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RESEARCH ARTICLE

Implementation of Format Preserving Encryption using AES with GCM Mode

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ABSTRACT

All over the world there are 7.83 billion people, 4.66 billion of them are active Internet users. Large amount of sensitive data is handled through internet. Most of the sensitive data are structured data types which should be encrypted. While using traditional database encryption algorithms, the length and format of the structured data is changed. The original field on the table and the encrypted field are different in size, format and data type. Especially the traditional encryption algorithms are not suitable for the field which is used as an index field. It leads to some additional work to handle the encrypted field. Format Preserving Encryption or Data type Preserving Encryption is special type of encryption in which the original and encrypted field are same in data type and format. After encryption, the encrypted filed is never changed. The format and data type are same as original filed. In this paper I proposed a special type of encryption that is AES based Format Preserving Encryption for structured data types on cloud.

Keywords: Cloud security, Cryptography, Format Preserving Encryption, AES based FPE, Security for structured data types.

INTRODUCTION

Format Preserving Encryption is a new technique for encryption structured data such as credit card number, social security number Bank account number etc. The database is the main resource provided by the cloud. It consists of both structured and unstructured data.

Most of the sensitive information are structured data which should be handled in a secured way. Strong Encryption and Authentication algorithm are required for structured data [1]. In Cryptography, Encryption algorithm converts the original information such as plaintext into unreadable secret information such as cipher text. In traditional encryption algorithms, the encrypted value is not same as plaintext in length and format. The encrypted value requires modification to the database and also changes of queries related to the database. To overcome this problem, applying one of the modern cryptography algorithm that is Format Preserving Encryption algorithm can be applied to structured data.

Importance of Format Preserving Encryption

In normal encryption, the length and format of the Plaintext and Cipher text are entirely different. The database structure is changed by the new encrypted value. The reconstruction of database is a very difficult process. If randomization was used in the encryption algorithm then referential integrity of the data base was also exaggerated. The index of the column contains encrypted values and then the index is unusable for encrypted data. An encryption algorithm not only alters the structure of the database it also alters the queries passed to the database. Changing of database and queries are complex tasks and also cost prohibitive [2].

Most of the block ciphers generate length preserving ciphertext. N bit block is mapped into another N bit block. But the data type of cipher text is not same as plain text. Format preserving encryption is a combination of length and data type conserving encryption [3].Using Format Preserving Encryption the modification to the database structure, application program and front end is reduced. The cost of updating the database and the application program is also minimized. Most of the encrypted columns are fixed as an index of the table to speed up the searching operation. FPE does not change the index. In Relational Database Management, Referential integrity of the database is also maintained. Use of FPE enables improving database security in a transparent way on many applications [4].

Format Preserving Encryption Modes

The National Institute of Standards and Technology (NIST), published two modes FF1and FF3 for FPE. FF1, originally called FFX (Format-preserving Feistel-based Encryption), was proposed by Bellare *et al.*, and FF3 corresponds to the BPS-BC component proposed by Brier et al. Both operation modes are based on a non-binary Feistel structure [5]. FF1 needs extra input tweak to avoid the dictionary attack. It is very complicated to implement. It is more expensive. The operating mode of BPS is simple and efficient. A block cipher with a larger block size is to be preferred with BPS. It does not ensure data integrity. NIST has concluded that FF3 is no longer suitable as a general-purpose FPE method.Researchers have identified vulnerabilities in all NIST approved FPE modes where the domain size is small.Both FF1 and FF3 algorithms are based on Fiestel Network. In Fiestel network the input is divided into two halves and inter relating a nonlinear function only to the right half. The result is added into the left half, and subsequently left and right halves are swapped. Since the nonlinear part requires most of the computation, two rounds of a Feistel cipher require about the same effort as a unchanging transformation [6].

Block Cipher Mode of Operation

We have two different approaches for data security. Data at rest and data in transit. Encryption plays a major role in data protection for securing data both in transit and at rest. While encryption data at rest data integrity is not important, only the stored data should be secured but in case of data at transit it plays a major role. Data integrity ensures that the data is not modified during the transmission. AES block cipher modes such as ECB, CBC, OFB, CFB and CTR provides only confidentiality but not ensure the integrity of the data. AES CTR mode is suitable for implementing Format Preserving Encryption. It is an AES block cipher mode that changes AES into a stream cipher. The mode is the simplest and most elegant of the confidentiality-only schemes. AES-CTR is simple and can be pipelined and parallelized. AES-CTR also supports pre computation of key stream. The length of the cipher text is

same as length of the plaintext. But for data integrity, additionally HMAC algorithm should be used along with AES-CTR. AES-CTR algorithm can be parallelized but HMAC cannot be parallelized [7]. To achieve both confidentiality and integrity on Format Preserving Encryption, we proposed an algorithm using AES with GCM mode. It achieves both confidentiality and integrity. It does not require any additional HMAC functions for ensuring data integrity.

FPE Using AES with GCM Mode

AES with Galois/counter mode (GCM) trusts the counter mode of encryption with the new Galois mode of authentication. It can be parallelized hence the throughput of the encryption algorithm can also be increased. It takes four inputs such as plaintext(P), secret key(K), Initial Vector (IV) and Authenticated Data(A) and produces Cipher text(C) and authenticated tag(T). The length of the plain text and cipher text are same. It handles only integer data, hence the proposed algorithm requires some additional mapping process to convert the given plaintext into set of integers and during decryption it is reversed.

The mapping is performed before and after encryption. The proposed algorithm handles integer domain. The string to be encrypted is stored in a character array. During the process of mapping, a string is processed to remove the special characters and encoded to integer using an index table. The plaintext consists of a sequence of n bit strings, in which the bit length of the last bit string is u, and the bit length of the other bit strings is 128.

The sequence is denoted $P_1, P_2, \ldots, P_{n-1}, P_*$ and the bit strings are called data blocks, n although the last bit string, $P*$, may not be a complete block. Similarly, the ciphertext is denoted n as $C_1, C_2, \ldots, C_{n-1}, C_*$, where the number of bits in the final block C_* is u. The additional authenticated data A is represented as $A_1, A_2, \ldots, A_{m-1}, A_{*m}$. The authenticated decryption operation is similar to the encrypt operation, but with the order of the hash step and encrypt step reversed [8]. The authentication process within GCM is based on a hash function, called GHASH1, that structures multiplication by a fixed parameter, called the hash subkey, within a binary Galois field.

Performance of FPE Using AES with GCM Mode

- AES with GCM mode is based on counter mode which can be implemented on parallel way. The throughput of the encryption algorithm is also increased.
- GCM uses only forward direction. For the implementation of both encryption and decryption same set codes are used. Hence the storage requirement is reduced. In hardware implementation same set of circuits are used.
- Single secret key is used as input. The hash key and IV are derived from the single key during the encryption and decryption process. Only the secret key is need to be stored and no need to store the hash key and IV hence the storage requirement is reduced.
- GCM with 4K storage is faster than those modes on messages less than 1024 bytes in length, and GCM with 256 byte storage is faster than CBC-HMAC-SHA1on the same messages.
- GCM supports the message of arbitrary length. It does not require the message length in advance. It calculated the length, when the message arrives.

CONCLUSION

There is a powerful need for privacy of sensitive fields before data is shared with any cloud provider, semi-trusted vendors, partners etc. Network telemetry data, transaction logs etc. are frequently required to be shared for benefiting from a variety of Software-as-Service applications. Such sensitive data fields are of well-defined data formats. While designing privacy for sensitive fields, it may be desirable to preserve the length of the inputs, in order to avoid any re-constructing of packet formats or database columns of existing systems. The proposed algorithm is a flexible and arbitrary domain cipher. Format preserving encryption would be welcomed for many real-time

applications. Especially for cloud environment in which the structured data should be handled in a more secured way.

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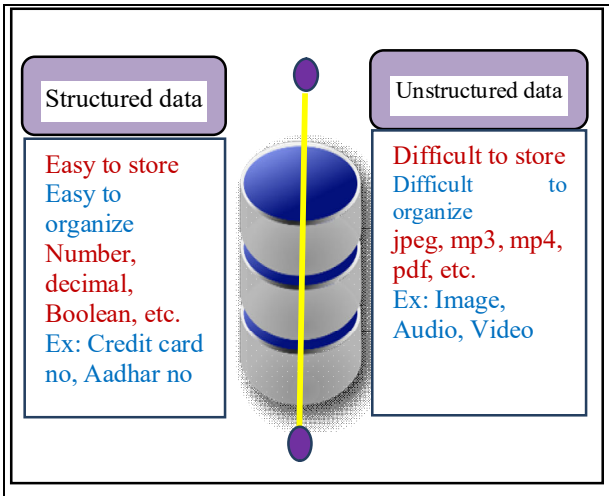

Figure 1: Structured Vs Unstructured data

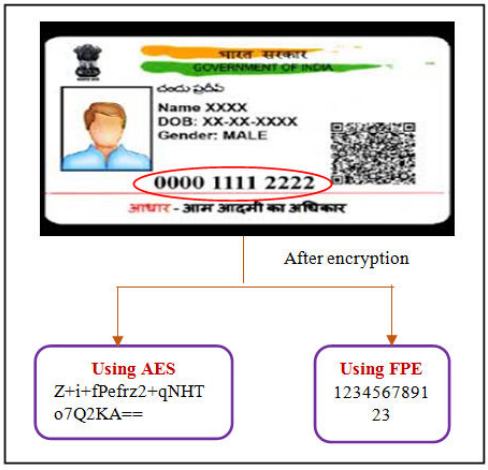

Figure 2: Aadhar number before and after encryption

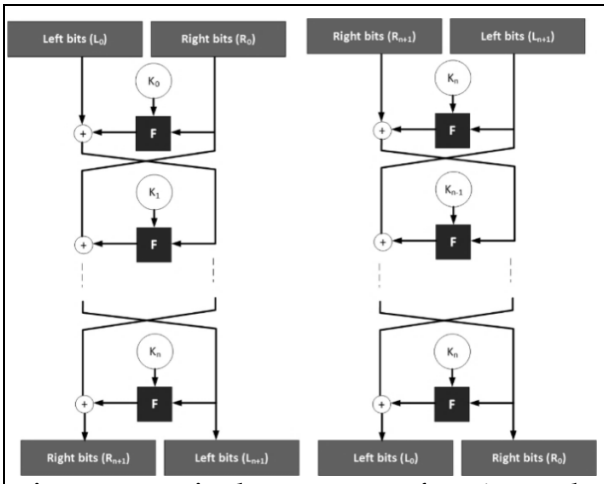

Figure 3: Feistel structure of FFX mode encryption

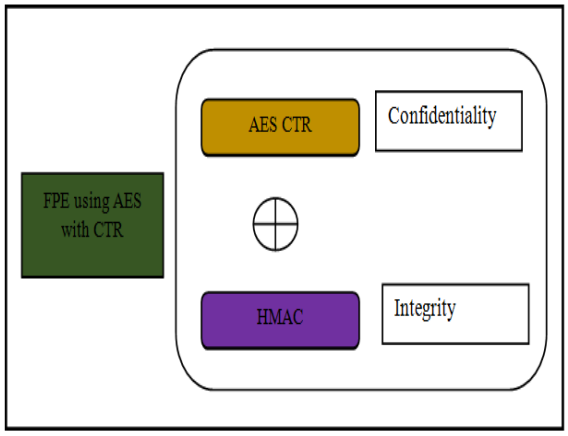

Figure 4: FPE using AES with CTR mode

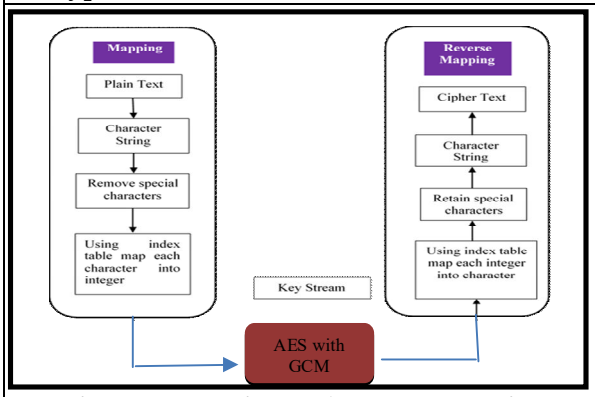

Figure 5: Mapping and Reverse mapping

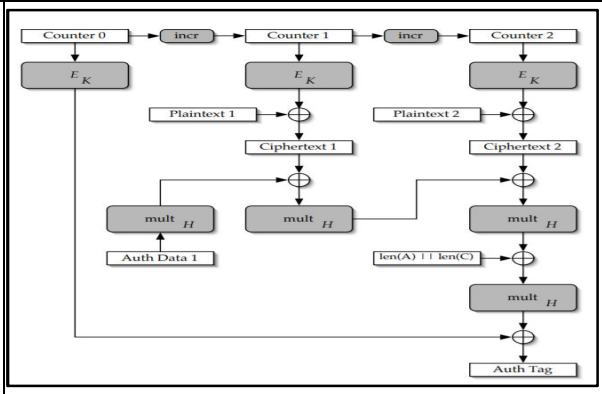

Figure 6: AES with GCM encryption

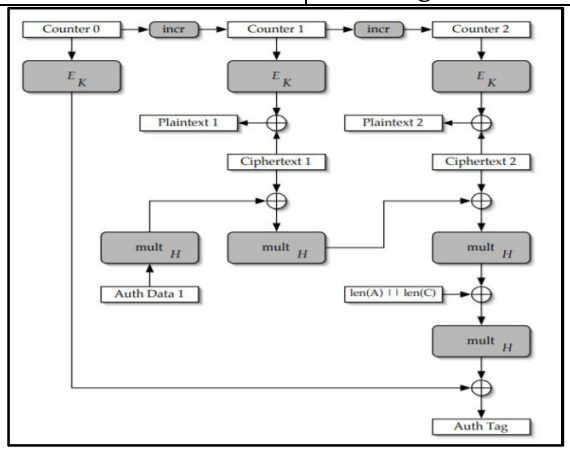

Figure 7: AES with GCM decryption

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RESEARCH ARTICLE

Psychological Conflicts and Mental Trauma in Bessie Head's *A Question of Power* and *A Woman Alone*

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ABSTRACT

Bessie Head is one of the rare female novelists who gives extraordinary contemporary voice. Her novels are deals about a small country in South Africa. Being bi-racial women, she overcomes many issues in existing South Africa. In order to escape these pressures, she settled in Botswana as an exile and there she came to know the realities of alienation, racial prejudice, rejection and victimisation. As a Crusader for sexual and social injustice for all men and women because the mixed marriage act was implemented in Apartheid South Africa, her favourite theme is interpersonal relationships and their possibility for individual growth and regeneration. Bessie Head wants to create a 'new world' of new men and women.

Keywords: Psychological Conflicts, Mental Trauma, inner Struggle, alienation.

Psychological Conflicts and Mental Trauma in Bessie Head's *A Question of Power* and *A Woman Alone*

Psychoanalysis is both methods of scientific investigation and a discipline that is concerned with the role of the unconscious in the mental life of the subject. It is initially based on the interpretation of the analysis and free associations within the context of the transference in the analytic situation. According to Webster's dictionary Psycho analysis means "a method of analyzing psychic phenomena and treating emotional disorders that involves treatment sessions during which the patient is encouraged to talk freely about personal experiences and especially about yearly childhood and dreams." It is a process of treating mental and emotional problems by having the patient talk about dreams, feelings, memories, etc. Psychoanalytic criticism adopts the methods of reading. Sigmund Freud introduced the term 'Psychoanalysis.' The literary texts argue things like dreams; express the secret unconscious desires and anxieties of the author. This literary work is an embodiment of the author's own neuroses and issues.

Psychological analysis of a particular character within a literary text is possible but all such characters are generally considered to be predictions of the author's psyche. This approach confirms the importance of literature, as it is structured on a literary key for the decoding. Sigmund Freud himself wrote,

The dream-thoughts which we first come across as we proceed with our analysis often strike us by the unusual form in which they are expressed; they are not clothed in the prosaic language usually employed by our thoughts, but are on the contrary represented symbolically by means of similes and metaphors, in images resembling those of poetic speech (26).

Like psychoanalysis, this critical endeavor seeks evidence of unresolved emotions, psychological conflicts resist ambiguity and tenderness within what might be a monolithic literary work. The writer's personal experience like his childhood traumas, family life, sexual conflicts, fixations, and such will be traceable within the behavior of the characters in the literary work. To the contrary, psychological material will be exposed indirectly, disguised, or encoded (as in dreams) through principles such as 'symbolism', 'condensation' and 'displacement.'

Bessie Head the South African apartheid woman novelist revives in her novels an intense moral idealism which effectively counterbalances her harsh realistic images of racism, sexism and economic injustices. In Bessie Head's novels these external forces of evil and oppression are always intertwined within the private lives and self-awareness of her characters. *A Question of Power* and *A Woman Alone* taken for analysis deals not only the external political issues, but also the moral and Psychological crisis in every individual character.

In *A Question of Power*, Bessie Head deftly handles the protagonist Elizabeth's acute mental disturbance to make possible the epic confrontation between good and evil. Elizabeth was born in a South African mental hospital to an insane mother. Her mother had committed suicide when the child was at six. Bessie Head herself was also born to bi-racial parents. She was brought by adopted parents and later fell mentally ill. Her revolution from the world of desolation built up by the abuse of power is the main theme in the novel. Bessie Head examines this desolation in a mythological way by the characters- Sello and Dan who plague Elisabeth's dreams. Forms of oppression or power are de-politicized or identified as the desire for either sexual or spiritual domination over the other. Throughout her life of alienation and inner battles with mental illness, Elizabeth was able to deal with her struggles: "I like the general atmosphere because I don't care whether people like me or not me. I am used to isolation" (QP 72). Elizabeth's moves into this stage of isolation and loneliness, Elizabeth creates her own world where she lives with three inner figures- Sello, Dan and Medusa. Elizabeth's madness helps her to create whom she often encounters and engages with.

Albeit most of her persuasion seems like her anxiety, mental torture and inner struggle Elizabeth learns to know many things. She understands about life from her conversation with Sello and Dan. She desires to have Sello as her friend who gives form and shape not only her philosophical world but also her spiritual world with the meaning of love, life and God.

As the days progress, Elizabeth appears to be more dependent on Sello. Head suggests that due to Elizabeth's hallucinations of seeing Sello, she allows her to have company and share her struggles with someone who gives medical advice. Throughout Elizabeth's spiritual journey, she not only looks at human history but also considers a solution to the problem of cruel and harsh attitudes. She believes that harsh attitude of the humans is the reason for others suffering. Therefore Elizabeth aims to practice softness and compassion to mankind. Due to this lesson of kindness, she learns that both communication and sharing are most important factors for humans to interact with people within same society.

While Head was in Botswana in her early time, she never shared her feelings and thoughts with anyone else. Elizabeth's sharing quality might have brought peace to her mind. Therefore her ability to share her spiritual journey, thoughts and struggle with Sello plays an important role that helps to lead Elizabeth away from a life of madness and illness. Elizabeth respects her friendship with Sello, though this friendship exists in another world. Sello represents a part of Elizabeth who eventually alleviates her loneliness and help her cope with the anxiety that comes from her mental illness. Sello is a figure that symbolizes Elizabeth's ability to work forward overcoming her illness whereas Elizabeth learns the opposite lessons of life from Dan through mental anguish and Trauma.

Dan is an utter contrast to Sello who is much more destructive in nature. He is a sexually perverted person who tortures Elizabeth in various ways. He represents the Power of patriarchal society and male domination over the female figure in South Africa. Elizabeth experiences oppression composed by the female power through Dan's activities and learns to survive under pressure. She gets an awakening to encounter male power as a victim. Dan induces her to commit suicide as he says again and again " you're going to commit suicide " but Elizabeth never consider his words and does not allow herself to be killed. She also argues against Dan when he says, "Die, die, die, you dog! I hate you! I hate you! ". Elizabeth replies that, "why, why, why? What I have done?" This argument with Dan exposes the inner quality and power of Elizabeth. Elizabeth portrays him as a teacher even though Dan's approach is like an enemy. Dan plays the role of a villainous character, Elizabeth gains strength and the ability to cope because of her longing for Botswana. Elizabeth copes with her illness because she spends her time in the hallucinating visions of Dan and Sello. Although she is isolated from the rest of society, she is able to communicate with Sello and Dan within her new utopian world which she creates for herself.

Though it is not easy to fight back against the wicked forces within a society, in this novel *A Question of Power*, Head uses madness or insanity as one kind of adynamic force to fight back against apartheid violence, patriarchy, and racial political views because sometimes it is the only possible way to voice against these powerful authorities. Insanity is the tool that connects the ideas of madness and spirituality together to represent Elizabeth's struggle. Elizabeth encounters problems with her society and because of her own experience with struggles. She suggests possible worldly and spiritual solution for the problems she encounters. By observing Dan's character closely, the reader can witness Elizabeth's attempt to analyse the social defects of South Africa.

Elizabeth's mental peace proves that she has transformed herself from a state of not belonging to the sense of belonging. So Head's phrase "gesture of belonging" indicates the reconciliation of Elizabeth's body and soul, because *A Question of Power* is a fictional autobiography. Bessie Head also experiences the same mental illness like Elizabeth, the protagonist of this novel. Head firmly opposes to be an object of patriarchal power due to her writing of own experiences as a fictional work. Madness and insanity are a kind of strength and blessing to help her to write novels. Bessie Head's autobiography encourages all women to cope while living under any humiliations.

The next novel *A Woman Alone, autobiographical writings,* is a collection of Bessie Head's personal thoughts and an indispensable tool for understanding her works. It was collected and published posthumously in 1990. Her writings have seen increased scholarly and critical acclaim in the period after her death.

The life of Bessie Head was exclusively prosaic. Her early life was full of pain and uncertainty. Her marriage life was a failure and even she broke out due to this relationship. She was stable in her personal life after entering into the literary world. It created the beginning of her life to take on familiar contours. She was an unreliable witness of her own pathetic life. Certainly she became an investigation into the enigma of human prejudice. In the process of unraveling the strands of her anguished life story, she encountered the sufferings, deprivation, crippling alienation and most of all her personal confusion. This personal confusion is at the centre of Bessie Head's troubled life. Her life has been divided into three major periods which is her early life in South Africa ,exile in Botswana and finally as a Botswana citizen.

Bessie Head was an African born woman who roseto become an internationally recognized author. The writings are intended as a 'piece – meal' portrait of this life, a mosaic of sketches, essays and personal notes making the present work primarily a biographical study. As a South- African colored, Bessie Head was subjected to all the brutalities meted out to these citizens not born white, and she as a first generation child of bi- racial origin, bore the full brunt of South Africa's discriminatory legislations. Her place of birth, foster childhood, adolescence as an orphan, her failed marriage and experiences as a non-white ghetto around the cities of South Africa form the background to the first phase.

Botswana became a new beginning. Although as a refugee from South Africa, she was not officially welcomed and her troubles did not end with her arrival in Botswana. She suffered a lengthy and debilitating nervous breakdown around 1969. This may have been congenitally induced. Her mother appeared to have suffered from a progressive psychosis, and Bessie was throughout her life acutely conscious of the fragility of her mental balance. Her breakdown appears to have occurred in the form of sporadic attacks which were spread over a period of two years.

The third phase divided her life in securing the Botswana citizenship. In1977 she had applied for citizenship and was turned down. A new sense of alienation began to develop within her, and in an interview with Jean Marquard in the same year she said bitterly, "I have liked Botswana very much although I have got nothing out of loving a country that didn't want me." (9)

Last phase of her life was very important. From her new vantage point as a recipient of local and international acclaim, she could look back and put her life into a meaningful perspective. Head bravely challenges the exclusionary rule and practices of the South African state based on race and gender and relating to patriarchal culture in Botswana. She rejected the title of a feminist. She used her fiction as a crusade for the equality of black people, especially black women. Head's exploration of womanhood in South Africa presents the politics of the apartheid regime. Similarly Head identifies the problems between the patriarchal nation of Botswana and the apartheid regime of South Africa and how both structures use power to oppress the powerless of the black women who were the most vulnerable. Head constantly argues that misusing of power stood in the way of recognition of the reverence of all creation, including black women. So Head decided to write novels in English. This represents most of the liberal authors who contributed to the national liberation frontt by exposing the brutality of South African Apartheid. Being a victim of the apartheid movement, Head migrated to Botswana where she continued to write about the experiences as a coloured woman under apartheid. Head chose English instead of any other African language in order to get close attention and for a wider international audience which could be addressed to.

Head always had a moral integrity which has connected the psychotic disorder of personal identity with brutality and oppression in society. In Head's world, the transformations begin and new worlds are created or at least there is hope at the end of all turmoil and agony which reflects the women's empowerment. Not only in her fiction but also in her personal life reflected in her autobiographical writings and even in her short stories and its collections, she has given to the readers the traumatic personal and political identity of a bi racial woman. There lies on optimistic note to humanity with a visionary zeal which Head derived from the eastern sphere of religious and spiritual quest which gets reflected in her writings through her own live experiences.

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RESEARCH ARTICLE

Image Restoration using Least Mean Fourth Based Full Adaptive Non-linear Order statistic Filters

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ABSTRACT

This paper presents the modification of nonlinear normalized least mean fourth algorithm with the help of Taylor series expansion of instantaneous output error. Here the cost function is used as the fourth power of instantaneous error function. The updation of different parameters of the learning rule is done with gradient descent algorithm and Taylor series expansion. The order statistics L and C filters are modified using the above learning rule and applied for the image restoration problem. These algorithm's performances are better than the least mean fourth (LMF) and normalized least mean fourth (NLMF) application.

Keywords: Non-linear filtesr, Adaptive filters, Order Statistic filters, LMF, NLMF.

INTRODUCTION

Images are corrupted by different types of noises such as blur due to optical system abbreviations, atmospheric turbulence, motion, and diffraction during image acquisition and statistical degradation due to noise while transmitting through different types of channels. Different authors have developed order-statistics filters [1-7], adaptive filters [8-11], and Wiener filters [12] which are nonlinear in nature. Different types of techniques have been adapted in order to remove noise from the degraded images. The adaptive filtering techniques have been introduced in areas of signal and image processing. The well-known filters are finite impulse response (FIR) or lattice filters, which are not suitable for nonlinear channel transmission, impulsive noises, and non-stationary images. The non-linear filters [26] like median filters (order-statistics) have been adopted to remove nonlinear noise like impulse noise etc. In this case, it removes the lines but distorts the edges [27] and blurs the details of the images at low signal-to-noise ratio (SNR) values. The median weighted filters and center-weighted filters, which are the modification of median filters, overcome the drawbacks like edge preservation and blur removal from the image.

The adaptive filtering techniques in image restoration suffer from drawbacks like computational complexity in terms of the learning rate, speed of convergence, and mathematical complexities (addition and multiplication). In a neural model[13-18], which is treated as one of the nonlinear models of image restoration [2], the restoration process is based upon the two stages process, like the learning of parameters using neural network and reconstruction of images with the help of learned parameter of the model. The parameter learning is done based upon the minimization of energy function or cost function and is carried out with a gradient descent algorithm. This procedure is treated as a robust one, and the stability of the network model is based upon the consequence of learning with minimization of cost function from time to time. Since the image signals are time-varying, and non-stationary, nonlinear filters have been used to remove noises from the corrupted images. Digital image filtering is based on the local image content (pixel value), and image statistics vary at the pixels of the Image. The basic idea of such type of filtering is to smoothen noise at the homogeneous region. But at the edges, it preserves the details of the signal. The order statistics adaptive filters like L-filter [19], Ll filter [20], and ranked order filters have been used for this purpose. The basic idea of order statistics filter is data ordering i.e the data across the odd size of the window, which is a 2D signal i.e N×N arranged in the ascending order (one dimensional signal of $1\times N^2$ size). The weights assigned with each data are updated in the heuristic manner according to LMS/Normalized LMS algorithms. The essential advantages of the NLMS algorithm as follows: (i) It automatically varies the step size parameters according to the norm of the input signal, (ii) it doesn't depend on the statistics of the input signal, (iii) it can be able to track the input variation and (iv) it is based on the minimization of mean square error. The LMS-L filters do not preserve the details of the signals when the window size is increased. But Ll(C) filter is designed to overcome the problems associated with the L filter by incorporating temporal order and ranked order information on the input sequence of the signal [20-21].

The polynomial type of error is called as the least mean fourth algorithm (LMF), which performs the training process, when the signal is embedded with Gaussian, and also the non-Gaussian types of noises. LMF filter [22] achieves a better trade-off between the transient and steady-state behavior of the adaptive filter. But the stability is the prime problem for the least mean fourth algorithm. Normalized LMF (NLMF) algorithm [22-25] came into the practice for achieving global stability. In the Normalized LMS (NLMS) algorithm, the weight vector is updated by the weighted sum of the input vector's squared norm. But in the case of normalized least mean fourth algorithm, the numerator of weight vector update the term in the fourth-order of the regressor, which provides the more stable state of the algorithm. In our present communication, we have been using different versions of LMF adaptive filters on the order sequence of data of order statistics filter to remove Gaussian as well as impulse noise (non - Gaussian noises) from the images. The proposed paper is organized as follows: Following the introduction, section-2 provides the cellular structure of window chosen for input data of distorted image and application of FA-LMF and FA-NLMF algorithms for L and Ll filter. Section-3 provides results achieved by those filters using the above algorithm and concludes by a conclusion in section-4

Adaptive Non-linear Order Statistic Filters.

LMF-L Filter

As the median filter suffers from streaking and edge jitters, non-linear filters (L-filters) have been developed to overcome these problems by taking the linear combinations of order statistics, making the algorithm a robust one. L-filters are treated as the running estimators, which compromises between non-linear operation (ordering) and linear operation (weighting). Such a filter's output is the weighted value of image data values corrupted with moving window's noise. The nature of the weighted vector signifies the type of filter.

The original image'd' of $p \times q$ (225×225) size is corrupted with Gaussian or non-Gaussian noise '**n** (k)', while transmitting or capturing of images. The corrupted Image is represented as x such that

$$\mathbf{x}(k) = \mathbf{d}(k) + \mathbf{n}(k) \quad . \tag{1}$$

Where, k= (i,j) is denoted as pixel coordinates. The large pictures of size $p \times q$ is divided into window size of 3x3 or 5x5 and so on $I_1 \times I_2$. The filter window image can be represented as:

$$\mathbf{x}(n) = \begin{bmatrix} x(i-1, j-1) & x(i-1, j) & x(i-1, j+1) \\ x(i, j-1) & x(i, j) & x(i, j+1) \\ x(i+1, j-1) & x(i+1, j) & x(i+1, j+1) \end{bmatrix} \quad (2)$$

The $I_1 \times I_2$ window can be arranged in a lexicographic order (row-wise) as Nx1 vector. Considering the window by raster scanning method of linear size $N = I_1 \times I_2$. This vector can be represented as

$$\mathbf{X}(k) = [x(i-1,j-1), x(i-1,j), x(i-1,j+1), x(i,j-1), x(i,j), x(i,j+1), x(i+1,j-1), x(i+1,j), x(i+1,j+1)]$$
$$= [x_1(k), x_2(k) \ldots\ldots x_s \ldots\ldots (k)] \quad (3)$$

The ordered input vector $\mathbf{x}_m(k)$ can be represented as

$$\mathbf{x}_m(k) = [x_{(1)}(k), x_{(2)}((k) \ldots\ldots x_{(t)}(k) \ldots\ldots x_{(N)}(k)]^T, \quad (4)$$

where, $x_1(k) \le x_2(k) \le \ldots\ldots\ldots\ldots \le x_N(k)$ are the ordered pixel values of the corrupted observed Image of small window size. The corresponding filter output y(k) of the L-filter can be expressed in terms of the weighted sum of the inputs as

$$u(k) = \sum_{i=1}^{N} w_i(k) x_i(k) = \mathbf{w}^T X_m \ . \quad (5)$$

Where, $\mathbf{w} = (w_1(k), w_2(k) \ldots\ldots\ldots w_N(k))^T$ is the L-filter weight vector with the constraint $W^T I = I^T W = 1$

The nonlinear output y(k) with adaptive gain a(k) is taken as

$$y(k) = a(k)\phi(u(k)) = \frac{a(k)}{1 + e^{-u(k)}} \quad (6)$$

where, $\phi(u(k)) = \frac{1}{1 + e^{-u(k)}}$ is the cost function of the LMF algorithm, which can be expressed as

$$E(k) = \sum_k e^4(k) \quad (7)$$

where, e(k)=d(k)-y(k) and d(k) is the undistorted (pure) image at different pixels, the weight updating rule is given by

$$\mathbf{w}(k+1) = \mathbf{w}(k) - \eta \nabla_w E(k) \ . \quad (8)$$

Where, η >0 is learning rate parameter of the algorithm. Since e(k) is the function of d(k),a(k),w(k) and x(k) and can represented as

$$e(k) = f(\mathbf{d}(k), \mathbf{w}(k), \mathbf{x}(k), a(k)) \tag{9}$$

Expanding with Taylor's series

$$e(k+1) = e(k) + \sum_{k=1}^{N} \frac{\partial(e(k))}{\partial(\mathbf{w}_n(k))} . \nabla w_n + \text{Higher order terms} \tag{10}$$

where, $\nabla_w(E(k)) = \frac{\partial(E(k))}{\partial(\mathbf{w}_n(k))} = \frac{\partial(e^4(k))}{\partial(e(k))} . \frac{\partial(e(k))}{\partial(\mathbf{w}_n(k))}$

$$= 4e^3(k) . \frac{\partial(\mathbf{d}(k) - a(k)\phi(u(k)))}{\partial \mathbf{w}_n(k)}$$

$$= 4e^3(k) \left[-a(k) \frac{\partial(\phi(u(k)))}{\partial(u(k))} . \frac{\partial(u(k))}{\partial(\mathbf{w}_n(k)} \right]$$

$$= -4e^3 a(k) \phi'(u(k)) . \frac{\partial(\mathbf{w}^T \mathbf{x}_m)}{\partial(\mathbf{w}_n(k))}$$

$$= -4e^3 a(k) \phi'(u(k)) X_m(k)$$

So, the weight updation can be represented as :

$$\mathbf{w}_n(k+1) = \mathbf{w}_n(k) + 4\eta e^3 a(k) \phi'(u(k)) \mathbf{x}_m(k) \tag{11}$$

Since the window is changing from time to time, the input vector $\mathbf{x}_m$ also changes, so that step size also varies as per the input vector. We can replace $\eta \rightarrow \eta(k)$, hence equation (11) can be replaced as:

$$\mathbf{w}_n(k+1) = \mathbf{w}_n(k) + 4\eta(k) e^3 a(k) \phi'(u(k)) \mathbf{x}_m(k) \tag{12}$$

By considering the constraint $w^T I=1$, we can decompose the weight vector and input vector as

$$\mathbf{w}_n(k) = (w_1(k), \ldots . w_{\gamma-1}(k) \mid w_\gamma(k) \mid w_{\gamma+1}(k) \ldots . w_N(k))^T \tag{13}$$

$$\mathbf{x}_m(k) = (x_1(k), \ldots . x_{\gamma-1}(k) \mid x_\gamma(k) \mid x(k)_{\gamma+1} \ldots . x(k)_N)^T \tag{14}$$

where, $\gamma = \frac{N+1}{2}$. The equation (13) and (14) one truncated to **wt**(k)) and **xt**(k) such that the weight updation rule can be adapted as per equation(11)

$$\mathbf{wt} = (w_1(k), w_2(k) \ldots . w_{\gamma-1}, w_\gamma, w_{\gamma+1} \ldots \ldots . w_N(k)) \tag{15}$$

$$\mathbf{xt}(k) = (x_1(k), x_2(k)..... x_{\gamma-1}, x_\gamma, x_{\gamma+1}..... ..x_N(k)) \quad (16)$$

the corresponding weights are updated as

$$\mathbf{wt}(k+1) = \mathbf{w}(k) + 4\eta(k)e^3 a(k)\phi'(u(k))\mathbf{xt}(k) \quad (17)$$

And $$w_\gamma(k+1) = w(k) = 1 - \sum_{\gamma=1}^{N-1} w_\gamma(k+1) \quad (18)$$

The equation (11) is reduced to

$$\mathbf{w}_n(k+1) - \mathbf{w}_n(k) = \Delta w_n(k) = 4\eta(k)e^3 a(k)\phi'(u(k)\mathbf{x}_m(k) \quad (19)$$

The partial differentiation of error w.r.t. weight can be derived as:

$$\begin{aligned}
&\frac{\partial(e(k))}{\partial(\mathbf{w}_n(k))} = \frac{\partial(\mathbf{d}(k) - \mathbf{y}(k))}{\partial \mathbf{w}_n(k)} = -\frac{\partial \mathbf{y}(k)}{\partial \mathbf{w}_n(k)} \\
&= -\frac{\partial[a(k)\phi(u(k))]}{\partial \mathbf{w}_n(k)} = -a(k)\frac{\partial\phi(u(k))}{\partial \mathbf{w}_n(k)} \\
&= -a(k)\frac{\partial\phi(u(k))}{d(u(k))}.\frac{\partial u(k)}{d\mathbf{w}_n(k)} \\
&= -a(k)\phi'(u(k)).\frac{\partial w^T.\mathbf{x}_m}{\partial \mathbf{w}} \\
&= -a(k)\phi'(u(k)).\mathbf{x}_m(k)
\end{aligned} \quad (20)$$

Expanding the error function by Taylor series we get

$$e(k+1) = e(k) + \sum \frac{\partial e(k)}{\partial \mathbf{w}_n(k)}.\Delta w_n(k) + \sum \frac{\partial e(k)}{\partial a_n(k)}.\Delta a(k) + \sum \frac{\partial e(k)}{\partial \mathbf{x}_n(k)}.\Delta \mathbf{x}_n(k) + ... + H.O.T \quad (21)$$

Where HOT represents Higher Order terms. Taking the first two terms for the learning rate parameter, we get

$$e(k+1) = e(k) + \sum \frac{\partial e(k)}{\partial \mathbf{w}_n(k)}.\Delta w_n(k) \quad (22)$$

Substituting the value of $\frac{\partial e(k)}{\partial \mathbf{w}_n(k)}$ from equation (20) and $\Delta w_n(k)$ from (19) in equation (22) we get

$$e(k+1) = e(k) + \left[-a(k)\phi'(u(k))\mathbf{x}_m(k)\right]\left[4\eta(k)e^3(k)a(k)\left|\phi'(u(k))\right|\mathbf{x}_m(k)\right]$$

$$\Rightarrow e(k+1) = e(k) - 4\eta(k)e^3(k)a^2(k)\left|\phi'(u(k))\right|^2\left\|\mathbf{x}_m(k)\right\|^2$$

$$\Rightarrow e(k+1) = e(k)\left[1 - 4\eta(k)e^2(k)a^2(k)\left|\phi'(u(k))\right|^2\left\|\mathbf{x}_m(k)\right\|^2\right] \quad (23)$$

as $e(k+1) \to 0$, we get $1 - 4\eta(k)e^2(k)a^2(k)\left|\phi'(u(k))\right|\left\|\mathbf{x}_m(k)\right\|^2 = 0$

$$\Rightarrow \eta(k) = \frac{1}{4e^2(k)a^2(k)\left|\phi'(u(k))\right|^2\left\|\mathbf{x}_m(k)\right\|^2} \quad (24)$$

The stability of the adaptive algorithm can be improved through normalization as it has been done in case of normalized LMS [25-26]. It has been chosen that the learning rate parameter lies between 0 and 2. The time-varying learning parameter equation (24) depends upon the input power, noise power, and weight initialization. As the input power approaches zero, the learning rate parameter will diverge. To make it stable, a small constant term δ is added to its denominator of equation (24). Hence it can be expressed as

$$\eta(k) = \frac{1}{4e^2(k)a^2(k)\left|\phi'(u(k))\right|^2\left\|\mathbf{x}_m(k)\right\|^2 + \delta} \quad (25)$$

The optimal learning rate $\eta(k)$ determines the convergence of non-linear gradient descent algorithm, for uniform convergence $e(k) \to 0$ as $k \to \infty$. Hence from the equation (23) we have $e(k+1) \le \left[1 - 4\eta(k)e^2(k)a^2(k)\left|\phi'(u(k))\right|^2\left\|\mathbf{x}_m(k)\right\|^2\right]e(k)$ such that

$$\left[1 - 4\eta(k)e^2(k)a^2(k)\left|\phi'(u(k))\right|^2\left\|\mathbf{x}_m(k)\right\|^2\right] < 1,$$

$$\Rightarrow 0 < \eta(k) < \frac{2}{4e^2(k)a^2(k)\left|\phi'(u(k))\right|^2\left\|\mathbf{x}_m(k)\right\|^2} \quad (26)$$

Similarly, if the gain varies from one window to another window, we can update the gain term according to the steepest descend algorithm, which can be expressed as

$$a(k+1) = a(k) - \alpha(k).\frac{\partial E(k)}{\partial a(k)}$$

$$= a(k) - \alpha(k).4e^3(k).\frac{\partial(\mathbf{d}(k) - \mathbf{y}(k))}{\partial a(k)}$$

$$= a(k) - \alpha(k).4e^3(k).\left[-\frac{\partial \mathbf{y}(k)}{\partial a(k)}\right]$$

$$= a(k) - 4\alpha(k)e^3(k).\left(-\frac{\partial a(k)\phi(u(k))}{\partial a(k)}\right)$$

$$= a(k) - 4\alpha(k)e^3(k)[-\phi(u(k)]$$

$$= a(k) - 4\alpha(k)e^3(k)\left[-\frac{a(k)\phi(u(k)}{a(k)}\right]$$

$$= a(k) + 4\alpha(k)e^3(k)\left[\frac{\mathbf{y}(k)}{a(k)}\right]$$

or $$a(k+1) = a(k) + 4\eta\alpha(k)e^3(k)\phi(u(k)) \quad (27)$$

Where α(k) is the time-varying learning parameter for gain updation. The gain updation term diverges as the error term becomes large, so it can also be normalized, which can be expressed as

$$a(k+1) = a(k) + 4\alpha(k)\frac{e^3(k)\phi(u(k))}{\|\mathbf{x}(k)\|^4}$$

$$= a(k) + 4\alpha(k)\frac{e^3(k)\phi(u(k))}{\|\mathbf{x}(k)\|^4}$$

$$= a(k) + \frac{4\alpha(k)e^3(k)\phi(u(k))}{\beta + \|\mathbf{x}(k)\|^2\left(\|\mathbf{x}(k)\|^2 + e^2(k)\right)} \quad (28)$$

Value of β is chosen such that $\beta << E\left(\|\mathbf{x}(k)\|^4\right)$. If it will not be of any significant effect on the average performance of the algorithm, we can represent the next error as

$$e(k+1) = e(k) + \sum\frac{\partial e(k)}{\partial \mathbf{w}_n(k)}.\Delta w_n(k) + \sum\frac{\partial e(k)}{\partial a_n(k)}.\Delta a(k).$$

$$\frac{\partial e(k)}{\partial a_n(k)} = \frac{\partial(\mathbf{d}(k) - \mathbf{y}(k))}{\partial a(k)} = -\frac{\partial \mathbf{y}(k)}{\partial a(k)} = -\frac{\partial(a(k)\phi(u(k)))}{\partial a(k)} = -\phi(u(k)).$$

From Eqn. (27) at $t \to \infty, [w_n(k+1) - w(k)] \to 0$ i.e $\Delta w_n \to 0$

Eqn. (21) reduces to

$$e(k+1) = e(k) + \sum\frac{\partial e(k)}{\partial a(k)}.\Delta a(k)$$

$$= e(k) - 4\alpha(k)e^3(k)\phi^2(u(k))$$

$$= e(k)\left[1 - 4\alpha(k)e^2(k)\phi^2(u(k)\right] \quad (29)$$

at $t \to \infty \quad e(k+1) = 0$, hence $1 - 4\alpha(k)e^2(k)\phi^2(u(k)) = 0$

$$\alpha(k)) = \frac{1}{4e^2(k)\phi^2(u(k))} \quad (30)$$

When the denominator of above becomes very small or zero, it will diverge. So, a very small quantity λ is added to the denominator, which will not affect the sum.

$$\alpha(k)) = \frac{1}{4e^2(k)\phi^2(u(k)) + \lambda} \quad (31)$$

The updated gain from equation (27) can be expressed as

$$a(k+1) = a(k) + \frac{4e^3\phi(k)}{4e^2(k)\phi^2(u(k)) + \lambda} \quad (32)$$

Algorithm (L-filter)

Step-1: The pure Image of size p×q can be read.

Step-2: The weight vector **w** can be initialized such that $\sum_{i=1}^{N} w_i = 1$. The parameters η, α, λ, β are to be initialized.

Step-3: The original image **d** is corrupted by noise (**n**), such that $\mathbf{x}(k) = \mathbf{d}(k) + \mathbf{n}(k)$. The intensity of the window of the corrupted Image is to be taken.

Step-4: **x**(k) is padded with zeros by extension of the row above and below and column left and right to ascertain the boundaries with zero intensity.

Step-5: Input image is to be divided in to numbers of windows of size 3×3 or 5×5.

Step-6: Windows are to be converted into into $N\times1$ vector where $N = I_1 \times I_2$ and such vectors are obtained are represented as $\mathbf{x}_N(k) = \left[x_1(k), x_2(k), \ldots\ldots\ldots x_s(k) \ldots\ldots\ldots x_N(k)\right]$.

Step-7: $x_N(k)$ vector is arranged in in ascending order

$$\mathbf{x}_m(k) = \left[x_1(k) < x_2(k) \ldots\ldots\ldots x_t \ldots\ldots\ldots < x_N(k)\right]$$ where k=1 to p×q.

Step-8: The maximum number of iteration is to be defined.

Step-9: The following parameters are to be evaluated u(k),y(k),E(k),η(k),α(k),a(k+1), using equations (5),(6),(7),(25),(31),(32) respectively .

Step-10: weight vector is updated according to formula (19)

Step-11: If total number of pixels are evaluated , go to step 12; else, go to step-5

Step-12: For calculating the efficiency and performance of the algorithm, following parameters like MFE, PSNR and SSIM are calculated [28].

Step-13: Using learned weight vector and other parameters using eqn.(6) ,the intensity at each pixel is calculated , for image restoration.

Step-14: Mean fourth error is plotted with respect to each iteration to ascertain the consequence of the algorithm.

LMF C-Filters (Ll-Filters)

C-Filter incorporates both temporal and ranked-ordered information of the input sequence, called as a combination filter. So C filter can be treated as L-filter with the coefficient of Xi, dependent on its temporal position and a FIR filter with the coefficient of the X_i dependent on its rank with in the window. Hence, the selected weights are ordered according to the order of pixels value in an image window by which restoration at high pass region can be performed without blurring between low to high pass or high to low pass region. Also, it prevents divergence of updated weight matrix in successive adaptive iterations due to ranked order property.

The original image d of $N \times N$ size is corrupted with Gaussian or Non-Gaussian noise **n**(k) while transmission or capturing of Images. The corrupted Image X is represented such that

$$\mathbf{x}(k) = \mathbf{d}(k) + \mathbf{n}(k) \tag{33}$$

Where k=(i,j) is denoted as pixel coordinates .The large pictures of size(NxN) is divided into window size of 3x3 or 5x5 and so on (I_1xI_2). The filter window image can be represented as:

$$\mathbf{x}(n) = \begin{bmatrix} x(i-1,j-1) & x(i-1,j) & x(i-1,j+1) \\ x(i,j-1) & x(i,j) & x(i,j+1) \\ x(i+1,j-1) & x(i+1,j) & x(i+1,j+1) \end{bmatrix} \tag{34}$$

The $I_1 \times I_2$ window can be arranged in lexicographical order (row-wise) as Nx1 vector. By scanning the window by raster scanning method where $N=I_1 \times I_2$.

$$\mathbf{x}_c(k) = [x(i-1,j-1), x(i-1,j), x(i-1,j+1), x(i,j-1), x(i,j), x(i,j+1), x(i+1,j-1), x(i+1,j), x(i+1,j+1)]$$

$$= [x_1(k), x_2(k) \ldots\ldots x_s \ldots\ldots (k)] \tag{35}$$

The ordered input vector $\mathbf{x}_c(k)$ can be represented a

$$\mathbf{x}_c(k) = ([x_1(k), x_2(k), \ldots\ldots x_t(k), \ldots\ldots x_N(k)])^T$$

The C -filter Coefficient matrix is represented by

$$\mathbf{w} = \begin{pmatrix} w_{11} & w_{12} & \ldots\ldots\ldots w_{1N} \\ w_{21} & w_{22} & \ldots\ldots\ldots \\ w_{N1} & w_{N1} & \ldots\ldots\ldots w_{NN} \end{pmatrix} \tag{36}$$

The ranked Order vector $\mathbf{w}_c(k)$ can be defined on as

$$\mathbf{w}_c(k) = w(R(x_i), i) \tag{37}$$

Where R (x_i) is the rank of the ordered input vector **x**(k)

From Eqn.(37) it can be observed that weights of pixels in an image frame, are selected with rank order. Hence, one can prevent the divergence of the weight vector , during the time of adaptation. The corresponding filter output y(k) of C-filters can be expressed in terms of the weighted sum of the inputs as

$$u(k)=\sum_{i=1}^{N} w_{ci}(k)x_i(k)=\mathbf{w}_c{}^T\mathbf{x}_c \quad (38)$$

normalized output $u_n(k)$ can be represented as

$$u(k)=\sum_{i=1}^{N}\frac{w_{ci}(k)x_i(k)}{\sum_{i=1}^{n}w_{ci}(R(x_i),i)}=\frac{\mathbf{w}_c{}^T\mathbf{x}_c}{\sum_{i=1}^{n}\mathbf{w}_c(R(x_i),i)} \quad (39)$$

Hence, the non-linear output y(k) can be expressed as

$$y(k)=a(k)\phi(u(k))=\frac{a(k)}{1+e^{-u(k)}} \quad (40)$$

From L-filter derivation, we can obtain similar expressions : $\eta(k),a(k+1),\alpha(k),e(k+1)$ from equations (25),(28),(31) ,and (29) respectively.Hence, the expression for

$$\mathbf{w}_{cn}(k+1)=\mathbf{w}_{cn}(k)+4\eta(k)e^3a(k)\phi'(u(k))\mathbf{x}_m(k) \quad (41)$$

Algorithm (C-filter)

Step-1: The pure Image of size p × q has been read.

Step-2: The parameters like weight matrix **w**, step size parameter η(k)**,** adaptive gain a (k), other constant parameters λ and δ are initialized.

Step-3: The original image '**d**' is corrupted noise **n.** So the corrupted Image becomes $\mathbf{x}(k)=\mathbf{d}(k)+\mathbf{n}(k)$ **Step-4:**x(k) is padded with zeros by extension of the row above and below,and column left and right to ascertain the boundaries with zero intensity.

Step-5: Number of Iteration is specified (say max).

Step-6: Input image is to be divided into numbers of windows of size 3×3 or 5×5.

Step-7: Windows are to be converted into $N\times1$ vector. Where $N=I_1\times I_2$ and such vectors are represented as $\mathbf{x}_N(k)=[x_1(k),x_2(k),\ldots\ldots x_s(k)\ldots\ldots x_N(k)]$.

Step-8: $\mathbf{x}_N(k)$ vector is arranged in ascending order such that $x_1(k)<x_2(k)\ldots\ldots x_t\ldots\ldots\leq x_N(k)$

$\mathbf{x}_m(k)=[x_{(1)}(k),x_{(2)}(k),\ldots\ldots x_{(t)},\ldots\ldots<x_{(N)}(k)]^T$, where k=1 to P × Q

Step-9: The ranked Order vector $\mathbf{w}_c(k)$ is obtained from C matrix $\mathbf{w}_c(k)=w(R(x_i),i)$.

Step-10: Following terms are evaluated using equations as follows
u(k),y(k),E(k),η(k),α(k),a(k+1), using equations (39),(40),(7),(25),(31),(32) respectively .

Step-11: The weight vector is updated according to the formula (41)

Step-12: If the total number of pixels are evaluated, go to step 13 else, go step-6

Step-13: For calculating the efficiency and performance of the algorithm, the following parameters like MFE, PSNR, and SSIM are calculated [28].

Step-14: Using learned weight vector and other parameters using Eqn.(6) , the intensity at each pixel is calculated, for image restoration.

Step-15: Mean fourth error is plotted with respect to each iteration to ascertain the algorithm's consequence.

SIMULATION RESULTS DISCUSSION

In this paper simulation work is carried out on Lena image using non linear full adaptive filter of least mean fourth criterion and order statistic L and C filter, with the availability of reference source. The image of Lena is distorted with by Gaussian, salt & pepper and speckle noises of strength 10dB, 5dB and 0dB separately. The filter coefficients are initialized in such way that their sum is unity. The entire image is used to train the full adaptive filter using non linear full adaptive FA- LMF and FA-NLMF algorithms, which are stable in comparison to LMS and NLMS. The derivation is based on Taylor series expansion of instantaneous output error, which is truncated to first order in the course of derivation of the updation algorithm. For non linear filtering problem , curves of FA-NLMF algorithm reaches to which looks better from better from the performance of mean square error characteristics.

Image Corrupted With Salt & Pepper Noise

In our present work , the pure image of Lena is made corrupted by salt and pepper noise of strength 10dB, 5dB and 0dB respectively. For training purpose, the whole image of Lena is taken in to consideration. The cost function for training purpose is taken as non linear function of fourth power of the error i.e. full adaptive Least mean fourth(FA-LMF) algorithm applied in order statistic L and C filters, of, basically FALMF (FA-LMF-L, FA-LMF-C) filters. But LMF filters have some stability problems, hence normalized FA-LMF(FA-NLLMF) provides global minimum in its least mean fourth characteristics , having advantages over FA-LMF algorithms. In NLMF algorithm, the weight vector updation is normalized by dividing by fourth power of norm of the regressor or by the product of the second power of the regressor and sum of the second power of the regressor and square of error term. For different step size parameter (η),0.1-1.9 and different SNR values, 0dB,5dB and 10dB ,noisy image is trained and observed better result when η=0.1 for all algorithms. When noise strength 10 dB and $\eta \geq 0.1$, LMS and NLMS algorithm diverges under full image training, but full adaptive LMF series gives better result by converging in its mean fourth characteristics.

FA-NLMF-C provides better result and visualization (Fig 2. (j)). among the entire filter in the series due to its temporal and ranked order properties as observed PSNR=42.75dB and SSIM=0.92, for 10dB of SNR. But for increased noise strength, less PSNR and SSIM value observed (Table-1): for SNR=5dB, observed PSNR=35.49 and SSIM= 0.83, while for SNR=0dB, PSNR and SSIM values decrease to 25.94 and 0.43 respectively. FA-NLMF-L filters gives better results in comparison to FA- NLMF filter due to its weighing and orderly arrangement of image array as observed PSNR=38.39 and SSIM= 0.88,where as reduced PSNR and SSIM observed in case of FA-NLMF filter ,34.62 and 0.82 respectively. From Fig.3 it has been observed that FA-LMF-C and FA-LMF-L shows better performance in comparison to LMF filter. For higher noise strength 5db and 0dB LMF filter shows little bit divergence but order statistics L and C version of LMF converges with respect to iteration. Fig.4 -6 shows the stability of NLMF and its order statistic L and C filter with respect to η ,as outputs restored images are appears similar in perception and also their measuring parameters are closer or same in some cases.

Image Corrupted With Gaussian & Speckle Noise

In case of Gaussian noise with noise strength of SNR=10dB, FA-LMF-L filter restores image with PSNR=34.67dB and SSIM=0.85, while LMF-C filter restores with better quality of vision with PSNR=35.52dB, and SSIM=0.85. Simulations are carried out for Gaussian and speckle noises for different strength of noises. For different step size it has been observed better visuality in case of normalized full adaptive LMF (FA-NLMF) version of C-filter than L filter, those perform better in case of Gaussian noise. Adaptive- NLMF-L filter restores image with PSNR=35.87 and SSIM=0.86, where as NLMF-C filter with PSNR=36.89 and SSIM=0.87, for Gaussian noise of strength, SNR=10dB (Table-2). For stronger noise strengths such as 5dB and 0dB of SNR, the output obtained with less PSNR and SSIM as tabulated in Table-2. Similarly, in case of speckle noise, for FA-NLMF-L filter, the noisy image is restored with PSNR=33.87 and SSIM=0.81, while for normalized LMF-C filter observed PSNR=35.74 and SSIM-0.84 with noise strength SNR-10dB as from Table-3.

CONCLUSION

The fully adaptive normalised nonlinear gradient descent algorithm based on LMF criteria has been introduced in this paper for image restoration .The selection and adaption of weights, constant terms and learning rate have been derived using Taylors series expansion of instantaneous output error. For training purpose if we use the whole image ,we get very blurring LMF and NLMF and distorted for LMS algorithm .So it is better to take a small region of image having edge and homogeneous regions. The performance of FA-NLMF algorithm for L and C filter is quite satisfactory and almost matched with original image for small SNR of 10db irrespective of the choice of learning rate parameter. The FA-NLMF-C filter performs better than the FA-NLMF-L filter in image observation as well as for evaluation parameter like MFE, PSNR and SSIM.

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Tabl-1. Different simulated parameters like MFE, PSNR, and SSIM for efficient evaluation of filters at different learning rate(η)when the image is corrupted with salt & pepper noise of different strength (10dB, 5dB, 0dB).

FILTER TYPE	Value Of η	SNR=10dB			SNR=5dB			SNR=0dB		
Salt & pepper Noise		MFE	PSNR	SSIM	MFE	PSNR	SSIM	MFE	PSNR	SSIM
FA-LMF	0.1	5.4*10^(-7)	33.57	0.80	3.0*10^(-6)	28.12	0.71	4.8*10^(-5)	21.80	0.35
	0.5	1.8*10^(-6)	30.68	0.78	6.3*10^(-6)	27.23	0.69	6.5*10^(-5)	21.14	0.32
	1	6.3*10^(-6)	28.97	0.74	9.2*10^(-6)	25.93	0.59	1.2*10^(-4)	18.77	0.28
	1.9	7.3*10^(-6)	26.98	0.72	9.5*10^(-6)	25.54	0.58	1.8*10^(-4)	18.35	0.27
FA-LMF-L	0.1	8.3*10^(-8)	38.16	0.89	8.6*10^(-7)	33.58	0.78	2.8*10^(-5)	25.01	0.38
	0.5	9.3*10^(-8)	38.12	0.88	9.8*10^(-7)	31.16	0.71	4.3*10^(-5)	23.67	0.36
	1	1.4*10^(-7)	37.26	0.87	9.1*10^(-7)	32.97	0.73	4.4*10^(-5)	23.65	0.35
	1.9	1.7*10^(-7)	36.68	0.87	9.6*10^(-7)	32.12	0.72	4.7*10^(-5)	22.03	0.34
FA-LMF-C	0.1	7.1*10^(-8)	38.79	0.89	7.3*10^(-7)	34.74	0.81	2.0*10^(-5)	25.27	0.35
	0.5	9.7*10^(-8)	38.11	0.87	8.3*10^(-7)	33.74	0.79	1.9*10^(-5)	25.46	0.43
	1	1.1*10^(-7)	37.91	0.85	8.7*10^(-7)	33.19	0.77	2.4*10^(-5)	24.88	0.41
	1.9	3.4*10^(-7)	36.98	0.82	9.5*10^(-7)	31.34	0.75	2.9*10^(-5)	24.32	0.38

FA-NLMF	0.1	5.9*10^(-7)	34.62	0.82	1.1*10^(-6)	30.69	0.72	4.2*10^(-5)	23.88	0.33
	0.5	4.0*10^(-7)	35.57	0.83	1.3*10^(-6)	30.24	0.72	4.3*10^(-5)	22.97	0.33
	1	7.4*10^(-7)	32.72	0.80	1.6*10^(-6)	30.15	0.71	4.5*10^(-5)	22.43	0.32
	1.9	7.7*10^(-7)	32.16	0.80	1.6*10^(-6)	30.11	0.71	4.8*10^(-5)	21.92	0.31
FA-NLMF-L	0.1	8.8*10^(-8)	38.39	0.88	7.1*10^(-7)	34.81	0.82	2.3*10^(-5)	25.13	0.38
	0.5	8.1*10^(-8)	38.67	0.89	8.2*10^(-7)	33.13	0.80	2.6*10^(-5)	25.04	0.38
	1	8.4*10^(-8)	38.59	0.88	8.6*10^(-7)	33.05	0.79	2.7*10^(-5)	24.83	0.37
	1.9	8.7*10^(-8)	38.41	0.88	8.8*10^(-7)	32.91	0.78	3.3*10^(-5)	24.76	0.35
FA-NLMF-C	0.1	1.1*10^(-8)	42.75	0.92	2.1*10^(-7)	35.49	0.83	1.5*10^(-5)	25.94	0.43
	0.5	3.5*10^(-8)	41.99	0.91	3.8*10^(-7)	35.15	0.81	2.3*10^(-5)	25.03	0.41
	1	4.3*10^(-8)	41.78	0.91	3.8*10^(-7)	34.90	0.81	2.7*10^(-5)	24.37	0.39
	1.9	4.6*10^(-8)	41.49	0.91	3.9*10^(-7)	34.86	0.81	2.7*10^(-5)	24.31	0.39

Tabl-2. Different simulated parameters like MFE, PSNR, and SSIM for efficient evaluation of filters at the learning rate(η=0.1)when the image is corrupted with Gaussian noise of different strength (10dB, 5dB, 0dB).

FILTER TYPE	SNR=10dB			SNR=5dB			SNR=0dB		
Gaussian Noise	MFE	PSNR	SSIM	MFE	PSNR	SSIM	MFE	PSNR	SSIM
FA-LMF	7.2*10^(-7)	33.02	0.81	1.1*10^(-6)	31.68	0.78	4.2*10^(-6)	29.86	0.72
FA-LMF-L	2.4*10^(-7)	34.67	0.85	4.8*10^(-7)	33.02	0.81	1.2*10^(-6)	30.73	0.75
FA-LMF-C	2.2*10^(-7)	35.52	0.85	4.3*10^(-7)	33.78	0.82	1.0*10^(-6)	31.97	0.76
FA-NLMF	4.1*10^(-7)	33.89	0.82	1.0*10^(-6)	31.89	0.78	3.5*10^(-6)	30.09	0.72
FA-NLMF-L	1.4*10^(-7)	35.87	0.86	2.8*10^(-7)	34.67	0.83	7.8*10^(-7)	32.67	0.79
FA-NLMF-C	1.2*10^(-7)	36.89	0.87	2.4*10^(-7)	34.83	0.84	5.2*10^(-7)	33.11	0.79

Tabl-3. Different simulated parameters like MFE, PSNR, and SSIM for efficient evaluation of filters at learning rate(η=0.1)when the image is corrupted with speckle noise of different strength (10dB, 5dB, 0dB).

FILTER TYPE	SNR=10dB			SNR=5dB			SNR=0dB		
Speckle Noise	MFE	PSNR	SSIM	MFE	PSNR	SSIM	MFE	PSNR	SSIM
FA-LMF	1.2*10^(-6)	31.93	0.73	5.3*10^(-6)	27.82	0.70	2.1*10^(-5)	25.34	0.48
FA-LMF-L	6.3*10^(-7)	32.81	0.79	7.2*10^(-6)	27.64	0.67	1.7*10^(-5)	26.31	0.50
FA-LMF-C	3.6*10^(-7)	34.37	0.81	1.2*10^(-6)	30.91	0.72	1.0*10^(-5)	26.72	0.52
FA-NLMF	1.2*10^(-6)	30.91	0.74	3.8*10^(-6)	29.77	0.72	1.8*10^(-5)	25.68	0.49
FA-NLMF-L	5.4*10^(-7)	33.87	0.81	1.1*10^(-6)	31.95	0.72	1.2*10^(-5)	26.82	0.52
FA-NLMF-C	2.2*10^(-7)	35.74	0.84	1.0*10^(-6)	31.92	0.73	1.0*10^(-5)	26.72	0.52

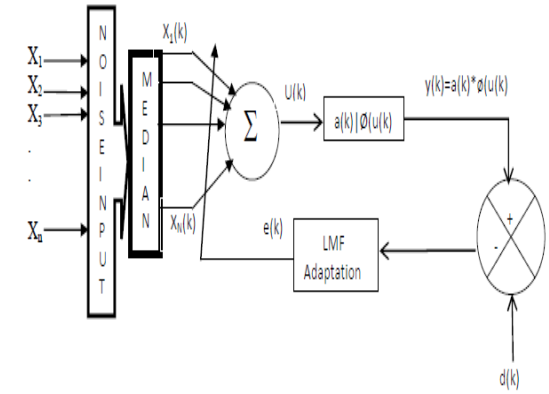

Fig 1.(a). Block diagram for Adaptive L filter

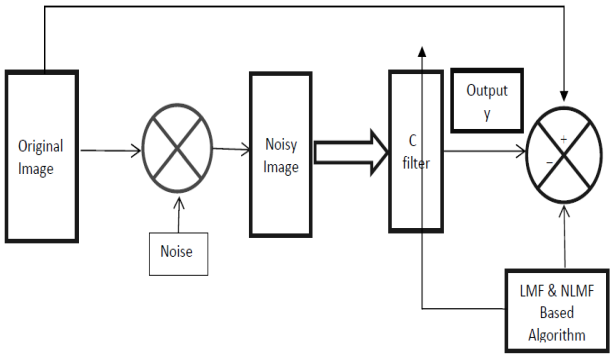

Fig.1. (b). Block diagram for C filter

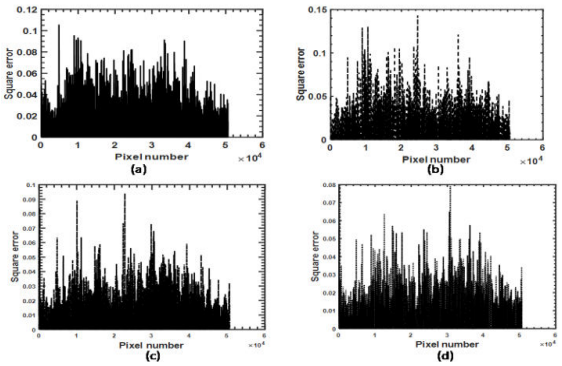

Fig.1(c). Square error characteristic of different filters. (a) LMS filter, (b) NLMS filter, (c) FA-LMF filter, (d) FA-NLMF filter.

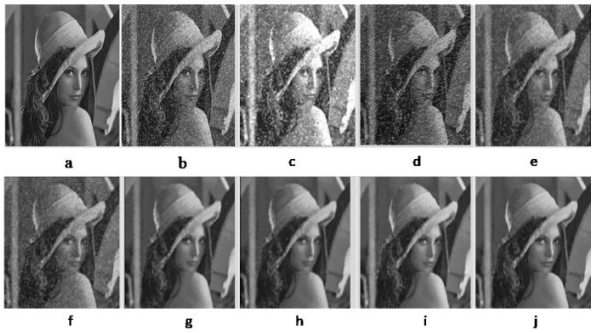

Fig.2 .(a) Pure image, (b) noisy image, (c) restored using LMS filter,(d) restored using NLMS filter. Fig .2 (e)-(j):Restored using non liner full adaptive ,(e)FA-LMF filter,(f)FA-NLMF filter,(g)FA-LMF-L filter,(h)FA-NLMF-L filter,(i)FA-LMF-C filter,(j)FA-NLMF-C filter.

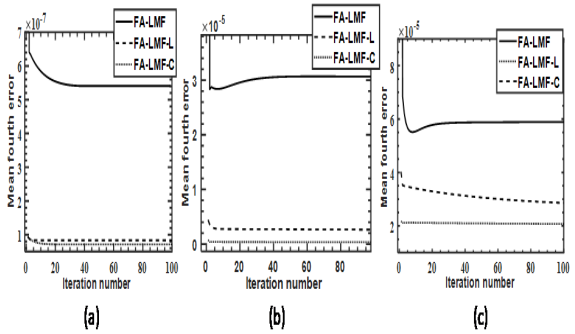

Fig.3.Mean fourth error characteristics (MFE) for Non linear full adaptive LMF filter and order statistic L and C filters different noise strength SNR (a) SNR=10dB,(b) SNR=5dB, (c) SNR=0dB.

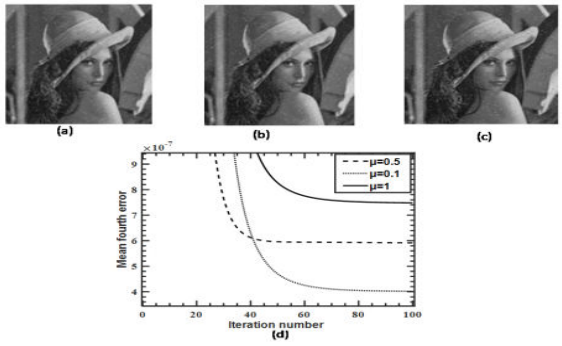

Fig.4. Restored images and MFE characteristics for NLMF filter for different values of step size (η). (a) Restored image for η=0.1, (b) Restored image for η=0.5,(c) Restored image for η=1, (d) MFE for η=0.1,0.5 and 1.

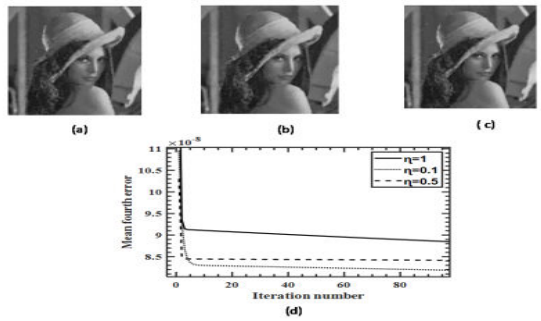

Fig.5. Restored images and MFE characteristics for NLMF-L filter for different values of step size (η). (a) Restored image for η=0.1, (b) Restored image for η=0.5, (c) Restored image for η=1, (d) MFE for η=0.1,0.5 and 1.

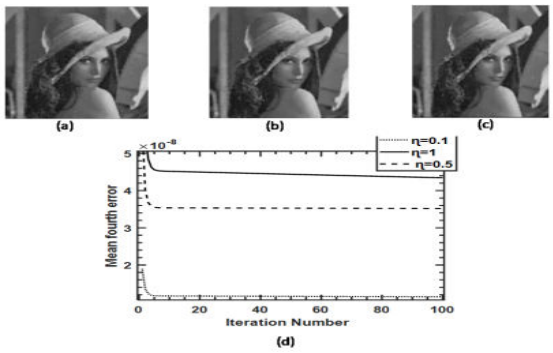

Fig.6. Restored images and MFE characteristics for NLMF-C filter for different values of step size (η). (a) Restored image for η=0.1, (b) Restored image for η=0.5, (c) Restored image for η=1, (d) MFE for η=0.1,0.5 and 1.

Fig.7.Noisy and restored images: Gaussian noisy image with noise strength (a) SNR=10dB, (b) SNR=5dB, (c) SNR=0dB. Restored images (d) for SNR=10db using FA-NLMF, (e) for SNR=5dB using FA-NLMF, (f) for SNR=0dB using FA-NLMF, (g) for SNR=10dB using FA-NLMF-L, (h) for SNR=5dB using FA-NLMF-L, (i) for SNR=0dB using FA-NLMF-L, (j) for SNR=10dB using FA-NLMF-C, (k) for SNR=5dB using FA-NLMF-C, (l) for SNR=0dB using FA-NLMF-C, filters.

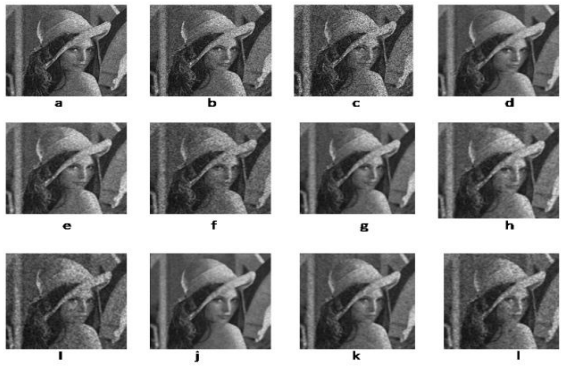

Fig.8.Noisy and restored images: Speckle noisy image with noise strength (a) SNR=10dB, (b) SNR=5dB, (c) SNR=0dB. Restored images (d) for SNR=10db using FA-NLMF, (e) for SNR=5dB using NLMF, (f) for SNR=0dB using FA-NLMF, (g) for SNR=10dB using FA-NLMF-L, (h) for SNR=5dB using FA-NLMF-L, (i) for SNR=0dB using FA-NLMF-L, (j) for SNR=10dB using FA-NLMF-C, (k) for SNR=5dB using FA-NLMF-C, (l) for SNR=0dB using FA-NLMF-C, filters.

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REVIEW ARTICLE

A Review: Polymers in Floating Drug Delivery System

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ABSTRACT

The substances which are formed as a result of condensation of the monomers are called polymers. The classifications of polymers are generally based on structure, source and monomer. Polymers are widely applied in the formulation of the Floating Drug Delivery System to modify drug release, drug targeting and improve gastric retention. Floating Drug Delivery System is low-density system that has sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting the gastric emptying rate for a long period of time. In Low-density approach the globular shells apparently having a lower density than that of gastric fluid can be used as a carrier for drug for its controlled release. In order to overcome the problem, multiple unit floating systems were developed, which reduce the inter subject variability and prevent dose-dumping. Several attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. Some of the most common polymers used in the floating drug delivery system are cellulose derivatives like HPMC. Application of polymers in the floating drug delivery system has been successful for various drugs like Rosiglitazone.

Keywords: Polymer, Classification, Advantages, Disadvantages, Floating Drug Delivery System, Classification, Factors affecting FDDS, and Polymers used in FDDS.

INTRODUCTION [1-4]

The substances which are formed as a result of condensation of monomers are called polymers [1]. Jöns Jacob Berzelius coined the term "polymer" in 1833. He didn't mention any rules for naming polymers based on molecular formula [2]. Polymer includes polymer physics and polymer chemistry, which are studied in the fields of polymer science, biophysics, and macromolecular science [3,4].

CLASSIFICATION

Based on monomer

Homopolymers

Homopolymers also known as homomers are defined as the type of polymers in which the monomers are the same compound.

Heteropolymers

Heteropolymers also known as copolymers are defined as the types of polymers in which the monomers are the different compound.

Based on structure

The vast majority of the polymers around us are comprised of a hydrocarbon spine and it's a long chain of connected carbon and hydrogen molecules, conceivable because of the tetravalent idea of carbon. A couple of instances of a hydrocarbon spine polymer are polypropylene, poly-butylene, polystyrene. Additionally, there are polymers which rather than carbon have different components in its spine. For instance, Nylon, which contains nitrogen iotas in the rehashed unit spine. Some polymers might contain a mixture of the various basic structures. The four basic polymer structures are as follows:

a) Linear polymer
b) Branched polymer
c) Cross-linked polymer
d) Networked polymer

Linear Polymers[5,6]

Direct polymers take after with long chains. The long chains are by and large reinforced together by the more fragile Vander Waals or hydrogen holding. direct polymers are regularly thermoplastic. Since these holding types are moderately simple to break with heat, what breaks the connections between the long anchors permitting the chains to stream past one another. This permits the material to be remolded. After cooling the connections between the long chains change, i.e., the polymer solidifies.

Example: Polyethylene PVC, polystyrene and polyamides.

Branched Polymers[6,7]

Direct polymers with the expansion of more limited chains dangling from the spine structures extended polymers. Since these more limited chains can confine with proficient pressing of the polymers, spread polymers will in general be less small than comparable direct polymers. Since the more modest chains don't connect starting with one long spine then onto the next, high temperature will normally break the connections between the stretched polymer chains and permit the polymer to be a thermoplastic, regardless of some complex extended polymers that oppose this dissolving and consequently separate prior to relaxing. For example they are thermosetting:

Example: low density polythene glycogen, starch, etc.

Crosslinked Polymers[5,6]

Cross connected polymers look like stepping stools. The chains interface starting with one spine then onto the next. Along these lines, not at all like direct polymers which are fortified together by more fragile Vander Waals powers, cross connected polymers are integrated through covalent holding This a lot more grounded security makes most cross connected polymers thermosetting, with a couple of exemptions for the standard cross connected polymers that end up intruding on their cross-joins at moderately cool temperatures.

Example: Elastomers include natural rubbers, styrene butamide block copolymers, and fluoroelastomer, polybutadiene and nitrile rubbers.

Networked Polymers[7,8]
Organized polymers are intricate that are intensely connected to shape a solitary complex organization of three-dimensional linkages. Scarcely, these polymers mellow when warming without corrupting the hidden polymer structure and are in this manner thermosetting polymers.

Based on source
a) Natural polymer
b) Synthetic polymer
c) Semi-synthetic polymer

Natural Polymer
The wellsprings of regular polymers are either creatures or plants. Consequently, they are called plant and creature polymers. These polymers are shaped by either addition polymerization or buildup polymerization. Polymers are widely found in nature. Our body also is comprised of numerous normal polymers like nucleic acids, proteins, etc.
Example: Jute, silk, wool, leather, natural rubber, lichen, etc.

Synthetic Polymer[9,10]
The engineered polymers are characterized as the filaments acquired by polymerization of straightforward compound atoms in lab are manufactured strands.
Example: Nylon, terylene, polyethene, polystyrene, synthetic rubber.

Semi-Synthetic [10]
They are gotten from normally happening polymers and go through additional synthetic alteration.
Example: cellulose nitrate, cellulose acetate.

ADVANTAGES OF POLYMER[11-15]
- ✓ High atomic weight polymer
- ✓ Fast polymerization rate.
- ✓ Allows expulsion of warmth from the framework.
- ✓ Viscosity stays near that of water and isn't reliant on sub-atomic weight.
- ✓ The eventual outcome can be utilized all things considered, shouldn't be adjusted or handled.
- ✓ The polymer is gotten unadulterated.
- ✓ Large castings might be arranged straight forwardly.

DISADVANTAGES OF POLYMER [11-15]
- ✓ For dry (separated) polymer, water evacuation is an energy-escalated measure.
- ✓ Surfactants and polymerization adjuvants-hard to eliminate Designed to work at high change of monomer to polymer.
- ✓ This can bring about critical chain move to polymer. It can't be utilized for buildup, ionic or Ziegler-Natta polymerization.
- ✓ Very low sub-atomic loads are gotten.

FLOATING DRUG DELIVERY SYSTEM[16-18]
Drifting Drug Delivery System are low-thickness framework that have adequately lightness to skim over the gastric substance and stay light in the stomach without influencing the gastric discharging rate for significant stretch of time. Gastro retentive frameworks can stay in the gastric area for a long time and subsequently fundamentally long the gastric home season of medications. Drawn out gastric maintenance improves bioavailability diminish drug waste and increment solvency of medications that are less dissolvable in high pH climate. Gastric maintenance gives new generous advantages and restorative prospects from patients.

CLASSIFICATION OF FLOATING DRUG DELIVERY SYSTEM[18]

Single Unit Floating

a) Effervescent
b) Non Effervescent

Multiple Unit Floating

a) Effervescent
b) Non Effervescent
c) Hollow Microsphere
d) Raft forming system

Single Unit Floating[19]

In Low-thickness approach the globular shells evidently having lower thickness than that of gastric liquid can be utilized as a transporter for drug for its controlled delivery. A light dose structure can likewise be acquired by utilizing a liquid filled framework that skims in the stomach. In coated shells popcorn, poprice, and polystyrol have been abused as medication transporters. Sugar polymeric materials, for example, methacrylic polymer and cellulose acetic acid derivation phthalate have been utilized to undercoat these shells. These are additionally covered with a medication polymer combination. The polymer of decision relying upon the kind of delivery wanted. The item skims on the gastric liquid while delivering the medication continuously over a drawn out span. Liquid filled skimming chamber kind of measurements structures incorporates consolidation of a gas-filled floatation chamber into a miniature permeable segment that houses a medication supply. Gaps or openings are available along the top and base dividers through which the Gastro-Intestinal Tract (GIT) liquid enters to break up the medication.

Effervescent floating dosage forms[20,21]

These are the framework sorts of frameworks which are planned with the assistance of swellable polymers like methyl cellulose, HPMC and chitosan alongside bubbly mixtures viz. Sodium carbonate, Calcium carbonate, Tartaric corrosive and Citric corrosive. These are figured in such explicit manner immediately it interacts with the acidic gastric substance CO2 is freed with capture in swollen hydrocolloids which gives lightness to measurement structures, for example, Famotidine, Amlodipine besylate. The ideal stoichio metric proportion of citrus extract and sodium bicarbonate for gas age is accounted for to be 0.76:1. For the most part Excipients incorporate HPMC, polyvinyl acetic acid derivation, Carbopol, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates.

Programmable medication conveyance frameworks for oral organization were created. It was another model gadget (3 cm long and 0.9 cm inside distance across) made to contain a tube shaped shell as oral container. Generally Excipients incorporate HPMC, polyvinyl acetic acid derivation, Carbopol, sodium alginate, calcium chloride, polyethylene oxide and polycarbonates.

Examples: HPMC, Calcium carbonate, Sodium carbonate

Non Effervescent Floating Dosage Form[22,23]

At least one gel framing, profoundly swellable cellulosic kind of hydrocolloids, hydroxyl ethyl cellulose, polysaccharides and grid shaping polymers like polycarbonates, polymethacrylate and polystyrene. One of the formulation techniques includes the blending of medication with a gel, which swells in contact with gastric liquid keeps a general trustworthiness of shape and mass thickness of short of what one inside the external coagulated hindrance. The lightness of measurement structure which accomplished because of the air ensnarement in to the swollen gel like design goes about as a repository and permits supported arrival of medication through the thick mass Drugs like Famotidine and levodopa. Models - colloidal gel boundary, miniature permeable compartment framework, alginate dots, and empty microspheres. Another is a Fluid-filled coasting chamber which incorporates fuse of a gas-filled floatation chamber into a miniature permeable part that causes a medication supply.

The detailing of ciprofloxacin was made out of 69.9% ciprofloxacin base, 0.34% sodium alginate, 1.03% thickener, 13.7% sodium bicarbonate, and 12.1% cross-connected poly vinyl pyrrolidine. The cross connected polymer PVP at first and the gel shaping polymers later framed a hydrated gel grid that ensnared the gas, making the tablet coast and be held in the stomach The hydrated gel network made a dissemination way for the medication, bringing about supported arrival of the medication.

Examples: polymethacrylates, polycarbonates, polyacrylates.

Multiple Unit Floating System[24,25]

In order to overcome problem, multiple unit floating systems were developed, which reduce the inter subject variability and prevent dose-dumping. The development of both Effervescent and Non-Effervescent multiple unit systems have been significant. The research has been focused and the scientists are still exploring the field of hollow microspheres, capable of floating on the gastric fluid and having improved gastric retention properties.

Non Effervescent [25,26]

A couple of examination work have announced the chance of growing such framework containing indomethacin, utilizing chitosan as the polymeric excipient. A different unit HBS containing indomethacin as a model medication arranged by expulsion measure is accounted for. A combination of medication, chitosan and acidic corrosive is expelled through a needle, and the exudate is straightforward. Chitosan hydrates and buoys in the acidic media causing gastric maintenance. Required medication delivery could be gotten by adjusting the medication polymer proportion.

Examples: Gel forming or highly swellable cellulose type hydrocarbon

Single layer floating tablets

They are defined by close blending of medication with a gel-framing hydrocolloid, which swells in contact with gastric liquid and keep up mass thickness of not as much as solidarity. The air caught by the swollen polymer presents lightness to these measurements structures.

Bilayer floating tablets

The bilayer tablet carries two layer prompt delivery layer and supported delivery layer. The quick delivery layer which delivery introductory portion from framework and the supported delivery layer ingests gastric liquid, shaping an impermeable colloidal gel obstruction on its surface, and keep a mass thickness of not as much as solidarity and consequently it stays light in the stomach.

Effervescent Multiple Unit[27,28]

The granules are a combination of medication pulverizes of two phases An and B, of which A contains 60 piece of HPMC, 40 pieces of polyacrylic corrosive and 20 pieces of medication and B contains 70 pieces of sodium bicarbonate and 30 pieces of tartaric corrosive. The 60 sections by weight of granules of stage and 30 sections by weight of granules of stage B are blended alongside an ointment and filled into case. In disintegration media, the container shell breaks down and frees the granules, which showed a skimming season of over 8 hours and supported medication arrival of 80% in about 6.5hours.

Examples: Sodium bicarbonate, citric acid or tartaric acid.

Hollow Microsphere[30,31]

Gliding microspheres are gastro-retentive medication conveyance frameworks dependent on non-bubbly methodology. Empty microspheres are in exacting sense, round void particles without center. These microspheres are typically free streaming powders comprising of proteins or engineered polymers, in a perfect world having a size under 200 micrometer. Strong biodegradable microspheres consolidating a medication scattered or disintegrated all through molecule framework have the potential for controlled arrival of medications. Gastro-retentive gliding microspheres are low-thickness frameworks that have adequate lightness to coast over gastric substance and stay in

stomach for delayed period. As the framework drifts over gastric substance, the medication is delivered gradually at wanted rate bringing about expanded gastric maintenance with decreased changes in plasma drug focus. Gastric liquid enters through the openings, breaks up the medication, and conveys the disintegrate drug for nonstop vehicle across the digestive system for investigation.
Examples: alginate, Eudragit S, agar and pectin.

Development of floating microspheres [19,31]
Empty microspheres (miniature inflatables), stacked with ibuprofen in their external polymer shells were set up by a novel emulsion-dissolvable dispersion technique. The ethanol: dichloromethane arrangement of the medication and an enteric acrylic polymer was poured in to a disturbed watery arrangement of PVA that was thermally controlled at 40°C. The gas stage created in scattered polymer bead by vanishing of dichloromethane framed in inward pit in microspheres of the polymer with drug. The miniature inflatables glided consistently over the outside of acidic disintegration media containing surfactant for more than 12 hours in vitro.

Mechanism of Floating Microspheres [19,30,31]
While microspheres interact with gastric liquid the gel formers, polysaccharides, and polymers hydrate to frame a colloidal gel hindrance that controls the pace of liquid entrance into the gadget and subsequent medication discharge. As the outside surface of the measurement structure breaks up, the gel layer is kept up by the hydration of the nearby hydrocolloid layer. The air caught by the swollen polymer brings down the thickness and presents lightness to the microspheres. Hence an insignificant gastric substance expected to permit legitimate accomplishment of lightness. Empty microspheres of acrylic tars, Eudragit, polyethylene oxide, and cellulose acetic acid derivation; polystyrene floatable shells; polycarbonate drifting inflatables and gelucire gliding granules are the new turns of events.

Methods of Preparation of Hollow Microspheres[19,30]
Empty microspheres are set up by dissolvable dissemination and dissipation techniques to make the empty internal center surface. Polymer is broken up in a natural dissolvable and the medication is either disintegrated or scattered in the polymer arrangement. The arrangement containing the medication is then emulsified into a fluid stage containing polyvinyl liquor to frame oil in water emulsion. After the development of a steady emulsion, the natural dissolvable is dissipated either by expanding the temperature under tension or by ceaseless mixing. The dissolvable evacuation prompts polymer precipitation at the o/w interface of drops, shaping hole and in this manner making them empty to confer the coasting properties.

List of Polymers used in Hollow Microspheres
Cellulose acetic acid derivation, Chitosan, Eudragit, Carbopol Acryl coat, Methocil, Acrylic pitches, Polyacrylates, Polyvinyl acetic acid derivation, Agar, Polyethylene oxide, Polycarbonates, and Polyethylene oxide.

Characterization of Hollow Microspheres[32-35]
Skimming microspheres are described by their micromeritic properties, for example, molecule size, tapped thickness, compressibility list, genuine thickness and stream properties. Molecule size is estimated utilizing an optical microscopy and mean molecule size was determined by estimating 200 to 300 particles with the assistance of aligned visual micrometer. Genuine thickness is dictated by fluid relocation technique; tapped thickness and compressibility list are determined by estimating the adjustment in volume utilizing a mass thickness mechanical assembly; point of rest is controlled by fixed channel strategy. The empty idea of microspheres is affirmed by filtering electron microscopy.

Raft Forming System [36-38]
Pontoon shaping framework is in much consideration for the conveyance of acid neutralizers and medication conveyance for gastrointestinal contaminations and problems. The fundamental instrument associated with pontoon

arrangement remembers the development of thick firm gel for contact with gastric liquids, where in each bit of the fluid swells shaping a consistent layer called pontoon. This pontoon coasts on gastric liquids due to a low thickness made by the development of CO2. It go about as a hindrance to forestall the reflux of gastric contant like HCL and compound into the throat. Skimming Rafts have been utilized in the treatment of Gastric esophageal reflux infection (GERD). Different of polymers are utilized like various polysaccharides, utilized in different examination works. The most broadly utilized pontoon framing specialists are Alginic corrosive, alginates and gelatin. Composition has drug, alginic acid, sodium bicarbonate, calcium carbonate, mannitol and a sweetener.

FACTORS AFFECTING GASTRIC RETENTION[37]

A few components incorporate like size, thickness and state of measurements structure, attendant admission of food and medications, for example, anticholinergic specialists e.g. atropine), sedatives e.g. codeine and prokinetic specialists are eg. propantheline metoclopramide and organic factors like sex, act, age, illness state and weight list eg. Diabetes, and so on.

Drugs Used In the Formulations of Gastro Specific Floating Dosage Forms[39]

- **Floating microspheres:** Aspirin, Griseofulvin, pnitroaniline, Ibuprofen, Ketoprofen, Piroxicam, Theophylline, Nifedipine, Nicardipine, Verapamil,Tranilast and Terfinadine.
- **Floating granules:** Diclofenac sodium, Indomethacin and Prednisolone.
- **Films:** Cinnarizine, Albendazole.
- **Floating tablets and Pills:** Acetaminophen, Acetylsalicylic acid, Ampicillin, Atenolol, Fluorouracil, Piretanide, Theophylline, Chlorpheniramine maleate, Aspirin, Calcium Carbonate, Fluorouracil, Prednisolone, Sotalol.
- **Floating Capsules:** Chlordiazepoxide hydrogen chloride, Ursodeoxycholic acid, Diazepam, Furosemide, Misoprostol, Levodopa, and Propranolol, Pepstatin.

FACTORS AFFECTING FLOATING DRUG DELIVERY SYSTEM[41-45]

Different endeavors have been made to hold measurement structure in the stomach as a method of expanding the maintenance time. These endeavors incorporate utilization of skimming dose structure (gas-producing framework and growing or extending framework), muco-cement framework, high-thickness framework adjusted shape framework, gastric-purging deferring gadgets and co-organization of gastric-exhausting postponing drugs.

Density[40]

Gastric maintenance time is capacity of measurements structure lightness that is subject to the thickness. A thickness of <1.0gm/cm3 is needed to show coasting property.

Size[41]

Measurements structure unit with a distance across more than 7.5 mm are accounted for to have an expanded GRT contrasted and those with a breadth of 9.9mm; it was seen that peristaltic waves secured the definition of previously mentioned size.

Nature of Meal[42]

Taking care of unpalatable polymer or unsaturated fat salts can change the motility example of the stomach took care of state, in this manner diminishing the gastric purging of medication and dragging out drug discharge.

Frequency of Feed[43]

The Gastro-maintenance time can increment by more than 400 minutes when achievement sive suppers are given contrasted with a solitary dinner due with the low recurrence of MMC;

Age [44]
Old individuals, particularly those over 70 years, have an altogether longer Gastro-maintenance time. In individuals, below 70 years, have a restricted Gastro-maintenance time.

Posture[44]
Gastro-maintenance time can differ among prostrate and upstanding walking conditions of patients. It is seen that upstanding position is more ideal in contrasted and prostrate position.

Viscosity of Polymer[44]
Medication delivery and drifting characters of FDDS are significantly influenced by the consistency of various evaluations of polymers and their collaboration. Low thickness polymers (e.g., HPMC K100 LV) are discovered to be more gainful than high consistency polymers (e.g., HPMC K4M) in improving the drifting properties of the measurement structure. Additionally, a reduction in the delivery rate was likewise found with an increment in polymer consistency.

Gender
Mean wandering GRT in guys (3.4 0.6 hours) is less contrasted and their age and race-coordinated with female partners (4.6 1.2 hours), paying little mind to the weight, tallness and body surface.

POLYMERS USED IN FDDS[25,55-59]
Probably the most widely recognized polymers utilized in gliding drug conveyance framework are cellulose subordinates like HPMC, EC. Eudragit is additionally broadly utilized. Engineered polymers which are utilized in the arrangement and plan of FDDS are costly to make. In this way, regular polymers like chitosan ought to be considered as another option. In one exploration study, which utilized chitosan as polymer and sodium lauryl sulfate as cross-connecting specialist, so marry better in-vitro drug discharge when contrasted with ordinary model.

Polymers are likewise utilized for upgrading the bio accessibility of medication. Improved enemy of diabetic impact was invested in FDDS of rosiglitazone maleate including polymers like HPMC and ethyl cellulose. The drifting properties or gastro-maintenance improved utilizing polymers like Eudragit. This is seen by improvement of muco-cement property. Enteric covering of coasting drug conveyance framework can be encouraged utilizing acrylic polymers. Controlled delivery can be given in this medication conveyance framework utilizing polymers extricated from xanthan and guar.

APPLICATIONS OF FLOATING DRUG DELIVERY SYSTEMS[60,61]
Coasting drug conveyance offers numerous applications on helpless bioavailability drugs in view of the restricted retention window in the upper piece of the gastrointestinal parcel. It holds the measurement structure at the site of assimilation and that upgrades the bioavailability.

Sustained Drug Delivery[60-62]
In this frameworks portion enormous in size and passing from the pyloric opening is restricted. New supported delivery gliding cases of Nicardipine hydrochloride were created and were assessed in vivo. Plasma focus time bends showed a more extended term for organization (16 hours) in the supported delivery gliding cases as contrasted and customary MICARD cases (8 hours).

Site-Specific Drug Delivery[60-62]
These structures are particularly priceless for drugs that are unequivocally acclimatized from stomach or the proximal piece of the little stomach related framework, E.g. riboflavin. Furosemide is fundamentally burned-through from the stomach followed by the duodenum as differentiated and standard MICARD compartments (8 hours).

Absorption Enhancement[60-62]

Medications which have helpless bioavailability at the site explicit retention from the upper piece of the gastrointestinal plot are likely possibility to be detailed as coasting drug conveyance frameworks, now and again expansion in the bioavailability of skimming measurements structures (42.9%) could be accomplished as contrasted and monetarily accessible LASIX tablets (33.4%).

CONCLUSION

Polymers are once in a while utilized in their unadulterated structure. Changes are done to improve the properties of the polymers. Contingent on the utilization, change is acted to meet the necessities of the material. Because of ideal properties of polymers it is broadly utilized in assorted fields like thickness, ophthalmology, directed medication conveyance framework (FDDS). In pretty much every field of dentistry they can be utilized effectively. The greater part of the polymers is utilized in Floating Drug Delivery System that is cellulose subordinates like EC, HPMC and Eudragit. The Eudragit is generally utilized in FDDS. The gliding properties or gastro-maintenance can be improved utilizing polymers like eudragit. This is seen by improvement of muco-bond. An enteric covering of drifting medication conveyance framework can be encouraged utilizing acrylic polymers. In research, the greater part of the polymers are utilized in FDDS in this way, we need to know more polymers, which can be useful for our future examination and Purposes.

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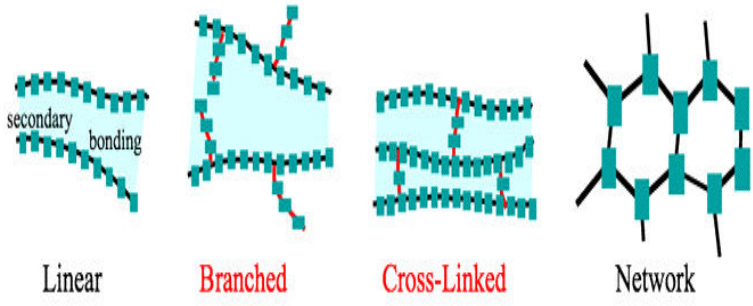

Fig.1. Classification of polymers

Fig.2. Natural Polymer

Fig.3. Synthetic polymer

Fig.4. Cellulose Acetate

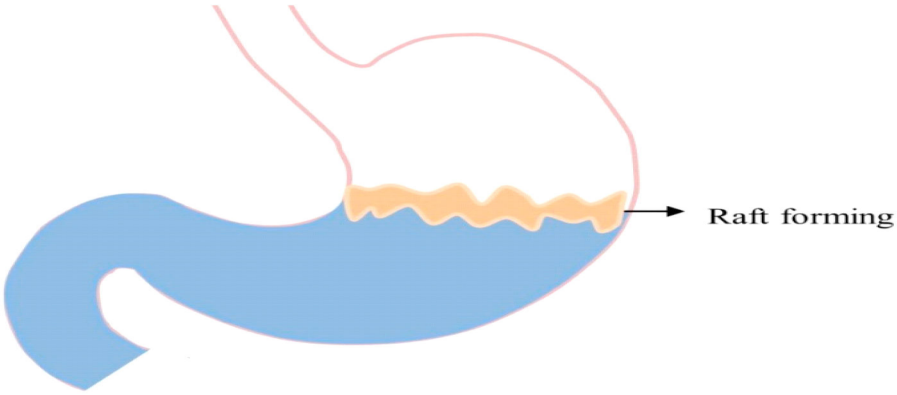

Fig.5. Raft Formation in Floating Drug Delivery System

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RESEARCH ARTICLE

Synthesis of TiO2@ZnO–CdS Nanocomposites and their Anti Inflammatory Activity

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ABSTRACT

Titanium dioxide (TiO_2) is used for water purification, because many chemical compounds and micro organism can be decomposed by oxidation and reduction processes.. In this study, the composite of TiO2 nanoparticles (NPs) @ mesoporous silica nanoparticles (MSNPs) (TiO2@ZnO) were prepared by the sol–gel method. The prepared TiO2@ZnO nanocomposite was modified by decorating Cadmium sulfide nanoparticles (CdS) (TiO2@ZnO–CdS) using a hydrothermal method. The composite was investigated for anti- inflammation of protein denaturation and proteinase inhibitory activity.

Keywords: nanocomposite, anti-inflammation, denaturation, inhibitory activity

INTRODUCTION

In recent years among the technologies used for the degradation of the environmental pollutants the photocatalytic technique gained interest moreover, it is regarded as the most innovative technique. The strongly oxidizing power of titanium dioxide nanoparticles (TiO_2 NPs) leads to pave its potential energy and environmental applications, such as solar cells, water splitting, super capacitor, sensors, biosensors, water purification and anti inflammatory activity.TiO_2 is considered as one of the most promising and challenge materials low toxicity, less chemical inert and high photo chemically stability [1]The TiO_2 nanoparticles mesoporous structure, highly surface area and porous nature higher photocatalytic activity in order to adsorption capacity for TiO_2 nanoparticles [2-4].The TiO_2

nanoparticles noble metal doping (Au,Pt,Ag) for certain subtracting metaloxide, carbon, polymer enhancing catalytic performance of photo induced reaction under the illumination of UV light [5-6]. In this routes employed for sensitizing TiO_2 and have proved in significantly enhancing the photo activity of TiO_2. The underlying mechanism being that the Fermi level of the metal is lower than TiO_2 and hence there can be an electron transfer from the conduction band of the semiconductor to the metal. The TiO_2 hollow microspheres, the results confirmed that the as – prepared products exhibited enhanced photocatalytic and microbial activity [8]. At once few researchers TiO_2 structure modifications of nanotube, nanorods, nanowires, nanosphere for further adapted 1D structure and 2D structure was more catalytic activity.

MATERIALS AND METHODS

Materials

The analytical grade were purchased from in Sigma Aldrich, Mumbai, India, were as Titanium (IV) chloride, ($TiCl_4$, 99.99 %), Cityltrimethyl ammonium bromide (CTAB, 99.98%), Tetra ethyl orthosilicate (TEOS, 99.99 %), Cadmium nitrate (99.98 %), absolute methanol, ethanol, ammonium hydroxide (NH_4OH, 99.99 %), sodium hydroxide (NaOH, 99.98 %), Hydrochloric acid (HCl, 99.98 %) were received from Merck.. All different chemicals employed in this work were of analytical grade. Unless otherwise specified, deionized double distilled water was used for the preparation of aqueous solutions.

Synthesis of TiO_2 nanoparticles (TiO_2NPs)

$TiCl_4$ (9 ml) was slowly introduced into deionized double distilled water in an ice bath (0°C) under constant stirring until it was completely dissolved and then 18ml of 30% NH_4OH was added to this suspension. The white titanium hydroxide ($Ti(OH)_4$) was allowed to stand for 1 h. Then, the obtained TiO_2 NPs were filtered, washed with deionized double distilled water and dried at 100°C in a vacuum oven for 3 h.

Synthesis of TiO_2@ZnO–CdS nanocomposite

1 g of TiO_2 and 50 ml of 1.0 M $ZnSO_4$ solution was added drop wise into 30 ml of 2.0 M NH_4CO_3 solution under vigorous stirring at 60°C in water bath for 1 h. The white precipitate was isolated by filter and washed for three times with double distilled water and ethanol, dried in a vacuum oven at 60°C for 24 h. Finally, the product was calcined at 600°C for 1 h to obtain powder of TiO_2/ZnO. The CdS NPs were deposited on the surface of TiO^2@ZnO nanocomposite through a chemical reduction method. In the typical synthesis, 1 g of the preformed TiO_2@ ZnO nanocomposite was dispersed in 250 ml of deionized double distilled water with continuous stirring for 30 min to get a homogeneous distribution of TiO_2@ZnO nanocomposite. The Cd $(NO_3)_2$(5wt%)was added and stirred towards the reduction of cadmium ions upon the drop wise addition of $NaBH_4$ until the colour changed to yellow. The appearance of the greenish yellow colour indicated the formation of TiO2@ZnO–CdS nanocomposite and the solution was continuously stirred for another 30 min. The TiO_2@ZnO–CdS nanocomposite was filtered washed thoroughly with deionized double distilled water, dried at 60°C for 3 h and finally calcination at 450°C for 3 h.

Methodology for Anti Inflammatory Process

Albumin Denaturation: About 0.2 ml of eggs albumin (from hens egg) was comprised 5 ml of reaction mixture, 2 ml of varying concentrations of sample (20-100 µg/ml), and 2.8 phosphate- buffered saline (PBS pH 6.4). The control was served as similar volume of double distilled water. Then the mixture was incubated at 37ºC in biochemical oxygen demand incubator for 15 min and then heated at 70º C for 5 min. After cooling their absorbance were measured at 660 nm at pure blank. Diclofenacsodium (standard drug) was used as reference drug and treated as such for the determination of absorbance. The percentage inhibition of protein denaturation was calculated as below [9].

$$\text{Percent inhibition} = \frac{\text{Abs control/ Abs treated}}{\text{Abs treated}} \times 100$$

Antiproteinase: The test was performed according to the modified method. The reaction mixture (2 ml) was containing 0.06 mg aspirin, 20 mM Tris-HCl buffer (pH7.4) and 1 ml test sample of different concentrations (20 -100 µg/ml). The mixture was incubated at 37º C for 5 min and then 1 ml 0.8% (w/v) casein was added. The mixture was incubated for an additional 20 min. 2 ml of 70% perchloric acid was added to complete the reaction. Cloudy suspension was centrifuged. The absorbance of the supernatant was maintained at 210 nm. The buffer solution is used as a blank. The experiment was performed in triplicate. The percentage inhibition of proteinase inhibitory activity was calculated.

$$\text{Percentage inhibition} = \frac{\text{(Abs control / Abs sample)}}{\text{Abs control}} \times 100$$

RESULTS AND DISCUSSION

Inhibition of Albumin Denaturation: Protein denaturation is a process in which proteins lose their tertiary and secondary structure by application of external stress or compound. The compound such as strong acid, strong base, concentrated Inorganic salt, an organic solvent or heat. Denaturation is a protein is a well- documented cause of inflammation. As part of investigation on the mechanism of the anti- inflammation activity ability of sample to inhibit protein denaturation was studied. Inhibition of albumin denaturation of activity at different concentration as shown in Figure 1& Table 1.It was effective in inhibiting heat induced albumin denaturation maximum inhibition of 71% was observed at the concentration of 100 µg\ml. Diclofenac is a standard anti inflammation drug shows the maximum inhibition 80% at the concentration of 100 µg\ml compared with control.

Antiproteinase Action: Neutrophils are known to be a rich source of serine proteinase and are localized at lysosomes. It was previously reported that leucocytes proteinase play an important role in the development of tissue damage during inflammatory reactions and significant level of protection was provided proteinase inhibitors. Anti proteinase activity at different concentration as shown in Figure 2& Table 2. It shows the maximum inhibition of 62% at 100µg\ml. Aspirin shows maximum inhibition 66% at 100µg\ml.

CONCLUSION

The TiO2@ZnO–CdS nanocomposite was investigated for anti- inflammation of protein denaturation and proteinase inhibitory activity were calculated. Maximum inhibition of 85% was observed for Albumin denaturation, while 70% for Antiproteinase Action

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Table-1*: In vitro* activity of the samples using albumin denaturation

S.NO	CONCENTRAION	% OF ALBUMIN DENATURATION	
		SAMPLES	DICLOFENAC
1	20	40	55
2	40	46	62
3	60	48	73
4	80	55	78
5	100	75	85

Table-2 : *In vitro* activity of the samples using anti proteinase action

S.NO	CONCENTRAION	% OF ANTI PROTENASE ACTIVITY	
		SAMPLE	ASPIRIN
1	20	33	43
2	40	36	51
3	60	40	58
4	80	44	69
5	100	66	70

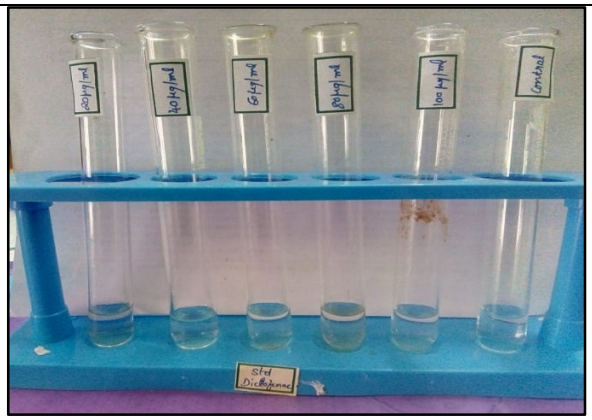

Figure 1: Inhibition of albumin denaturation of standard Diclofenac sodium

Figure 2: Anti proteinase action in samples

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RESEARCH ARTICLE

Baseline Study on Species Composition of Coleopterans in A Rural Area of Karakkamala, Wayanad District, Kerala, Southern India

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ABSTRACT

The present study was made based on the species composition of beetles in the 2 different area of the Karakkamala village of Wayanad District of Kerala. There are 27 species belongs to 7 families were recorded in the present study. The beetles are collected, taxonomically arranged and photographed. The identified families are Scarabaeidae, Cerambycidae, Chrysomelidae, Curculionidae, Coccinillidae, Carabidae and Bupristidae. Off which Scarabidae was the most dominant family which represents 9 different species. Cerambycidae and Chrysomelidae are the second largest family represented by 5 species in each family. The least number of species (1 species) was represented by the family Bupristidae. The present study revealed that the Non-residential area has the highest species composition than the residential area.

Keywords: Cerambycidae, Chrysomelidae, Curculionidae, Coccinillidae, Carabidae, Bupristidae.

INTRODUCTION

Coleoptera is an order of insects commonly called as beetles. The word "coleopteran" is from the Greek keleos, meaning "sheath", and pteron, meaning "wing", thus "sheathed wing". The reason for the name is that most beetles have two pairs of wings, the front pair, and the "elytra", being hardened and thickened into a sheath-like or shell-like protection for the rear pair and for the rear part of the beetle's body. The order coleopteran includes more species than any other order; constituting almost 25% of all known life forms [1-3]. Approximately 15,088 species of beetles were recorded from India [4]. The species composition of beetles is very wide. They are found in all major habitats, except marine and the Polar Regions. There are particular species that are adapted to practically every kind

of diet. The family Scarabaeidae is the largest family of insects which contains more than 30000 species in the world [5]. *Coleoptera* are found in nearly all natural habitats, that is, vegetative foliage, from trees and their bark to flowers, leaves, and underground near roots, even inside plants like galls, tissue, including dead or decaying ones[6]. About of beetle species are phytophagous in both the larval and adult stages, living in or on plants, wood, fungi, and a variety of stored products, including cereals, tobacco, and dried fruits. Because many of these plants are important for agriculture, forestry, and the household, the beetle can be considered as pest [7]. Beetles are not only pests but can also be beneficial, usually by controlling the populations of pests. One of the best, and widely known, examples is the ladybug or ladybird (family Coccinellidae). Both the larvae and adults are found feeding on aphid colonies. Other ladybugs feed on scale insects and mealy bugs. If normal foods sources are scarce, they may feed on other things, such as small caterpillars, young plant bugs, honeydew, and nectar. Ground beetles (family Carabidae) are common predators of many different insects and other arthropods, including fly eggs, caterpillars, wireworms, and others [8].

With reference to coleopteran, excellent faunal treatises have been prepared by [9] who described fifteen new species from Kerala. Beetles are exceedingly variable both ecologically and biologically. Most of the beetles are terrestrial herbivores; many are predatory, frequently with highly specialized host ranges or life cycles (Forest Science Project (FSP) Technical Report). While the identity and activity of a few of the forest beetles are well known, most of those other than the major pests have been little studied. Their complex ecosystem roles have not been elucidated. Although some of this deficiency is owing to a general lack of emphasis on total ecosystem function and dynamics, it is well known that lack of identification manuals has severely hindered studies of the whole beetle component of forest diversity [10]. The most common lifecycle type in beetles is holometaboly, whereby individuals emerge from eggs as larvae, develop through several instars, pupate, and eventually emerge as adults. Sexual reproduction is predominant, although parthenogenesis (i.e., production of viable, unfertilized eggs) also occurs. More specialized or unusual life cycles, which include the occurrence of active and inactive larval instars in parasitoid species, also are known in Coleopteran [11]. India is well known for richness of coleopterans fauna and against an estimated total of 179 families of Coleopterans, about 103 families are known from India, of the 3,50,000 described species from all over the world, 15,000 species under 2,000 genera are known from India (Biswas, 1995). The short-term investigation was made on the species composition of *Coleoptera* occurring in a rural area of Karakkamala in Wayanad district of Kerala state, Southern India.

MATERIALS AND METHODS

The present work was made in Karakkamala Village, Wayanad District, Kerala, India. There are two area such as Residential and Non-Residential were selected from the village for the investigation. The field study was made on the beetle diversity in the selected areas. The work was carried out for the period of five months from September 2020 to January 2021.

Study Area

The study area is the Karakkamala village under Vellamunda panchayath of Mananthavady Taluk, Wayanad district in the Northern Kerala (Fig. 1). The study was carried out with special reference to the Ward X of the village. It is away from the city. Station-1: Residential: This is an area with occasional buildings and houses where people live (Fig. 2). Station-2:Non-Residential: It is containing mixed vegetation such as coffee plants, coconut trees, banana, vegetable garden, rubber plantations, etc. (Fig. 3).

Collection of insects

The specimens were collected from homestead, trees, plants, household articles etc. The collection of samples were made at various time of the day like morning, noon, afternoon, evening and at night. The area under study was

taken in a keen observation. The collected specimens were photographed by mobile camera having good quality. After photography the specimens were left alone.

Methods of collection
Different collecting and trapping methods were used to collect the insect sample.

Hand collection
This is the most commonly used and simple method for collection of insects. Most beetles are harmless and were collected by hand. They were collected from ground, flowers, leaves, and barks, branches of trees, soil, leaf litter and stored food products.

Butterfly nets: Butterfly nets were employed for catching flying beetles.

Beating: Beating is a profitable method of collecting that provides specimens rarely encountered by other means. Insects were beaten or shaken from foliage or blossom, and even dead branches may yield specimens that would otherwise go unnoticed. Beating was done at any time but not be done when the vegetation is wet from early morning dew or rain. The best times are usually early or late in the day. A stout stick can be used to beat foliage with sharp downward strokes while holding the beating tray beneath. The short abrupt shakes was done which provide the most specimens. Sometimes shrubs and tree branches were heavily shaken so that beetles may fall on already spread large white sheets [12].

Searching: Most of the specimens were collected manually by active visual search. Insects found by searching are collected by hand and forceps.

Light trap: Some beetles were collected during night with a source of white light. Light trap was used to collect the nocturnal beetles.

Pitfall trap: Beetles were collected using Cebo-Suspendido-Rejilla pitfall traps [13-15]. Each trap consisted of a plastic basin (210 mm in diameter and 150 mm in depth), buried to its rim in soil and containing a water-formalin-liquid soap mixture. One liter of fresh dung was placed on a strip of wire grid (2.5cmx2.5cm) at the top of the basin. A set of four replicate traps, with each replicate at each corner of a 100m² plot was placed in the study site. The trap was visited every day.

Identification method
The details such as the date of collection, collected habitat, colour and other relevant data of the insect was recorded. The beetle was collected first, later it was identified with the help of standard reference book [16] and further confirmed by experts and web based materials.

Data analysis
As beetles are reported to be the diverse group of insects. The main focus of this study is to assess the species composition of beetles in this region. The list of collected species were given in the Table 1.

RESULTS

A total of 27 species of coleopterans belonging to 27 genera of 7 families were identified during the study. There are 7 distinct families such as Scarabaeidae, Chrysomelidae, Cerambycidae, Curculionidae, Carabidae, Coccinillidae and Bupristidae were identified. The list of beetles recorded is given in the Table 1. Off 7 Families, Chrysomelidae and Cerambycidae were the next dominant families having 5 species. The family Curculionidae represent 3 species. 2 species of each were recorded in families Carabidae and Coccinellidae. Bupristidae represented by a single species

only. There are 12 species recorded from residential area and the list of beetles recorded in this area was given in the Table 2 and Table 3 represent the list of beetles recorded from the non-residential area. There are 15 species are identified from this area. So non-residential area shows highest species diversity than residential area. It is reported that the family Chrysomelidae, Coccinellidae and Bupristidae were present only in non-residential area. Similarly family Carabidae can record from the residential area in this study. From the pie chart (Fig.4) it is confirmed that the Scarabaeidae represents the most dominant family which contributes 33%. Chrysomelidae and Cerambycidae are the second highest family which contributes 19% each. Curculionidae contributes 11% from the study area. Coccinellidae and Carabidae shows the equal number of species thus contributes 7% each. Bupristidae was the least recorded family that contributes only 4%.

Fig.5 shows that the number of species recorded from the residential area. Totally 12 species are identified from this area. Among these, 5 species belongs to the family Scarabaeidae. Off the total 9 Scarabidae species, 5 were reported from residential area. The family Cerambycidae and Carabidae contain 4 and 2 species respectively. Off the total, 5 Cerambycidae species 4 were reported from residential area. Similarly the Carabid species reported from the same area. Only one species of the Curculionidae family has been reported from here. Fig.6 shows the number of species recorded from the Non-residential Area. Totally 15 species were identified from this area. Among these, 5 species comes under the family Chrysomelidae. 4 species belongs to the family Scarabaeidae. The family Curculionidae and Coccinellidae contain 2 species each. Similarly the family Cerambycidae and Bupristidae contain only one species each.

DISCUSSION

The result of present study shows that Scarabidae (33%) were the most dominant family followed by Chrysomelidae (19%), Cerambycidae (19%), Curculionidae (11%), Carbidae (7%), Coccinellidae (7%) and Bupristidae (4%). Total 27 species belonging to 7 different families of beetles were collected and identified in this study. The dominant families observed in the present study was almost similar to the studies conducted in different parts of the country. A total of 12 species belonging to 5 different families of beetles viz. Gyrinidae, Tenebrionidae, Carabidae, Scarabaeidae and Meloidae were collected and identified from various habitats in an investigation conducted on the coleopteran diversity from the vicinity of Semadoh-Makhala Road, Sipna Range, and Melghat Tiger Reserve of India in the month of October-November 2009[17]. Another investigation in and around Tarubanda village, Gugamal Range, Melghat Tiger Reserve was conducted from October 2010 to November 2010 and a total of 16 species of beetles were collected and examined, out of which 13 species belonging to 6 different families were identified from various habitats [18]. Authors have studied the diversity pattern of beetles in and around Joysagar Tank of Assam, India. There are 10 species of beetles belonging to 8 different families viz., Dytiscidae, Gyrinidae, Carabidae, Hydrophilidae, Chrysomelidae, Coccinellidae, Cerambycidae and Tenebrionidae were collected and identified.

Study on insect diversity in disturbed and undisturbed forests in the Kerala parts of Western Ghats showed maximum number of species from order *Coleoptera*. Families such as Chrysomelidae, Cerambycidae and Tenebrionidae were recorded to be dominant [19]. In the study on the insect fauna of Peechi-Vazhani Wildlife Sanctuary, 374 species of insects were recorded of which Coleoptera contributed 78 species. The beetles belonged to the families Chrysomelidae, Cerambycidae, Buprestidae, Bostrychidae, Platypodidae, Curculionidae and Scarabaeidae were reported [20]. A reconnaissance on animal diversity in Periyar Tiger Reserve, Kerala with special reference to invertebrates for a period of 15 days resulted in documenting 27 species of Coleopterans belonging to 20 families. Off these, Scarabaeidae showed greater abundance when compared to all other families [21]. A study on the abundance and richness of insects in Kazhakuttam Grama Panchayat in Kerala showed that most dominant insect order was *Coleoptera* represented by 10 families followed by Coccinellidae was the second most dominant family [22].

Various studies have revealed that Indian Himalayan Region harbors a rich diversity of beetles. Author [23] reported 186 species of beetles belonging to 18 families of order *Coleoptera* from Nival Zones of North-East Himalaya. Scarabaeidae was the most dominant family with 84 species followed by Salphylimidae (32), Tenebrionidae (17), Curculionidae (16), Dystiscidae and Hydrophilidae (7 each). Author [24] reported 190 species of beetles belonging to 26 families from North-East Himalaya. Tenebrionidae was the most dominant family with 55 species followed by Carabidae (23), Scarabaeidae (18) and Haliphidae (16). Author [25] reported 105 species of beetles belonging to 9 families from Western Himalayan Ecosystem. Chrysomelidae was the most dominant family with 35 species followed by Tenebrionidae (23), Carabidae (22), Scarabaeidae (21), Elateridae (5) Curculionidae (4), Meloidae (3), Cicindelidae and Lampyridae (1 each). Author [26] have recorded 49 species of Scarabaeid Coleopteran insects belonging to 4 families from Kullu Valley of Himachal Pradesh. Authors [27] have reported 20 species of Coleopteran insects from Nanda Devi Biosphere Reserve, Western Himalayas, Uttarakhand, India. Autohrs [28] have reported 17 species of beetles belonging to 6 families from Shyampur forest range in Shivalik foothills of Haridwar, India. Recently, authors [29] have reported 56 species of Scarabaeid beetles belonging to 20 genera and 4 subfamilies from different landscapes of Himachal Pradesh, India. Authors [30] investigated the diversity, distribution and zoo-geographical notes on Longhorn Beetles (*Cerambycidae: Coleoptera*) of North-East India. They reported 562 species under 211 genera belonging to 56 tribes of 5 subfamilies of the family Cerambycidae from North-East Indian states. Species diversity of the scarab beetles of Madhya Pradesh and Chhattisgarh is quite rich and currently includes 134 species belonging to 11 subfamilies under four families of super family Scarabaeoidea [31-33].

CONCLUSION

The present study concluded that the beetle diversity was comparatively rich in Non-Residential Area than the Residential Area which might be due to the favorable environmental, habitat and feeding conditions prevailing in the Non-Residential Area. The present findings showed that the Scarabidae was the most dominant family represented with 9 species could be ascribed to higher reproductive efficacy. The results of present short term study shed light on beetle diversity in the Karakkamala village of Kerala state. The detailed long term investigation on the distribution and diversity of beetles in this area is highly essential to know the real biodiversity status on the particular group of fauna.

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Table-1: Total number of beetle species recorded from the Karakkamala, Kerala

S.No.	Common Name	Scientific Name	Family	Order
1	Dung beetle	*Copris fricator*	Scarabaeidae	Coleoptera
2	Coconut White Grub	*Leucopholis coenophora*	Scarabaeidae	Coleoptera
3	Rhinoceros Beetle	*Oryctes rhinoceros*	Scarabaeidae	Coleoptera
4	Brown rhinocerose beetle.	*Xylotrupes gidon*	Scarabaeidae	Coleoptera
5	Unknown	*Popillia cupricollis*	Scarabaeidae	Coleoptera
6	Unknown	*Neocalaphodiusmoestus*	Scarabaeidae	Coleoptera
7	Unknown	*Onitis philemon*	Scarabaeidae	Coleoptera
8	Unknown	*Anomala bengalensis*	Scarabaeidae	Coleoptera
9	Unknown	*Adoretus* sp.	Scarabaeidae	Coleoptera
10	Rice Hispa	*Discladispa armigera*	Chrysomelidae	Coleoptera
11	Pumkin Beetle	*Aulacophora foveicoies*	Chrysomelidae	Coleoptera
12	White Spotted Leaf beetle	*Monolepta signata*	Chrysomelidae	Coleoptera
13	Frog legged leaf beetle	*Sagra femorata*	Chrysomelidae	Coleoptera
14	Leaf beetle	*Altica* sp.	Chrysomelidae	Coleoptera
15	Cucurbit longicorn	*Apomecyna saltator*	Cerambycidae	Coleoptera
16	Monkeypod round headed long horn beetle	*Xystrocera globosa*	Cerambycidae	Coleoptera
17	Unknown	*Nupserha* sp.	Cerambycidae	Coleoptera
18	Unknown	*Acalolepta* sp.	Cerambycidae	Coleoptera
19	Unknown	*Pothyne* sp.	Cerambycidae	Coleoptera
20	Red palm weevil	*Rhynchophorus ferrugineus*	Curculionidae	Coleoptera
21	Banana root borer	*Cosmopolites sordidus*	Curculionidae	Coleoptera
22	Rice Weevil	*Sitophilus oryzae*	Curculionidae	Coleoptera
23	Harlequin /lady bird beetle	*Harmoniaaxyrids*	Coccinellidae	Coleoptera
24	Lady bird beetle	*Cycloneda sanguinea*	Coccinellidae	Coleoptera
25	Asian ground beetle	*Mochtherustetraspilotus*	Carabidae	Coleoptera
26	Ant nest beetle, flanged bombardier beetle	*Platyrhopalopsismellei*	Carabidae	Coleoptera
27	Jewel beetle/ wood borring betle	*Iridotaeniablanchardii*	Bupristidae	Coleoptera

Table 2: List of beetles recorded from residential area

S. No.	Scientific Name	Family
1	*Apomecyna saltator*	Cerambycidae
2	*Anomala bengalensis*	Scarabaeidae
3	*Neocalaphodiusmoestus*	Scarabaeidae
4	*Acalolepta* sp.	Cerambycidae

5	*Pothyne* sp.	Cerambycidae
6	*Onitis philemon*	Scarabaeidae
7	*Nupserha* sp.	Cerambycidae
8	*Mochtherustetraspilotus*	Carabidae
9	*Xylotupes gideon*	Scarabaeidae
10	*Sitophilus oryzae*	Curculionidae
11	*Platyrhopalopsismeleii*	Carabidae
12	*Adoretus* sp.	Scarabaeidae

Table-3: List of beetles recorded from non-residential area

S.No.	Scientific Name	Family
1	*Discladispa armigera*	Chrysomelidae
2	*Aulacophora faveicoles*	Chrysomelidae
3	*Monolepta signata*	Chrysomelidae
4	*Sagrafe morata*	Chrysomelidae
5	*Altica* sp.	Chrysomelidae
6	*Iridotaenia blanchardii*	Bupristidae
7	*Cosmopolites sordidus*	Curculionidae
8	*Rhynchphorus ferrugineus*	Curculionidae
9	*Harmonia axyrids*	Coccinillidae
10	*Cyclonedas anguinea*	Coccinillidae
11	*Xystrocera globosa*	Cerambycidae
12	*Popilliacupricollis*	Scarabaeidae
13	*Copris fricator*	Scarabaeidae
14	*Leucopholis coenophora*	Scarabaeidae
15	*Oryctes rhinoceros*	Scarabaeidae

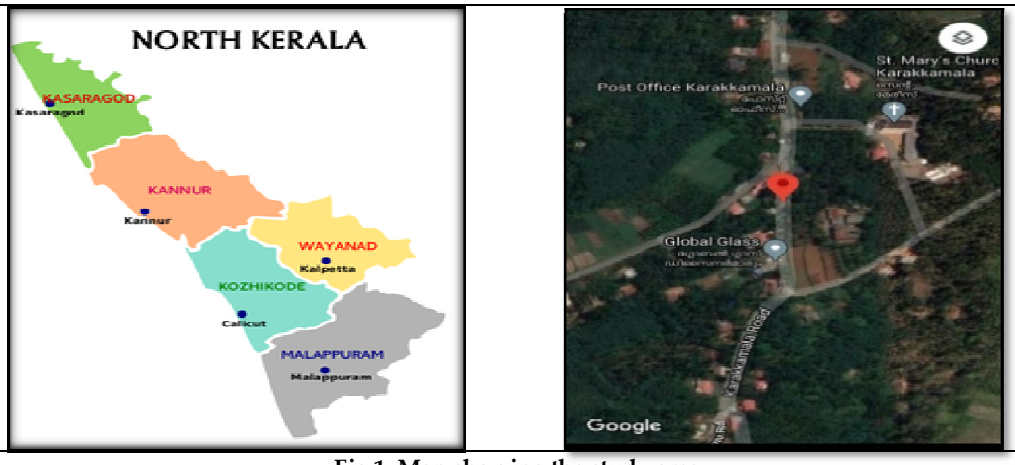

Fig 1: Map showing the study area

Fig 2:Residential Area

Fig 3: Non-Residential Area

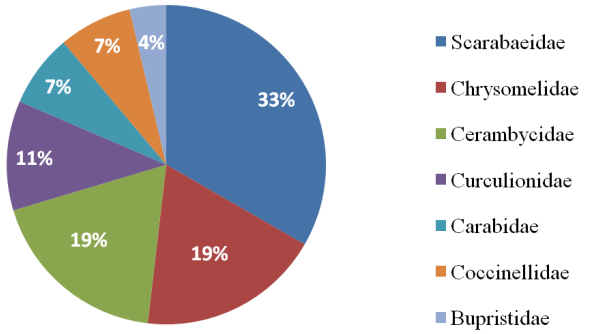

Fig 4: Graphical representation of the Coleoptera family recorded during study

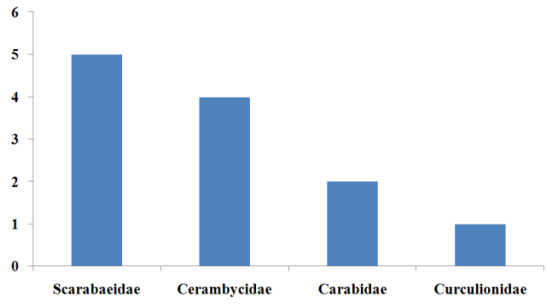

Fig 5: Species composition of insects from the residential area

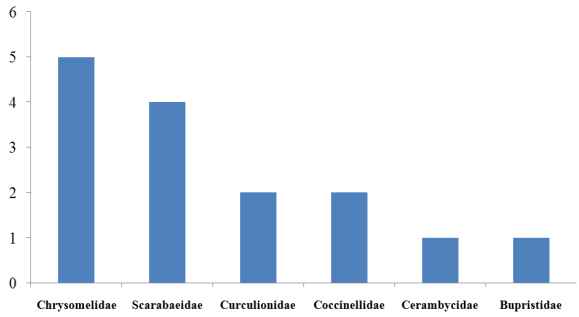

Fig 6: Species composition of insects from non-residential area

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RESEARCH ARTICLE

A New Approach for Solving Hexadecagonal Fuzzy Assignment Problem

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ABSTRACT

An assignment problem is a specific case transportation problem. The optimal assignment problem aims to assign a task (work) to a person to minimizing the total time. The fuzzy problem is changed into a crisp problem by using the Robust ranking technique. In this article, an alternative method is opted for finding the solution of hexadecagonal fuzzy assignment problem. The optimum solution of the hexadecagonal fuzzy assignment problem is derived by using suggested method which is illustrated with example.

Keywords: Alternative method, Hexadecagonal fuzzy number, Robust ranking method, Ones assignment method, etc.,

INTRODUCTION

One of the subclasses of transportation problem is the assignment issue. Assignment problem plays a vital in decision-making problems. The goal of optimum assignment is assigning a jobs to persons depends upon their potency to do the job. In fuzzy assignment problem, the cost(time) are taken as a fuzzy number.

L.A.Zadeh [18] presented the idea of fuzzy in real life situations. Bellmann and Zadeh [4] use the fuzzy definition to solve decision making problems .the solutions of fuzzy linear programming problems are often effective according to H.J.Zimmermann [19]. M.S.Chen [5] solved a fuzzy assignment problem. Amit Kumar and Anila Gupta [1] solved the fuzzy assignment and fuzzy traveling salesman problem with various membership functions. Chi Jen Lin and Ue Pyng Wen [6] solved the fuzzy assignment problem using a labeling algorithm. Kuhn [8] created a new method named the Hungarian method for solving the assignment problems.

R. Jahirhussain and P. Jayaraman [7] ranked the fuzzy numbers using Robust ranking method. T.S.Pavithra and C.Jenita [10] ranked the dodecagonal fuzzy numbers using a new ranking technique. Stephen Dinagar and S. Kamalanathan [13] discussed the fuzzy assignment problem with two different ranking techniques. . A.Nagoor Gani and V.N. Mohamed [9] solved a trapezoidal fuzzy assignment problem. Sunil Kumar Mehta et al [14] approached Taylor's series method for finding the solution to the assignment problem. D.Selvi et al [11] found the solution of the fuzzy assignment problem with the help of the magnitude method. A.Srinivasan and G.Geetharamani [12] used one's assignment method for for solving the fuzzy assignment problem.

Y.L.P.Thorani and N. Ravi Shankar [16] solved fuzzy assignment problems with generalized fuzzy numbers. Supriya Kar et al [15] found the solution to the generalized fuzzy assignment problem in which the cost of jobs and persons are trapezoidal fuzzy numbers. Anchal Choudhary et al [2] applied a branch and bound technique for solving the fuzzy assignment problem. S.Yahya Mohamed and M.Divya [17] solved the fuzzy traveling salesman problem with α - cut and ranking technique.

S. Narayanamoorthy and P. Vidhya [12] applied a branch and bound method for solving the fuzzy assignment problem. S. Dhanasekar et al [7] used an improved Hungarian method for finding the solution of a fuzzy assignment problem. Charles Robert Kenneth et al [4] found a solution of fuzzy assignment for maximizing the profit. Pranab Biswas and Surapati Pramanik [14] applied the multi-objective fuzzy assignment in Military affairs. D. Premalatha and P. Murugan [15] solved the heptagonal fuzzy assignment problem using one assignment method. S.Vimala and S.Krishna Prabha [22] solved the fuzzy assignment problem using ones assignment method. M. Khalid et al [9] approached a new method called the improved ones assignment method for solving the assignment problems.

In this article, we approached a different ranking technique for ranking the hexadecogonal fuzzy number. Fuzzy assignment problems can be transposed into crisp problems by using the ranking technique and an optimal solution is obtained by using one's assignment method.

Preliminaries

Definition 2.1. A membership function mapping element of a domain space or the universe of discourse X to the unit interval [0,1] were characterized by a fuzzy set.

(i.e) $\widetilde{A} = \{x, \mu_{\widetilde{A}}(x) ; x \in X\}$ .Here $\mu_{\widetilde{A}}(x) = 1$

Definition 2.2.A fuzzy set A of the universe of discourse X is called normal fuzzy set implying that there exists at least one $x \in X$ Such that $\mu_{\widetilde{A}}(x) = 1$

Definition 2.3. The support of the fuzzy set in the Universal set X is the set that contains all the elements of X that have anon- zero membership grade $\widetilde{A}$. (i.e) $Supp(\widetilde{A}) = \{x \in X / \mu_{\widetilde{A}}(x) > 0\}$

Definition 2.4. A fuzzy set $\widetilde{A}$ defined on the set of real numbers R is said to be a fuzzy number if its membership function $\mu_{\widetilde{A}}(x): R \to [0,1]$ has the following properties

(i) A must be a normal and convex fuzzy set

(ii) $\alpha_{\widetilde{A}}$ must be a closed interval for every $\alpha \in [0,1]$

(iii) The support $\widetilde{A}$ must be bounded

Definition 2.5. A fuzzy number $\widetilde{A}$ is a triangular fuzzy number which is denoted by $\widetilde{A} = (A_1, A_2, A_3)$ whose membership function is defined by

$$\mu_{\tilde{A}}(x)=\begin{cases}0 & x<A_1\\ \dfrac{x-A_1}{A_2-A_1} & A_1\le x\le A_2\\ \dfrac{A_3-x}{A_3-A_2} & A_2\le x\le A_3\\ 0 & x>A_3\end{cases}$$

Definition 2.6. A fuzzy number $\tilde{A}$ is a trapezoidal fuzzy number which is denoted by $\tilde{A}=(A_1,A_2,A_3,A_4)$ whose membership function is defined by

$$\mu_{\tilde{A}}(x)=\begin{cases}0 & x<A_1\\ \dfrac{x-A_1}{A_2-A_1} & A_1\le x\le A_2\\ 1 & A_2\le x\le A_3\\ \dfrac{A_4-x}{A_4-A_3} & A_3\le x\le A_4\\ 0 & x>A_4\end{cases}$$

Hexadecagonal Fuzzy Number

A fuzzy number $\tilde{A}$ is a Hexadecagonal fuzzy number defined by $\tilde{A}=(A_1,A_2,A_3,A_4,A_5,A_6,A_7,A_8,A_9,A_{10},A_{11},A_{12},A_{13},A_{14},A_{15},A_{16})$ where $A_1,A_2,A_3,A_4,A_5,A_6,A_7,A_8,A_9,A_{10},A_{11},A_{12},A_{13},A_{14},A_{15},A_{16}$ are real numbers and its membership function is given by

$$\mu_{\tilde{A}}(x)=\begin{cases}0 & x<A_1\\ k_1\left(\dfrac{x-A_1}{A_2-A_1}\right) & A_1\le x\le A_2\\ k_1 & A_2\le x\le A_3\\ k_1+(k_2-k_1)\left(\dfrac{x-A_3}{A_4-A_3}\right) & A_3\le x\le A_4\\ k_2 & A_4\le x\le A_5\\ k_2+(k_3-k_2)\left(\dfrac{x-A_5}{A_6-A_5}\right) & A_5\le x\le A_6\\ k_3 & A_6\le x\le A_7\\ k_3+(1-k_3)\left(\dfrac{x-A_7}{A_8-A_7}\right) & A_7\le x\le A_8\\ 1 & A_8\le x\le A_9\\ k_3+(1-k_3)\left(\dfrac{A_{10}-x}{A_{10}-A_9}\right) & A_9\le x\le A_{10}\\ k_3 & A_{10}\le x\le A_{11}\\ k_2+(k_3-k_2)\left(\dfrac{A_{12}-x}{A_{12}-A_{11}}\right) & A_{11}\le x\le A_{12}\\ k_2 & A_{12}\le x\le A_{13}\\ k_1+(k_2-k_1)\left(\dfrac{A_{14}-x}{A_{14}-A_{13}}\right) & A_{13}\le x\le A_{14}\\ k_1 & A_{14}\le x\le A_{15}\\ k_1\left(\dfrac{A_{16}-x}{A_{16}-A_{15}}\right) & A_{15}\le x\le A_{16}\\ 0 & A_{16}<x\end{cases}$$

where $0 < k_1 < k_2 < k_3 < 1$

Operations of Hexadecagonal Fuzzy number

The Arithmetic operations of Hexadecagonal Fuzzy numbers are presented here .

Let $\tilde{A}_{HXDFN} = (A_1, A_2, A_3, A_4, A_5, A_6, A_7, A_8, A_9, A_{10}, A_{11}, A_{12}, A_{13}, A_{14}, A_{15}, A_{16})$ &

$\tilde{B}_{HXDFN} = (B_1, B_2, B_3, B_4, B_5, B_6, B_7, B_8, B_9, B_{10}, B_{11}, B_{12}, B_{13}, B_{14}, B_{15}, B_{16})$

be two the hexadecogonal fuzzy numbers. The addition, subtraction, and scalar multiplication of hexadecagonal fuzzy numbers can be defined as follows

$$\tilde{A}_{HXDFN} + \tilde{B}_{HXDFN} = \begin{bmatrix} A_1 + B_1, A_2 + B_2, A_3 + B_3, A_4 + B_4, A_5 + B_5, A_6 + B_6, A_7 + B_7, A_8 + B_8, A_9 + B_9, \\ A_{10} + B_{10}, A_{11} + B_{11}, A_{12} + B_{12}, A_{13} + B_{13}, A_{14} + B_{14}, A_{15} + B_{15}, A_{16} + B_{16} \end{bmatrix}$$

$$\tilde{A}_{HXDFN} - \tilde{B}_{HXDFN} = \begin{bmatrix} A_1 - B_{16}, A_2 - B_{15}, A_3 - B_{14}, A_4 - B_{13}, A_5 - B_{12}, A_6 - B_{11}, A_7 - B_{10}, A_8 - B_9, \\ A_9 - B_8, A_{10} - B_7, A_{11} - B_6, A_{12} - B_5, A_{13} - B_4, A_{14} - B_3, A_{15} - B_2, A_{16} - B_1 \end{bmatrix}$$

$$\alpha\tilde{A}_{HXDFN} = [\alpha A_1, \alpha A_2, \alpha A_3, \alpha A_4, \alpha A_5, \alpha A_6, \alpha A_7, \alpha A_8, \alpha A_9, \alpha A_{10}, \alpha A_{11}, \alpha A_{12}, \alpha A_{13}, \alpha A_{14}, \alpha A_{15}, \alpha A_{16}]$$

$$\alpha\tilde{B}_{HXDFN} = [\alpha B_1, \alpha B_2, \alpha B_3, \alpha B_4, \alpha B_5, \alpha B_6, \alpha B_7, \alpha B_8, \alpha B_9, \alpha B_{10}, \alpha B_{11}, \alpha B_{12}, \alpha B_{13}, \alpha B_{14}, \alpha B_{15}, \alpha B_{16}]$$

Robust Ranking Method

The robust ranking technique for Hexadecagonal fuzzy numbers is defined as follows. If $\tilde{A}$ is a fuzzy number then the Robust Ranking is defined by $Y(\tilde{A}) = \int_0^1 (0.5)(a^L, a^U) d\alpha$ where

$$(a^L, a^U) = \begin{bmatrix} (b-c)\alpha + a,\ d - (d-c)\alpha, (f-e)\alpha + e, h - (h-g)\alpha, (j-i)\alpha + i, l - (l-k)\alpha, \\ (n-m)\alpha + m, p - (p-o)\alpha \end{bmatrix}$$

(4.1)

Mathematical Formulation of Fuzzy Assignment Problem

The fuzzy assignment problem can be stated in the following matrix form

Persons	**Jobs**			
	1	**2**	**----**	**N**
1	$\tilde{t}_{11}$	$\tilde{t}_{12}$		$\tilde{t}_{1n}$
2	$\tilde{t}_{21}$	$\tilde{t}_{22}$		$\tilde{t}_{2n}$
---	**---**	**---**	**--**	**---**
N	$\tilde{t}_{1N}$	$\tilde{t}_{2N}$		$\tilde{t}_{NN}$

Mathematical formulation of the fuzzy assignment problem is given by

$$\text{min}imize\ \tilde{Z}^{**} = \sum_{i=1}^{N}\sum_{j=1}^{N} \tilde{t}_{ij}\tilde{y}_{ij}$$

Subject to the constraints

$$\sum_{i=1}^{N} \tilde{y}_{ij} = 1,\ i = 1,2,...N \qquad \&$$

$$\sum_{j=1}^{N} \tilde{y}_{ij} = 1,\ j = 1,2,...N$$

where $\tilde{x}_{ij}$ is the decision variable and $\tilde{t}_{ij}$ is the fuzzy time of j[th] job to i[th] person. By using ranking technique (4.1), first we defuzzify the fuzzy value into crisp value for solving the problem.

One Assignment Method

The working rule for one assignment method is given below

Rule 1: Select the minimum or maximum element (in the case of minimization or maximization) of every row in the time matrix (say a_i) and put it on the right of the matrix

	1	2	3		n	
1	t_{11}	t_{12}	t_{13}	...	t_{1n}	a_1
2	t_{21}	t_{22}	t_{23}	...	t_{2n}	a_2
3	t_{31}	t_{32}	t_{33}	...	t_{3n}	a_3
	...	...	...	...	...	...
n	t_{n1}	t_{n2}	t_{n3}	...	t_{nn}	a_n

After finding an element (minimum or maximum), divide every element of i[th] row of the matrix by a_i. This operation produce at least one ones in every row. If every row and column having ones then do the assignment, otherwise, go to rule 2.

	1	2	3		n	
1	t_{11}/a_1	t_{12}/a_1	t_{13}/a_1	...	t_{1n}/a_1	a_1
2	t_{21}/a_2	t_{22}/a_2	t_{23}/a_2	...	t_{2n}/a_2	a_2
3	t_{31}/a_3	t_{32}/a_3	t_{33}/a_3	...	t_{3n}/a_3	a_3
	...	...	...	...	...	...
n	t_{n1}/a_n	t_{n2}/a_n	t_{n3}/a_n	...	t_{nn}/a_n	a_n
	b_1	b_2	b_3		b_n	

Rule 2: Select the smallest value in every column in the reduced matrix (say b_j), and write it below the matrix in every column. Divide every element of j[th] column of the time matrix by b_j. After dividing an element in each column, we get at least one in every column. Make an assignment in terms of ones. If an optimal assignment doesnot occurs by using the steps (1) and (2) then go to step 3.

	1	2	3		n
1	t_{11}/a_1b_1	t_{12}/a_1b_2	t_{13}/a_1b_3	...	t_{1n}/a_1b_n
2	t_{21}/a_2b_1	t_{22}/a_2b_2	t_{23}/a_2b_3	...	t_{2n}/a_2b_n
3	t_{31}/a_3b_1	t_{32}/a_3b_2	t_{33}/a_3b_3	...	t_{3n}/a_3b_n
	...	...	...	...	...
n	t_{n1}/a_nb_1	t_{n2}/a_nb_2	t_{n3}/a_nb_3	...	t_{nn}/a_nb_n

Rule 3: Draw a minimum lines that cover all the ones in the reduced matrix. Choose the smallest element (say $\widetilde{d}_{ij}$) which is not covered by any of the lines. Divide all the uncovered elements by $\widetilde{d}_{ij}$. Now some new ones will appear in rows and column . Now do the optimal task .

Rule 4: If this new matrix also does not yield a complete optimum assignment, repeat steps 3 and 4 iteratively. A better assignment can be achieved by repeating the same process.

Example

Consider the following Hexadecagonal fuzzy assignment problem which consists of four jobs and four machines. In the time matrix, $\widetilde{t}_{ij}$ those times are hexadecagonal fuzzy times. The aim is to assign a job to person with minimum time.

Table I: Hexadecagonal Fuzzy Assignment Problem

	W_1	W_2	W_3	W_4
J_1	(1,2,3,4,5,6,7,8,9,10,11,12,13,14, 15,16)	(0,1,2,3,4,5,6,7,8,9, 10,11,12,13,14,15)	(1,3,5,7,9,11,13,15,17,19,21,23,25,27, 29,31)	(1,3,4,5,7,9,10,12,14, 15,16,18,20, 21, 22 ,24)
J_2	(2,4,6,8,10,12,14,16,18,20,22,24,26,28, 30,32)	(2,3,5,7,9,11,13,17, 19,23,29,31,35,37, 41,43)	(1,4,7,10,13,16,19,22 ,25,28,31,34,37, 40,43, 46)	(0,4,6,9,11,12,13,14, 15,16,19,21, 23, 25, 27,29)
J_3	(1,2,3,4,7,10,13,15 ,16,17,22,26,30,34, 35,36)	(2,4,6,8,9,13,15,16, 18,20,21,25,27,28, 30,31)	(1,2,3,4,5,7,9,11,13,17,21,25,27,31,32, 34)	(2,4,8,9,11,13,16,19, 20,22,24,25, 27, 29, 30,31)
J_4	(1,2,3,4,8,9,10,12, 13,15,17,18,20,22, 23, 24)	(0,2,3,5,6,7,9,10,13, 15,16,18,21,24,29, 34)	(3,4,7,10,11,13,15,16 ,18,21,24,28,30,34,36 ,44)	(1,2,4,5,7,8,10,11,13, 14,16,17,19, 20, 22,23)

The hexadecagonal fuzzy assignment problem can be put into mathematical format is

Minimize $\widetilde{Z}^{**} = \Re$ (1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16) $y_{11} + \Re$ (0,1,2,3,4,5,6,7,8,9,10,11,12,13, 14,15) $y_{12} + \Re$ (1,3,5,7,9,11,13,15,17,19,21,23,25,27,29,31) $y_{13} + \Re$ (1,3,4,5,7,9,10,12,14,15,16,18,20, 21,22,24) $y_{14} + \Re$ (2,4,6,8,10,12,14,16,18,20,22,24,26,28,30,32) y_{21} $+ \Re$ (2,3,5,7,9,11,13,17,19,23,29,31,35,37,41,43) $y_{22} + \Re$ (1,4,7,10,13,16,19,22,25,28,31,34,37,40, 43,46) $y_{23} + \Re$ (0,4,6,9,11,12,13,14,15,16,19,21,23,25,27,29) $y_{24} + \Re$

(1,2,3,4,7,10,13,15,16,17,22,26,30, 34,35,36) y_{31} + ℜ (2,4,6,8,9,13,15,16,18,20,21,25,27,28,30,31) y_{32} + ℜ (1,2,3,4,5,7,9,11,13,17,21,25, 27,31,32,34) y_{33} + ℜ (2,4,8,9,11,13,16,19,20,22,24,25,27,29,30,31) y_{34} + ℜ (1,2,3,4,8,9,10,12,13, 15,17,18,20,22,23,24) y_{41} + ℜ (0,2,3,5,6,7,9,10,13,15,16,18,21,24,29,34) y_{42} + ℜ (3,4,7,10,11,13,15,16,18,21,24,28,30,34,36,44) y_{43} + ℜ (1,2,4,5,7,8,10,11,13,14,16,17,19,20,22,23) y_{44}

Subject to the conditions

$$\sum_{i=1}^{4} \tilde{y}_{ij} = 1 \text{ and}$$

$$\sum_{j=1}^{4} \tilde{y}_{ij} = 1$$

Ranking of Hexadecagonal Fuzzy Number

To find the optimum value of the given Hexadecagonal fuzzy time given in table I, first, we convert the fuzzy values into the crisp values using the proposed ranking method (4.1) as shown in table II.

Crisp Assignment Problem of the Corresponding Hexadecagonal Fuzzy Assignment Problem

The crisp assignment problem of the corresponding Hexadecagonal fuzzy transportation problem is given in table 3.

Table II: Crisp assignment problem of the corresponding Hexadecagonal fuzzy assignment problem

	W_1	W_2	W_3	W_4
J_1	34	30.5	59	50.25
J_2	68	81.25	94	61
J_3	67.75	68.25	60.5	72.5
J_4	50.25	58	78.5	48

The given is balanced problem. By applying the proposed technique, we find the optimal assignment schedule and the optimum assignment time. The optimal assignment schedule is given by

$J_1 \to W_2$, $J_2 \to W_4$, $J_3 \to W_3$, $J_4 \to W_1$

Using (5.2) the optimal time is

$\tilde{t}_{12} + \tilde{t}_{24} + \tilde{t}_{33} + \tilde{t}_{41}$ = ℜ (0,1,2,3,4,5,6,7,8,9,10,11,12,13,14,15) y_{12} + ℜ (0,4,6,9,11,12, 13,14, 15,16,19,21,23,25,27,29) y_{24} + ℜ (1,2,3,4,5,7,9,11,13,17,21,25,27,31,32, 34) y_{33} + ℜ (1,2,3,4,8,9,10,12,13,15,17,18,20,22,23, 24) y_{41} = 30.5+ 61 +60.5+50.25 = 202.25 units.

The optimal assignment time =30.5+ 61 +60.5+50.25 = 202.25 units.

CONCLUSION

In decision-making challenges, the ranking of fuzzy numbers is important. In this study, we approached a different ranking technique for ranking the hexadecogonal fuzzy number. With the aid of the ranking method, the hexadecagonal fuzzy assignment problem can be transposed into a crisp assignment problem, and an optimal solution can be found by using one's assignment method, which is shown by an example.

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REVIEW ARTICLE

A Review: Epidemic Diseases

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ABSTRACT

The world has built up an expansion worldwide wellbeing framework as a defense against known and obscure irresistible sickness dangers. The framework comprises of different formal and casual organizations of associations that serve various partners; have changing objectives, modalities, assets, and responsibility; work at various provincial levels and cut across people in general, private-for-benefit, and private-not-revenue driven areas. The advancing worldwide wellbeing framework has done a lot to ensure and advance human wellbeing. Nonetheless, the world keeps on being stood up to by longstanding, arising, and reappearing irresistible infection dangers. These dangers contrast generally regarding seriousness and likelihood. They likewise have differing ramifications for dreariness and mortality, just as for an unpredictable arrangement of social and financial results. To different degrees, they are additionally manageable to elective reactions, going from clean water arrangement to guideline to biomedical counter measures. Regardless of whether the worldwide wellbeing framework as right now established can give powerful assurance against a unique exhibit of irresistible illness dangers has been raised doubt about by late flare-ups of Ebola, Middle East respiratory disorder, SARS, and flu and by the approaching danger of rising antimicrobial obstruction. The worry is amplified by quick populace development in regions with powerless wellbeing frameworks, urbanization, globalization, environmental change, common clash, and the changing idea of microbe transmission among human and creature populaces. This Council would fortify the worldwide wellbeing framework by improving cooperation and coordination across associations filling in information holes concerning (for instance) irresistible sickness reconnaissance, innovative work needs, financing models, production network co-ordinations, and the social and monetary effects of possible dangers; and making significant level, proof based proposals for overseeing worldwide dangers related with irresistible illness.

Keywords: worldwide wellbeing, worldwide wellbeing frameworks, irresistible sickness, symptoms, measure, WHO advices and reaction.

INTRODUCTION

An epidemic is the quick spread of irresistible disease to countless individuals in a given populace inside a brief timeframe. As per current ideas, an epidemic is characterized as the event locally or district of instances of an ailment or other wellbeing related occasions plainly in abundance of ordinary hope. The people group or locale, and the time span in which the cases happen are determined definitely. An epidemic disease isn't needed to be contagious, and the term has been applied to West Nile fever and the obesity epidemic (e.g. by the World Health Organization), among others. Consequently, epidemics allude to the "unordinary" event locally or area of disease, explicit wellbeing related conduct (e.g., smoking) or other wellbeing related occasions (e.g., car crashes) plainly in overabundance of "anticipated event". The quantity of cases differs as indicated by the disease-causing specialist, what's more, the size and sort of past and existing openness to the specialist [1,2].

Epidemics of infectious disease are generally caused by several factors including

Change in the biology of the host populace (for example expanded pressure or expansion in the thickness of vector animal groups)

1. Genetic change in the microorganism supply or the presentation of an arising microorganism to a host populace (by the development of microbe or have).
2. Generally, an epidemic happens when has insusceptibility to one or the other an set up microorganism or recently arising novel microbe is abruptly diminished beneath that found in the endemic balance and the transmission edge is surpassed.
3. The conditions which administer the episode of epidemics additionally incorporate tainted food supplies, for example, sullied drinking water and the movement of populaces of specific creatures, like rodents or mosquitoes, which can go about as disease vectors.
4. Certain epidemics happen at specific seasons. For instance, challenging hack happens in spring, while measles produces two epidemics, one in winter and one in March. Flu, the regular cold, and other diseases of the upper respiratory plot, like sore throat, happen transcendently in the colder time of year.
5. Disease flare-ups are generally brought about by a contamination, sent through individual to-individual contact, creature to-individual contact, or from the climate or other media.
6. Outbreaks may likewise happen following openness to synthetics or to radioactive materials. For instance, Minamata disease is brought about by openness to mercury.
7. Epidemics might be the outcome of debacles of another sort, for example, typhoons, floods, seismic tremors, dry spells, and so forth
8. Occasionally the reason for an episode is obscure, even after intensive examination.

TYPES OF EPIDEMIC DISEASES[3]

COMMON-SOURCE EPIDEMICS

Normal source epidemics are habitually, yet not generally, due to openness to an irresistible agent. They can result from tainting of the climate (air, water, food, soil) by modern synthetics or pollutant. E.g.,Bhopal gas misfortune in India and Minamata disease in Japan coming about because of utilization of fish containing a high centralization of methyl mercury.

Single Exposure Or "Point-Source" Epidemics

These are otherwise called "point-source" epidemics. The openness to the disease specialist is brief and basically synchronous, the resultant cases all create inside one brooding time of the disease. E.g., an epidemic of food harming. The principle highlights of a "point-source" epidemic are:

1. The epidemic bend rises and falls quickly, with no optional waves
2. The epidemic will in general be hazardous, there is a grouping of cases inside a restricted time period, and
3. More critically, every one of the cases creates inside one brooding time of the disease.

Continuous or Multiple Exposure Epidemics

On the off chance that the epidemic proceeds over more than one hatching period, there are either a constant or numerous openings to a typical source or a proliferated spread. Sometimes the openness from a similar source might be delayed – consistent, rehashed or irregular – not really simultaneously or place. For model, a whore might be a typical source in a gonorrhea flare-up, however since she will taint her customers throughout some undefined time frame there might be no unstable ascent in the quantity of cases. A well of tainted water, or a broadly disseminated brand of antibody (for example polio immunization), or food, could result in comparative outbreaks. In these occurrences, the subsequent epidemics will in general be more broadened or irregular. The flare-up of respiratory ailment, the Legionnaire's disease, in the mid year of 1976 in Philadelphia (USA) was a typical source, ceaseless or rehashed openness outbreak. This flare-up, as in other outbreaks of this sort, proceeded past the scope of one hatching period. There was no proof of who had contact with sick people and auxiliary cases among people.

PROPAGATED EPIDEMICS [5]

An engendered epidemic is regularly of irresistible cause and results from individual to-individual transmission of an irresistible specialist (e.g., epidemics of hepatitis A and polio). The epidemic as a rule shows a progressive ascent and tails off over an any longer time of time. Transmission proceeds until the quantity of susceptibles is exhausted or defenceless people are not, at this point presented to tainted people or delegate vectors. The speed of spread relies on group resistance, openings for contact and optional assault rate. Propagated epidemics are bound to happen where countless powerless are totalled, or where there is an ordinary inventory of new helpless people (e.g., birth, migrants) bringing down crowd invulnerability.

MIXED EPIDEMICS [6]

Few epidemics have highlights of both basic source epidemics and proliferated epidemics. The example of a typical source flare-up followed by auxiliary individual to-individual spread isn't uncommon. These are called mixed epidemics.

YELLOW FEVER-MALI

Yellow fever is an acute viral haemorrhagic disease, which is transmitted from the infected mosquitoes. The "yellow" is a name refers to the jaundice that affects by the some patients. Large epidemics of that the yellow fever take place when infected people bring out that the virus into the heavily occupy areas with a highly mosquito density, where most of the people have no immunity, due to the lack of vaccination. In these conditions, infected mosquitoes of *Aedesae gypti* species transmit the virus from person to person.

Yellow fever is a genuine, possibly dangerous influenza like sickness spread by mosquitoes. It's described by a high fever and jaundice. Jaundice is the yellowing of the skin and eyes, which is the reason this sickness is called yellow fever. This infection is generally pervasive in specific pieces of Africa and South America. It isn't treatable; however you can forestall it with the yellow fever immunization. The WHO Trusted Source appraises that 50% of individuals who create serious side effects of this condition will pass on. More seasoned grown-ups and those with traded off invulnerable frameworks are most in danger for genuine difficulties. From 3 November through 8 December 2019, three research centres affirmed instances of yellow fever including two passings (case casualty rate = 67%) were distinguished through the public observation framework in Mali. The principal case-patient was a 15-year-old young lady from a town in Kati region, Koulikoro locale, Mali. The second and third cases were in 17 and 25-year-elderly people men, nationals from Cote d'Ivoire, living in the locale of Bouguimi, Sikasso district, Mali. Each of the three cases tried positive for yellow fever by Immunoglobulin M (IgM) and reverse transcriptase polymerase chain response (RT-PCR) on 3 December 2019 at Institute Pasteur Dakar (IPD). The main argument was not immunized

against yellow fever and had no movement history outside of Kati District. In the mean time, the immunization status for the other two cases was obscure. Furthermore, there were nine suspected and three plausible cases detailed from the Bouguimi region, including three passings among the likely causes. The age of the suspected, plausible and affirmed cases ranges between 1 to 33 years, and the male to female proportion is 2:1. Among the revealed manifestations, fever, jaundice, and retching were the most well-known. Eight wellbeing territories of Bouguimi wellbeing area have been influenced, with Manankoro (four cases) and Mafelé (three cases) revealing the most elevated number. One presumed cause is forthcoming affirmation at the Institute Pasteur Dakar lab. On 5 December 2019, the Government of Mali authoritatively proclaimed a yellow fever flare-up in two locales of Sikasso and Koulikoro

CLASSIFICATION [9]

The clinical picture can be named gentle, moderate, serious or threatening. In gentle and moderate structures, the manifestations and research centre changes are less exceptional, with gentle thrombocytopenia and moderate expansion in transaminases. In this structure, there is typically no expansion in bilirubin. Serious sickness, then again, prompts exceptional thrombocytopenia and expanded transaminases, notwithstanding expanded creatinine. Dangerous yellow fever is that wherein spread intravascular coagulation is seen with fibrinogen utilization and gathering of D-dimer, notwithstanding the past changes.

DIAGNOSIS [9]

Clinically, it is hard to separate it from other viral infections in the underlying stage, and yellow fever ought to be considered on the whole cases with viable clinical appearances, regardless of whether gentle, and positive the study of disease transmission (having visited a danger zone inside 15 days preceding the beginning of side effects without being recently inoculated, or having been immunized inside under 30 days. Affirmation of the determination is made utilizing a technique for sub-atomic enhancement of the infection in the blood (highly delicate and explicit strategy, which may even permit to separate the sylvatic infection from the antibody strain), which exemplary happens up to fifth day of sickness. In the event of death, the determination can be affirmed in a few tissues in up to 24 hours; or by immune histo-chemistry.

SYMPTOMS

Yellow fever grows rapidly, with side effects happening three to six days after openness. The underlying manifestations of the contamination are like those of the flu infection. They include:

- Headaches
- Muscle throbs
- Joint throbs
- Chills
- Fever

INTENSE PHASE

This stage as a rule goes on for three to four days. Regular indications include:

- Headaches
- Muscle throbs
- Joint throbs
- A fever
- Flushing
- A loss of craving
- Shivers
- Backaches

After the intense stage is finished, indications will start to disappear. Numerous individuals recuperate from yellow fever at this stage, yet a few groups will build up a more genuine variant of this condition.

POISONOUS PHASE

The side effects that you encountered in the intense stage may vanish for as long as 24 hours. At that point, those manifestations will return, alongside new and more genuine indications. These incorporate

- Decreased pee
- Abdominal torment
- Vomiting (at times with blood)
- Heart musicality issues
- Seizures
- Delirium
- Bleeding from the nose, mouth, and eyes

This period of the infection is frequently lethal, yet just 15% of trused wellspring of individuals with yellow fever enters this stage.

CAUSES [10]

Yellow fever is brought about by yellow fever infection, an encompassed RNA infection 40–50 nm in width, the sort species and namesake of the family Flaviviridae. It was the principal sickness demonstrated to be contagious by separated human serum and sent by mosquitoes, by American specialist Walter Reed around 1900. The positive-sense, single-abandoned RNA is around 11,000 nucleotides in length and has a solitary open perusing outline encoding a polyprotein.

TRANSMISSION [11,12]

Yellow fever infection is basically sent through the chomp of the yellow fever mosquito Aedesaegypti, however other generally Aedes mosquitoes like the tiger mosquito (Aedesalbopictus) can likewise fill in as a vector for this infection. Like other arboviruses, which are communicated by mosquitoes, yellow fever infection is taken up by a female mosquito when it ingests the blood of a tainted human or another primate. Infections arrive at the stomach of the mosquito, and if the infection fixation is sufficiently high, the virions can taint epithelial cells and duplicate there. From that point, they arrive at the haemocoel (the blood arrangement of mosquitoes) and from that point the salivary organs. At the point when the mosquito next sucks blood, it infuses its spit into the injury, and the infection arrives at the circulatory system of the chomped individual.

Transovarial and transstadial transmission of yellow fever infection inside A. aegypti, that is, the transmission from a female mosquito to her eggs and afterward hatchlings, are shown. This contamination of vectors without a past blood supper appears to assume a part in single, abrupt breakouts of the infection.

TREATMENT [13]

There's no solution for yellow fever. Treatment includes overseeing manifestations and helping your invulnerable framework in fending off the contamination by

- Getting enough liquids, perhaps through your veins
- Getting oxygen
- Maintaining a solid circulatory strain
- Getting blood bondings
- Having dialysis on the off chance that you experience kidney disappointment
- Getting treatment for different diseases that may create

Immunization is the best way to forestall yellow fever. The antibody for yellow fever is offered as a solitary chance. It contains a live, debilitated variant of the infection that assists your body with making invulnerability. The Centers for Disease Control (CDC) recommends that any individual who is 9 months through 59 years of age and heading out to or living in a territory where the danger of yellow fever is available ought to be immunized.

Gatherings of individuals who shouldn't get the antibody incorporate

- People who have extreme sensitivities to eggs, chicken proteins, or gelatin
- Infants more youthful than a half year old
- People who have HIV, AIDS, or different conditions that bargain the Immune framework.

The antibody is viewed as incredibly protected. A solitary portion secures for in any event 10 years. The results may incorporate

- A gentle migraine
- Muscle torment
- Fatigue
- A second rate fever .

DRUG [14]

Since there is no remedy for the viral contamination itself, clinical treatment of yellow fever centresaround facilitating indications like fever, muscle torment, and parchedness. In view of the danger of inside dying, maintain a strategic distance from ibuprofen and other non-steroidal mitigating drugs on the off chance that you presume you have yellow fever. Hospitalization is frequently required.

ADVERSE REACTION [15]

The yellow fever immunization is for the most part thought to be one of the most secure. More than 400 million individuals have been immunized, with generally excellent outcomes as far as security and resistance. The reactogenicity of the antibody was observed in 10 clinical preliminaries somewhere in the range of 1953 and 1994. Gentle, self-restricted responses, like torment and blushing at the infusion site, and foundational responses, like fever, migraine, myalgia, and disquietude, seem five to seven days after immunization in a minority of those inoculated.

Genuine antagonistic responses purportedly brought about by the yellow fever immunization are uncommon. Instances of post-vaccinal encephalitis (neurotropic infection) from infection 17D have been portrayed in newborn children matured under 4 months (pace of 500–4,000 for each million dosages managed). The antibody is contraindications for newborn children matured under a half year, in this way setting up a more noteworthy edge of wellbeing. Lately, also, a few instances of genuine unfavorable responses connected with the antibody have been accounted for in clearly solid individuals who got the immunization in the United States (nine cases), Brazil (four cases), and Australia, Colombia, France, the United Kingdom,2 and Switzerland (one case each).

CONTRAINDICATIONS [16]

The yellow fever immunization ought not be directed to people in the accompanying gatherings Individuals with intense febrile illnesses, whose overall wellbeing status is undermined; Individuals with a background marked by extreme touchiness to chicken eggs and their subordinates . Pregnant ladies, besides in an epidemiological crisis and at the express suggestion of wellbeing specialists; People with illness related (for instance, malignancy, leukemia, AIDS, and so forth) or medication related immune suppression ;Infants matured under a half year (counsel the antibody's lab insert);People of all ages with a sickness including the thymus.

PRECUATIONARY MEASURES [17]

The yellow fever immunization can be directed to HIV patients, however just the individuals who are asymptomatic and have not yet evolved AIDS, or as the doctor decides. Hypothetically, organization of the yellow fever immunization to pregnant ladies isn't suggested; in any case, there is no verification that it causes fetal peculiarities. In choosing whether or not to inoculate, the epidemiological danger ought to be weighed against the danger of pregnant ladies getting the illness. It is suggested that the epidemiological danger of getting the illness versus the danger of an antagonistic occasion be assessed separately for explorers to enzootic zones who are over age 60

YELLOW FEVER VACCINATION [18]

Yellow fever immunization is a live, weakened infection readiness produced using the 17D yellow fever infection strain. Truly, the 17D immunization has been viewed as one of the most secure and best live infection antibodies at any point created. The infection is filled in chick incipient organisms vaccinated with a seed infection of a fixed section level. The 17D yellow fever antibody infection family is the establishment for both the 17D-204 genealogy and 17DD heredity. Antibody type 17D204 is utilized in both the United States and Australia, while immunization type 17DD is utilized in Brazil.

The two immunization types share 99.9% succession homology.

The 1YF-VAX® (fabricated by Aventis, Swift water, Pennsylvania) immunization is a freeze-dried supernatant of centrifuged incipient organism homogenate, bundled in 1-portion and 5-portion vials for homegrown use. The immunization ought to be put away at temperatures of 2ºC–8ºC (35ºF–46ºF) until it is reconstituted by the expansion of diluent (clean, physiologic saline) provided by the maker. Multidose vials of reconstituted antibody ought to be held at 2ºC–8ºC (35ºF–46ºF); unused immunization ought to be disposed of inside 1 hour after reconstitution.

STEPS TAKEN [18]

Setting up an Emergency Operations Center (EOC) for general wellbeing coordination of the flare-up in the areas of Sikasso, Koulikoro, and the influenced locale. Additionally, EOC has been initiated in Bamako city. A multidisciplinary quick reaction group was sent to direct examinations in the influenced regions of the Sikasso and Koulikoro areas. An arrangement to direct a top to bottom entomological review is in progress. Improved epidemiological reconnaissance, incorporating dynamic case finding in both the influenced areas, has been fortified. An extensive reaction plan is being created with the particular goals including groundwork for an International Coordination Group (ICG) solicitation to lead a yellow fever receptive mass immunization crusade.

Arrangement of hazard correspondence limits through the association of important partners. Public correspondence and mindfulness endeavors on yellow fever (signs, side effects, and inoculations) including anticipation measures. On 3 December 2019, a joint examination group (WHO Country Office and Ministry of Health) was conveyed to portray the danger and build up an intercession plan. Field examinations demonstrate immunization inclusion under 80% in Kati and 88% in Manakorodistricts.

STEPS TAKEN BY WHO [19,20]

In 2016, two connected metropolitan yellow fever episodes – in Luanda (Angola) and Kinshasa (Democratic Republic of the Congo), with more extensive worldwide exportation from Angola to different nations, including China – have shown that yellow fever represents a genuine worldwide danger requiring new essential reasoning. The Eliminate Yellow Fever Epidemics (EYE) Strategy was created to react to the expanded danger of yellow fever metropolitan flare-ups with worldwide spread. Controlled by WHO, UNICEF, and Gavi, the Vaccine Alliance, EYE upholds 40 nations and includes in excess of 50 accomplices.

The worldwide EYE Strategy is guided by three key targets: secure in danger populaces, forestall global spread of yellow fever, contain flare-ups quickly. These targets are supported by five skills of progress: 1. moderate antibodies and supported immunization market; 2. solid political responsibility at worldwide, provincial and nation levels; 3.

significant level administration with long haul organizations; 4. collaborations with other wellbeing projects and areas; and 5. innovative work for better instruments and practices. The EYE system is thorough, multi-segment and multi-accomplice. As well as suggesting inoculation exercises, it calls for building versatile metropolitan places, anticipating metropolitan availability, and fortifying the utilization of the International Health Regulations (2005). The EYE organization upholds yellow fever high and moderate danger nations in Africa and the Americas by fortifying their observation and lab ability to react to yellow fever cases and episodes. EYE accomplices additionally support the execution and manageability of routine inoculation projects and immunization.

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Table-1: Abbreviation

SI. NO	ABBREVIATION	FULL FORM
1	WHO	World Health Organization
2	CDC	Centre For Disease Control
3	HIV	Human Immunodeficiency Virus
4	AIDS	Acquired Immunodeficiency Syndrome
5	ICG	International Co-ordination Group
6	EOC	Emergency Operations Centre
7	YF	Yellow Fever
8	YF-VAX	Yellow Fever Vaccine

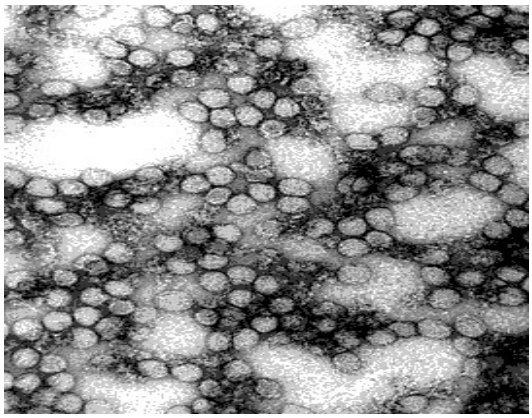

Fig. 1: Microscopic view of YF virus

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RESEARCH ARTICLE

Antimicrobial Activity of *Geastrum rubellum* - a Wild Edibale Mushroom Collected from Satakosia Reserve Forest, Mayurbhanj, Odisha, India

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ABSTRACT

In this present study, a wild edible mushroom *Geasstrum rubellum* was studied for its antimicrobial activity against some clinicals pathogens. Bacterial pathogen like; *Pseudomonas aeruginosa, Proteus vulgaris, Bacillus subtilis, Staphylococcus aureus, Shigellaflexneri, Klebsiella pneumonia* and fungal pathogens such as *Candida krusie, Candida albicans, Trichophyton mentagrophytes* were used. Culture filtrate the mushrooms species was tested against all the pathogens by the agar cup well method. On screening, it found that, bacterial pathogens *Shigella flexneri* and *Staphylococcus aureus* showed highest activity than *Bacillus subtilis* and *Klebsiella pneumonie*. At the same time, attractive antifungal activity was determined in *Candida albicans* and *Trichophyton mentagrophytes.* Growth rate was also studied for the species in two (PDA and MEA) media and better result found in MEA. Optimal metabolites production, was tested by the media effect of media (PDB and MEB) and incubation period (8days, 16days and 24days) and satisfactory activity in PDB incubated for 16 days against *Shigella flexneri*.

Keywords: Antimicrobial activity, bioactive compound, pathogens, metabolites, wild edible mushrooms.

INTRODUCTION

Mushroom is a general word mostly used for the fruiting body of the macro fungi belonging to basidiomycetes. It may be fleshy or hard body and can be epigeous and hypogeous [1]. Mushrooms are beautiful organisms mediates significant role in ecosystem function, and influence on human and human related activities of the daily life of us besides their utilization in industries, agriculture and medicines [2-4]. This community is one of the most diverse

group, approximately 75,000 described species but this very less number from actual number. Club fungi are the most advanced group contain about 30,000 known species [5]. Taxonomically, estimated about 140,000 species known as mushrooms forming fungi out of which only 10% in known [6].Mushrooms rich in several useful bioactive compounds and amino acids, vitamins B1, B2, C and D and minerals such as Zn, Na, Fe, Mg, P and low fat [7]. Some mushrooms are domesticated for commercial purposes; whereas, many mushrooms still grow wild in the forest undocumented. Mushrooms especially the wild mushrooms varieties are good sources of protein as they possess the constituents of non-essential amino acids with little amount of cholesterol in comparison to the cultivated one and mushroom now becoming a powerful agent to prevent malnutrition problem [8]. From ancient time, wild mushrooms have been consumed, it may be for their test and flavor [9].Antimicrobial properties of mushroom extracts, highlighting some low and high molecular weight compounds. Low molecular compounds, mainly are secondary metabolites, like; steroids, anthraquinones, benzoic acid derivatives, but also primary metabolites as, oxalic acid. High molecular compounds, mainly peptides and proteins. Edible mushrooms (*A. bisporus* and *P. sajor-caju)* were assayed in vitro for their antimicrobial activities byusing aqueous and organic solvent extracts. In their study, E. coli 390, E. coli 739, *Enterobacter aerogenes, P. aeruginosa* and *Klebsiella pneumoniae* were most sensitive to aqueous, ethanol, methanol and xylene extracts of these mushrooms [10]. *Pleurotus* species had a narrow antibacterial spectrum against Gram-negative bacteria and strongly inhibited the growth of the Gram-positive bacteria tested, including *B. subtilis*, and *M. luteus* [11]. The antimicrobial activity of various solvent extracts (methanol, ethanol, acetone and aqueous extract) of *G. lucidum* was tested against six species of bacteria: *E. coli, S. aureus, K. pneumoniae, B. subtilis, S. typhi* and *P. aeruginosa*. Acetone extract exhibited maximum antibacterial activity, while the most susceptible bacterium observed was *K. pneumoniae* [12]. Methanolic extracts of six wild mushrooms (*L. perlatum, C. cibarius, C. vermiculris, R. formosa, M. oreades, P. pulmonarius*) of Western Ghats of Karnataka, India showed significant antimicrobial activity against *B. subtilis, S. aureus, E. coli, P. aeruginosa* and *Candida albicans*[13].The solvent-based effectiveness of antibacterial activity of edible mushroom *L. tuberregium* (Fr.) Singer. In vitro antimicrobial properties of *L. tuberregium* culture filtrate extracted using four different solvent systems (Hexane, dichloromethane, chloroform and ethyl acetate) were the most active to inhibit the growth of *S. aureus, Micrococcus luteus, E. coli, Salmonella typhi* and *Shigella flexneri* [14].Therefore, in this present study, a wild edible mushroom has been selected for antimicrobial activity against some common human pathogens.

MATERIAL AND METHODS

Collection and Isolation of Mushroom Strain

The fruiting body of *Geasstrum rubellum* commonly known as earth star was collected from Satkosia reserve forest, Similipal, Mayurbhanj, at a young stage with the aid of sterile forceps, wrapped with sterile foil paper and transported to laboratory. It was washed thoroughly with several changes of sterile distilled water and air dried under laminar air flow chamber. Thereafter, the mushroom was aseptically broken exposing the inner tissue with the aid of a sterile blade. Several small segments of 2 × 2 mm of the sterile tissue were then transferred onto potato dextrose agar (PDA) and malt extract agar (MEA) media plates with the help of sterile knife and forceps. Approximately 4 mushroom segments per plate were inoculated. The plates were sealed with parafilm and incubated in room temperature for three days. The plated segmented were observed once a day for the growth of mushroom strain. Hypal tips growing out the plated segments were immediately transferred into PDA slant, purified and maintained at 4°C for subsequent experiments.

Determination of Fungal Growth in Different Media

Radial growth of the fungi was determined by placing the agar blocks of pure culture (3mm in diameter) of activity growing in petridishes containing PDA and MEA media. The plates were incubated in BOD incubator and observed once a day. The radial growth of the fungi in respectively medium were observed and recorded upto 14 days of incubation.

Antimicrobial Activity

Micro organisms

Antimicrobial activity was determined against six bacterial pathogen (*Pseudomonas aeruginosa, Proteus vulgaris, Bacillus subtilis, Staphylococcus aureus, Shigella flexneri, Klebsiella pneumonia*) and three pathogenic fungal pathogens (*Candida krusie, Candida albicans, Trichophyton mentagrophytes*). The test pathogens were obtained from the Institute of Microbial Technology (IMTECH), Chandigarh, India.

Antimicrobial Activity of Fungal Metabolites In Different Media

The fungus was cultured in two different media viz. Potato dextrose broth and Malt extract broth. The culture was the incubated at room temperature for 14 days by shaking on a rotary shaker at 120 rpm. The antimicrobial activity of different broth cultures of the fungus was determined by agar cup diffusion method against above mentioned six bacterial sp. and three pathogenic fungal sp. Muller Hinton agar plates were incubated with overnight culture of each bacterial pathogens' suspensions. Similarly, for the fungal pathogens, Sabouraud agar plates were inoculated with each fungal suspension. The plates with incubated organism were evenly spread out with sterile cotton swabs. Agar cups were prepared by scooping out the medium with sterile cork borer (7mm in diameter). The cups were then filled with 100µL of each fungal broth cultures in different media and incubated at 35±1°C for 24 hours for bacteria and 48 hours for fungal pathogens. The zone of inhibition was then measured in diameter with a transparent ruler.

Characterization of the Metabolites

The metabolites were partially characterized by thin layer chromatography (TLC). TLC plates of thickness 0.2mm were prepared with the silica gel GF254 on the glass plate and kept in onen for 2 hours. Plates were spotted with 1 mg/ml concentration of crude metabolite on the base line and run with hexane, ethyl acetate and water in the ratio 7:2:1 as mobile phase. After completion of the solvent front, the plates were taken out and dried. The plates were taken under TLC viewer on UV light for spot identification of the compound. The relative font (R_f) values were calculated using the formula; relative font (R_f) = Distance moved by the solute/Distance moved by the solvent. The identified bands were scraped with a glass slide and dissolved in ethyl acetate for future study.

RESULTS

Isolation and Morphological Identification

In this present investigation the source of organism was collected from Satkosia reserve forest, Mayurbhanj, Odisha. The species was characterized both by morphologically and microscopically. Based on its morphological characteristics, it was identified as *Geastrum rubellum,* commonly known as earth fungus. The characteristic features of the mushroom were as follows: the cap resembles like a sprouted flower. The fruiting body is creamy-ochraceous, scaly, bulb-shaped and sessile. The brittle outer peridium split at maturity into 5-8 pointed rays that reflex back revealing the cream coloured by the gleba in immature stage. The spore mass (gleba) is initially pallid and firm becoming brown and powdery (Fig. 1A). The spore was observed under microscope as brownish in colour and round shaped. The fungal strain was obtained as mycelia from fruiting body and radial growth of fungi was determined by culturing in two different media for 14 days (Fig. 1B). The observation shows that the maximum radial growth was observed in Malt extract agar medium than potato dextrose agar medium (Fig. 2). By the 14 days of incubation radial growth of 64mm was recorded in MEA media being the highest growth rate and the sane time 34mm radial growth was measured in PDA medium.

Antimicrobial Assay

The fungal species was determined for antimicrobial activity against a panel pathogen bacterial and fungal pathogen. The fungus was cultured in two different fungal broths (PDB and MEB). Preliminary antimicrobial

screening indicate that maximum antimicrobial activity was observed in Potato dextrose broth and nearly same result was found in Malt extract broth medium (Table-1). Bacterial pathogen i.e., *Shigella flexneri* and *Staphylococcus aureus* show highest activity than *Bacillus subtilis* and *Klebsiella pneumonie*. In case of fungal pathogen, high antifungal activity was determined in *Candida albicanes* and Trichophytonmentagrophytes whereas *Candida krusie* found with no activity (Fig. 3,4& 5).

Optimization of Maximum Metabolites Production

Effect of media (PDB and MEB) and incubation period (8days, 16days and 24days) were tested for optimal metabolites production. Activity of metabolites was tested against all pathogens (Fig. 6). Optimum activity was found in Potato dextrose broth (PDB) incubated for 16 days against *Shigella flexneri*. The strain was incubated in PDB for 16 days for further extraction of crude metabolites. The crude metabolites were extracted with ethyl acetate as organic solvent.

Thin layer chromatography (TLC)

The crude metabolite was subjected to separation by tlc. A single major distinct band was obtained which were visualized in short UV ranged at 254 nm. The Rfvalue of the major compound was calculated to be 0.81 (Fig. 7).

DISCUSSION

Wild mushrooms have been widely used as human food for centuries and have been appreciated for their texture and flavors as well as some suggested medicinal and tonic attributes. However, the awareness of mushrooms as a healthy food and as an important source of biologically active substances with medicinal potential has also emerged. Various activities of mushrooms have been studied which include antimicrobial, antifungal, antioxidant, antiviral, antitumor, cytostatic, immunosuppressive, antiallergic, antiatherogenic hypoglycaemic, anti-inflammatory and hepatoprotective activities [15]. Considering vast medicinal properties of wild edible mushrooms, in the present investigation a wild edible mushroom was studied for antimicrobial activity against a panel of human pathogenic microorganisms. Significant antimicrobial activity was observed in the crude extract with activity against almost all the tested pathogens. The metabolite was active against both bacterial and fungal pathogens. This indicates the metabolite to be broad spectrum in nature. There very little report on antimicrobial activity of *Geastrum rubellum*. Therefore, the present study is significant as this mushroom could be further exploited for antimicrobial agents. Recently, report antimicrobial activity of *geastrum s*p. against some clinically significant human pathogens [16]. The fruit bodies of *Geastrum* sp. have been chemically analyzed and shown to contain a number of bioactive compounds, including fungal sterols. The fungus also contains various fatty acids, notably myristic, palmitic, stearic, oleic, alpha-linolenic, and linoleic acid. Therefore, it may be attributed that the antimicrobial activity of this species may be due to presence of different chemical components. However, further study may elucidate more on their biological activities. The crude metabolites extracted from the mycelia wasanalyzed by simple preparative TLC. It was found that a single distinct band spotted in the TLC plate suggesting that the activity of the species due to presence of such molecule which need further purification and study.

Several workers have antimicrobial activity of extracts of mushrooms species as well as their phytochemical characteristics. In many instances it has been revealed that fruiting body and the mycelium contain compounds with wide ranging antimicrobial activity. Mushrooms are rich sources of natural antibiotics; in these, the cell wall glucans are well known for their immunomodulatory properties, and many of the externalised secondary metabolites (extracellular secretions by the mycelium) combat bacteria and viruses [17]. Other mushrooms compounds of therapeutic interests are the secondary metabolites as lectins, lactones, terpenoids, alkaloids, antibiotics and metal chelating agents, which are also important for the immune function of the organism. Mushrooms also contain a number of enzymes such as laccase, superoxide dismutase, glucose oxidase and peroxidase. I have been shown that

enzyme therapy plays an important role in cancer treatment preventing oxidative stress and inhibiting cell growth. Searching wild source may bring new natural product with antimicrobial properties that provide good protection against the infectious disease. Therefore, new wild edible mushrooms, as natural sources, could be introduced for this purpose. Medicinal mushrooms cultivation is lucrative and generates lots of employment opportunities and is suitable foe house wives and handicapped people. Considering all aspect, cultivation of medicinal mushrooms is a good avenue for the diversification of Indian horticulture. However, research and development on medicinal mushrooms should be strengthened to attain the goal. Our study suggests that exploring wild edible mushrooms may lead to the discovery of novel metabolites that might be use a new antimicrobial considering present health scenario of the world.

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Table-1: Antimicrobial activity of star fungus against pathogens in different media.

	Zone of inhibition in (mm)								
Media	**ck**	**ca**	**tm**	**pa**	**pv**	**bs**	**sa**	**sf**	**kp**
PDB	-	+++	+++	-	p	++	+++	+++	++
MEA	-	++	+++	-	-	++	++	++	++

PDA-Potato Dextrose Agar, MEA- Malt Extract Agar.

ck-Candida krusie, ca-Candida albicans, tm-Trichophyton mentagrophytes, Pa-Pseudomonas aeruginosa, pv- Proteus vulgaris, bs-Bacillus subtilis, sa-Staphylococcus aureus, sf-Shigella flexneri, kp-Klebsiella pneumonia.

-indicate no activity; p indicate partial activity; + indicate zone of inhibition 0≤10mm; ++ indicate zone of inhibition 10≤20mm; +++ indicate zone of inhibition 20≤30mm.

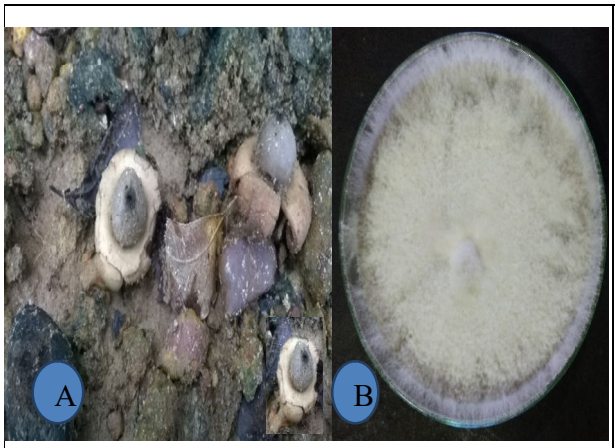

Fig.1: Showing (A) fruiting body and (B) colonial morphology of *Geastrum rubellum*.

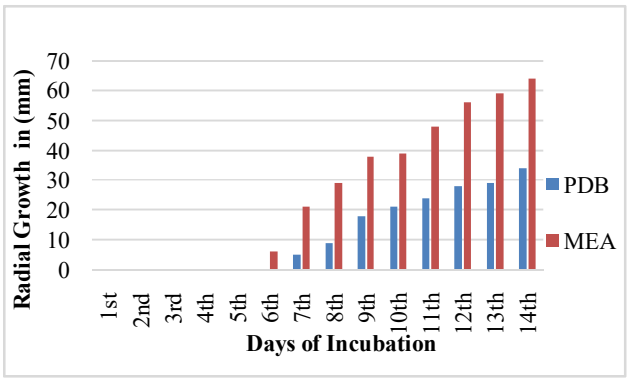

Fig.2: Graph showing the radial growth of *Geastrum rubellum*in PDA and MEA media

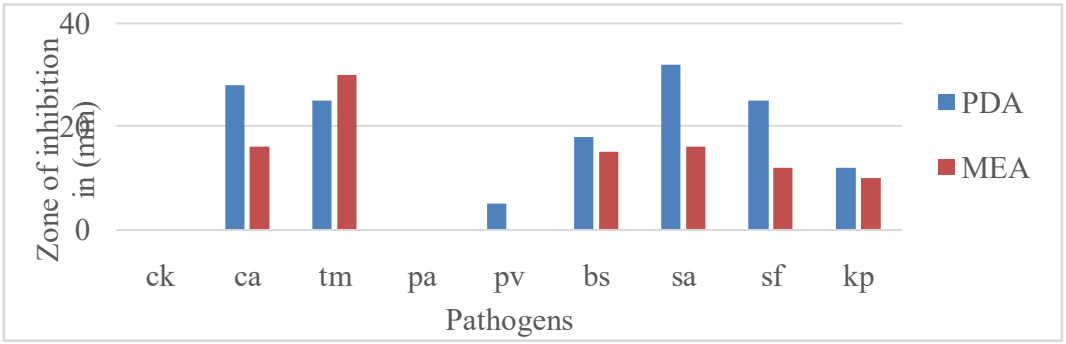

Fig.3: Graph showing the zone of inhibition against the pathogens in two media.

ck- Candida krusie, ca-Candida albicans, tm-Trichophyton mentagrophytes, Pa-Pseudomonas aeruginosa, pv- Proteus vulgaris, bs-Bacillus subtilis, sa-Staphylococcus aureus, sf-Shigella flexneri, kp-Klebsiella pneumonia.

PDA-Potato Dextrose Agar, MEA- Malt Extract Agar.

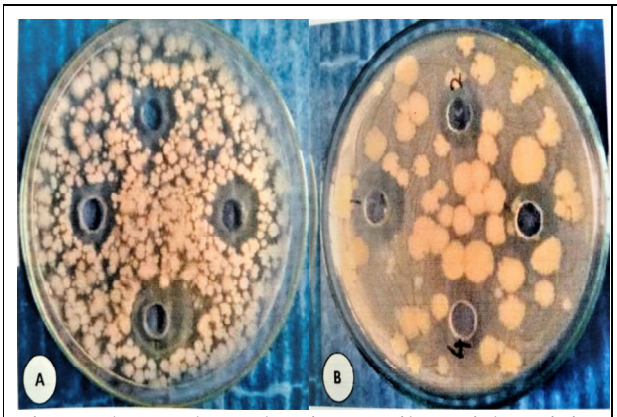

Fig.4: Photo plate showing antibacterial activity against (A)*Shigella flexneri* and (B) *Staphylococcus aureus.*

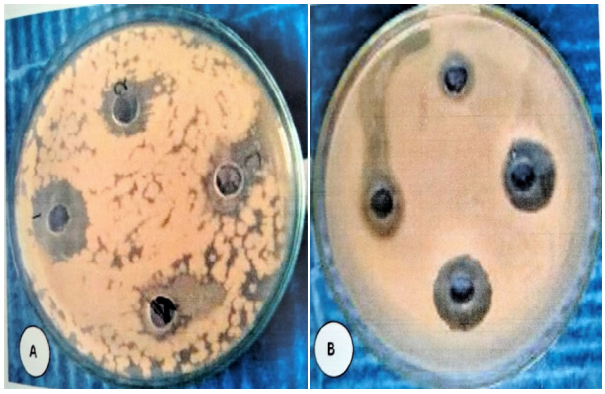

Fig.5: Photo plate showing antifungal activity against (A) *Candida albicans* and (B) *Trichophyton mentagrophytes.*

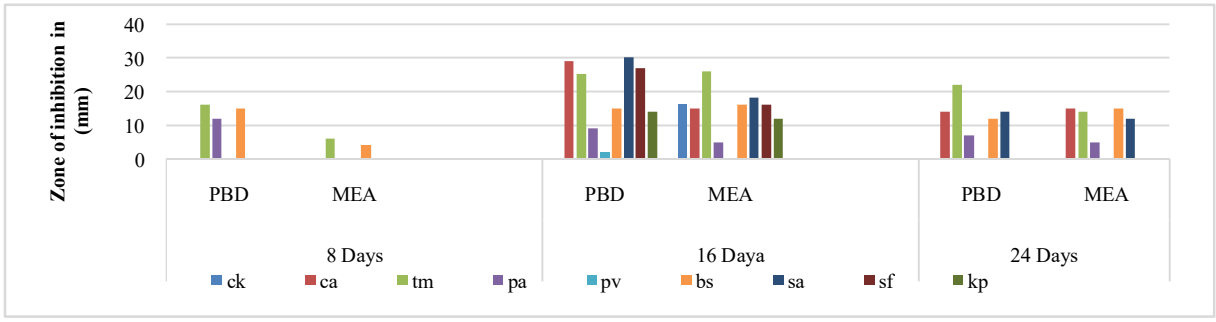

Fig.6: Graph showing the effect of different media and incubation time on the production of the metabolites and their activity.

ck-Candida krusie, ca-Candida albicans, tm-Trichophyton mentagrophytes, Pa-Pseudomonas aeruginosa, pv- Proteus vulgaris, bs-Bacillus subtilis, sa-Staphylococcus aureus, sf-Shigella flexneri, kp-Klebsiella pneumonia.

PDA-Potato Dextrose Agar, MEA- Malt Extract Agar

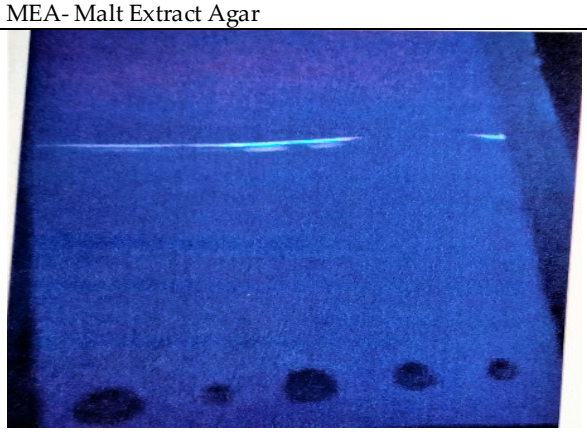

Fig.7: TLC plate showing the presence of single major distinct bands of crude compounds of *Geastrum rubellum.*

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RESEARCH ARTICLE

Power Line Transmission Failure Detection using Statistical Feature Classification Methods

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ABSTRACT

In an electrical power system, the high number of faults occurs in overhead transmission lines because of the greater length of the conductor exposure to the atmosphere. Therefore, Covered Overhead Conductors (COC's) are widely used. However, the standard protection devices are often unable to detect the conductor's phase-to-ground fault, which lead to Partial Discharge (PD). To overcome this, a robust real-time PD fault analysis system is required. A set of statistical methods such as Principal Component Analysis (PCA), Independent Component Analysis (ICA), Seasonal and Trend Decomposition using Loess (STL) and Hidden Markov Model (HMM) are used as feature extraction technique to decompose every raw voltage signal. Support Vector Machine (SVM) is used as a feature classification tool. Based on the performance evaluation metrics such as Precision, Recall, F1-Score it is observed that STL with SVM classifier provides the best prediction and classification results.

Keywords: Transmission Lines, Partial Discharge, Covered Overhead Conductors.

INTRODUCTION

The fault is a random character that may arise in the transmission line, resulting in the transmission line's incapacity to execute the needed function, as the fault can occur in any circumstances and at any point along the transmission

line. Because the conductor is exposed to the atmosphere for a longer period of time, the probability of failure or breakdown is more likely in overhead lines. As a result, insulated conductors are becoming increasingly used in overhead power transmission lines. Standard protection devices, on the other hand, are frequently unable to identify the conductor's phase-to-ground defect, as well as the more common tree or tree branch impacting conductor events, which only cause Partial Discharge (PD) activity rather than the overcurrent seen on bare conductors. To recognise PD activity in Covered Overhead Conductors (COCs), an effective pattern recognition algorithm is required.

Proposed Methodology

To overcome the faults occurs in overhead transmission lines, a robust real-time PD fault analysis system is required. MATLAB & Tensor Flow are used to analyze the waveform data and to develop a functional pattern recognition algorithm to detect PD activities on IOCs based on stray electrical field voltage measurement a set of statistical methods such as Principal Component Analysis (PCA), Independent Component Analysis (ICA), Seasonal and Trend Decomposition using Loess (STL) and Hidden Markov Model (HMM) are used as feature extraction technique to decompose every raw voltage signal. Figure 1 depicts the proposed method's block diagram. The proposed method focuses on each signal, where irregular noise information is most abundant. The method then produces a few data features from each component in the various instances. The data feature from the various instances is merged and stabilized at the future fusion stage. Data oversampling is also adopted to balance the number of PD signals and non-PD signals in the dataset. Finally, the features and known statuses are used to train a Support Vector Machine (SVM) classifier. Future PDs will be detected by the trained classifier.

Principal Component Analysis

Principal component analysis (PCA) is a statistical technique that lets you review the information contained in huge data tables utilizing a smaller set of "summing up index" that can be more simply visualized and analyzed. PCA has emerged as a widely useful method for dimensionality reduction. It is analyzed from the results that PCA performs well in various recognition tasks. PCA is a common method for estimating original data using lower-dimensional feature vectors. It is a way of recognizing patterns in data and expressing the data in such an approach to highlight their resemblance and dissimilarity.

Independent Component Analysis

Independent component analysis (ICA) is a statistical and numerical tool for revealing hidden components that drive groups of random variables, measurements, or signals. The ICA methodology can be thought of as an extension of the PCA methodology. ICA, on the other hand, optimises higher-order statistics like kurtosis, while PCA optimises the data's covariance matrix, which represents second-order statistics. As a result, PCA identifies uncorrelated components, whereas ICA identifies independent components.

Seasonal and Trend Decomposition Using Loess (STL)

STL is a multitalented and vigorous technique for decomposing time series. STL is an abbreviation for "Seasonal and Trend decomposition using Loess," while Loess is a technique for estimating non-linear associations. The STL technique was developed by Cleveland, Cleveland, McRae, & Terpenning.

Consider the subsequent time series model with trend and seasonality

$$y_t = T_t + S_t + r_t, t = 1,2,\ldots N \quad (1)$$

where y_t denotes the observation time, T_t is the trend in time series, S_t is the seasonal signal with period T, and the r_t denotes the remainder signal. Seasonality usually describes periodic patterns that vary near a baseline, and trend describes the continuous increase or decrease in seasonal-trend decomposition. Thus, typically it is assumed that the seasonal component S_t has a repeated pattern that changes gradually or even stays constant over time. In contrast, the trend component T_t is considered to change quicker than the seasonal component. Also, consider that the remainder r_t in this decomposition encompasses all signals other than trend and seasonality. Thus, in the majority

cases, it contains more than white noise as typically considered. In abnormality detection, assume r_t and can be further decomposed into two terms

$r_t = a_t + n_t$ (2)

where a_t denotes spike or dip, and n_t denotes the white noise.

Hidden Markov Model

The HMM method is a doubly stochastic model. A Markov chain is used to explain the transition between states, and the other stochastic process is applied to describe the statistical relation between state and observed variables. The state is not directly visible in the HMM, but the output, which may be used to detect the state's existence and properties, is. As a result, the strategy is known as the "hidden" Markov model. The HMM can be divided into two layers the hidden and the observation layer.

Support Vector Machines

SVMs are used as intelligent tools for identifying faulty lines and buses that is finding the location with respect to the Electrical Service Entry ESE. They were first introduced by Vapnik based on the structural risk minimization principle. The goal of SVM is to build a line of hyper-plane that may be used to identify distinct datasets. Support vectors are subsets of the training data that define the hyper-plane. Support vectors can create complex boundaries and maximize the margin separation through the quadratic minimizations. The SVM can solve both linear non-linear identification problems. Based on the principle of structural risk minimization, SVM could avoid the local-minimum issue which is the fundamental challenge of BP-ANN. The one-against-all (one-vs-rest) approach is most likely used to implement SVM multi-class classification.

Performance Metrics

The number of correct positive results divided by the number of positive results predicted by the classifier is what is known as precision. The number of correct positive outcomes divided by the total number of relevant samples equals recall (all samples that should have been identified as positive). The weighted harmonic mean of precision and recall is used to get the F1 score, which is a measure of a test's accuracy. The F1 Score ranges from (0,1). The formulas used for these performance evaluations are given below.

The precision index and the recall index for PD signals are:

$Precision = \frac{TP}{TP+FP}$ $Recall = \frac{TP}{TP+FN}$ (3)

The precision index and the recall index for non-PD signals are:

$Precision = \frac{TN}{TN+FN}$ $Recall = \frac{TN}{TN+FP}$ (4)

The harmonic mean of Precision and Recall is the F1-Score:

$F1 = 2\frac{Presision \cdot Recall}{Presision+Recall}$ (5)

RESULTS & DISCUSSIONS

The performance evaluation metrics of PCA with SVM classifier, is shown in Table 1& Figure 2. At the various instance of 5, 10 & 15, it is observed that Precision & Recall values are unstable, and the overall performance of the model based on F1-Score at the various instances is 53%, 54% & 58% respectively. The performance evaluation metrics of ICA with SVM classifier, is shown in Table 2& Figure 3. At the various instances of 5, 10 & 15, it is observed that Precision & Recall values are unstable, and the overall performance of the model based on F1-Score at the various instances is 65%, 65% & 68% respectively. The performance evaluation metrics of PCA + ICA with SVM classifier, is shown in Table 3& Figure 4. At the various instances of 5, 10 & 15, it is observed that Precision & Recall values are unstable, and the overall performance of the model based on F1-Score at the various instances is 67%, 67% & 65% respectively. The performance evaluation metrics of STL with SVM classifier is shown in Table 4& Figure 5.

At the various instances of 5, 10 & 15, it is observed that Precision & Recall values shows 73%, 75% & 76% of detected PD signals are true PD signals out of 82%, 83% & 87% successfully detected PD signals the F1-Score at the various instances are 77%, 79% & 81% respectively. The performance evaluation metrics of HMM with SVM classifier is shown in Table 5& Figure 6. At the various instances of 5, 10 & 15, it is observed that Precision & Recall values shows 67%, 69% & 71% of detected PD signals are true PD signals out of 77%, 78% & 80% successfully detected PD signals the F1-Score at the various instances are 71%, 73% & 75% respectively. At various instance of 5, 10 & 15 it is observed that Precision & Recall values shows 73%, 75% & 76% of detected PD signals are true PD signals out of 82%, 83% & 87% successfully detected PD signals the F1-Score at the various instances are 77%, 79% & 81% respectively. Based on the analysis of Prediction Evaluation Metrics shown in Table 6& Figure 7 for different statistical methods such as PCA, ICA, PCA + ICA, STL & HMM with SVM Classifier, it is observed that STL with SVM classifier provides the best prediction and classification results.

CONCLUSION

To overcome the faults occurs in overhead transmission lines, a robust real-time PD fault analysis system is proposed using a set of statistical methods such as Principal Component Analysis (PCA), Independent Component Analysis (ICA), Seasonal and Trend Decomposition using Loess (STL) and Hidden Markov Model (HMM) are used as feature extraction technique to decompose every raw voltage signal. Support Vector Machine (SVM) is used as a feature classification tool. At various instance of 5, 10 & 15 it is observed that Precision & Recall values shows 73%, 75% & 76% of detected PD signals are true PD signals out of 82%, 83% & 87% successfully detected PD signals the F1-Score at the various instances are 77%, 79% & 81% respectively. Based on the performance evaluation metrics such as Precision, Recall, F1-Score it is observed that STL with SVM classifier provides the best prediction and classification results.

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Table 1. Prediction Evaluation Metrics by PCA & SVM

Evaluation Category	Precision			Recall			F1-Score		
	Instance			Instance			Instance		
	5	10	15	5	10	15	5	10	15
PD Signals	0.59	0.59	0.63	0.48	0.50	0.54	0.53	0.54	0.58
Non-PD Signals	0.50	0.51	0.56	0.60	0.60	0.65	0.55	0.55	0.60

Table 2. Prediction Evaluation Metrics by ICA & SVM

Evaluation Category	Precision			Recall			F1-Score		
	Instance			Instance			Instance		
	5	10	15	5	10	15	5	10	15
PD Signals	0.70	0.69	0.72	0.60	0.61	0.64	0.65	0.65	0.68
Non-PD Signals	0.64	0.66	0.65	0.73	0.74	0.73	0.69	0.69	0.69

Table 3. Prediction Evaluation Metrics by PCA + ICA & SVM

Evaluation Category	Precision			Recall			F1-Score		
	Instance			Instance			Instance		
	5	10	15	5	10	15	5	10	15
PD Signals	0.68	0.69	0.69	0.67	0.66	0.61	0.67	0.67	0.65
Non-PD Signals	0.72	0.74	0.65	0.73	0.76	0.73	0.73	0.75	0.69

Table 4. Prediction Evaluation Metrics by STL & SVM

Evaluation Category	Precision			Recall			F1-Score		
	Instance			Instance			Instance		
	5	10	15	5	10	15	5	10	15
PD Signals	0.73	0.75	0.76	0.82	0.83	0.87	0.77	0.79	0.81
Non-PD Signals	0.67	0.69	0.74	0.55	0.57	0.58	0.61	0.62	0.65

Table 5.Prediction Evaluation Metrics by HMM & SVM

Evaluation Category	Precision			Recall			F1-Score		
	Instance			Instance			Instance		
	5	10	15	5	10	15	5	10	15
PD Signals	0.67	0.69	0.71	0.77	0.78	0.80	0.71	0.73	0.75
Non-PD Signals	0.65	0.64	0.65	0.52	0.52	0.54	0.58	0.57	0.59

Table 6. F1-Score of different Statistical Methods & SVM Classifier

F1-Score	PCA & SVM			ICA & SVM			PCA+ICA & SVM			HMM & SVM			STL & SVM		
	Instance			Instance			Instance			Instance			Instance		
	5	10	15	5	10	15	5	10	15	5	10	15	5	10	15
PD Signals	0.53	0.54	0.58	0.65	0.65	0.68	0.67	0.67	0.65	0.71	0.73	0.75	0.77	0.79	0.81
Non-PD Signals	0.55	0.55	0.60	0.69	0.69	0.69	0.73	0.75	0.69	0.58	0.57	0.59	0.61	0.62	0.65

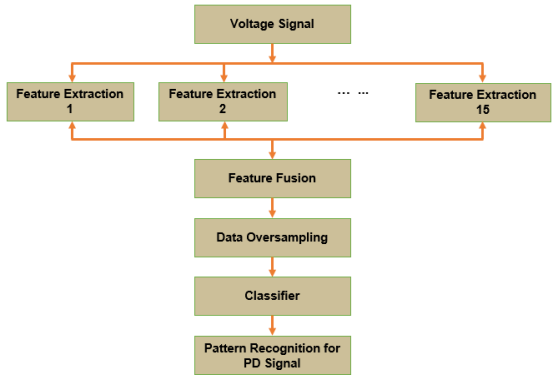

Figure 1. Block Diagram of the Proposed Method

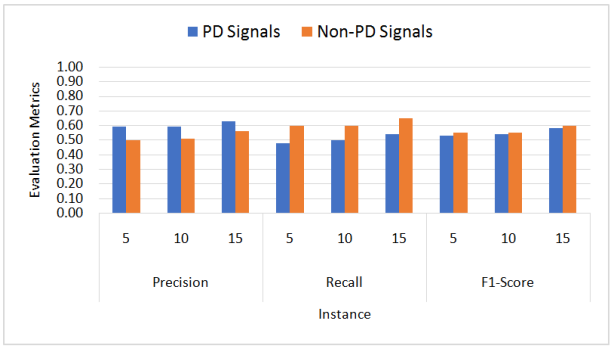

Figure 2 Prediction Evaluation Metrics Plot for PCA & SVM

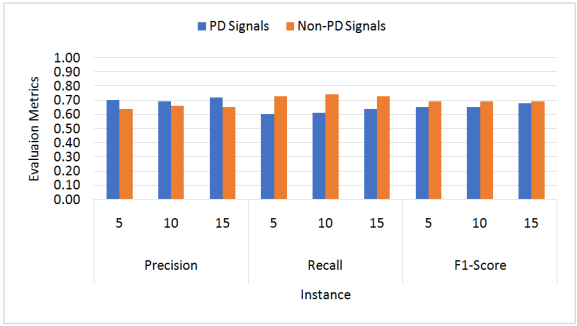

Figure 3. Prediction Evaluation Metrics Plot for ICA & SVM

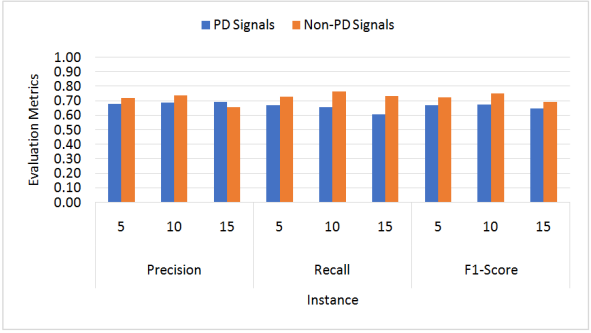

Figure 4. Prediction Evaluation Metrics Plot for PCA + ICA & SVM

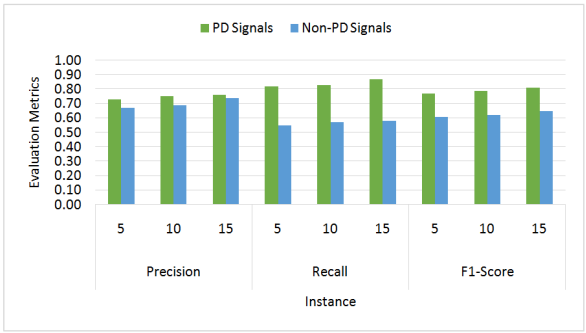

Figure 5. Prediction Evaluation Metrics Plot for STL & SVM

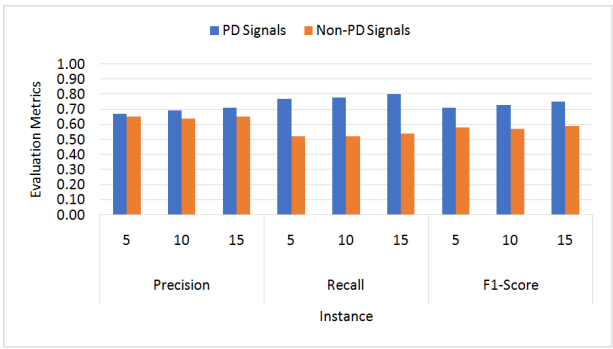

Figure 6. Prediction Evaluation Metrics Plot for HMM & SVM

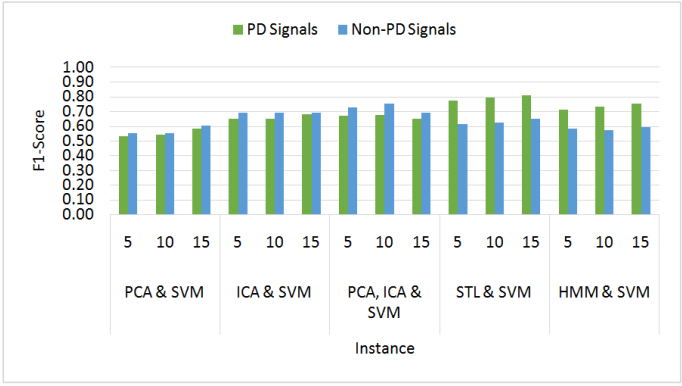

Figure 7. F1-Score Plot for different Statistical Methods & SVM Classifier

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REVIEW ARTICLE

A Review on Structural Evaluation and Strengthening of Flexible road Pavements using Falling Weight Deflectometer (FWD) Technique

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ABSTRACT

Most of the road network in Asian country encompasses a vital level of decay and thus needs major rehabilitation come. In general, most of those rehabilitation activities involve a replacement asphalt layer on the first pavement structure; information and analysis of the structural capability of the pavement are essential to perform a sturdy and economical rehabilitation style. it's necessary to see the structural capability of versatile pavements as an operation of the deflections made by the applying of a load. The techniques most employed in several countries to live pavement deflections are the Falling Weight Deflectometer (FWD) and the Benkelman beam, the primary one that works underneath dynamic loading and also the second device underneath static loading. the employment of devices underneath static loading has not been counseled by many style methodologies, together with AASHTO, however, these are still used widely in several countries together with the Asian countries. So, it's necessary to check the deflections by the Benkelman beam and falling weight deflectometer. During this study, deflections live by FWD techniques on thirty deflection observation points on a particular fifteen-kilometer versatile urban road stretch. Each test is performed at the same time on marking points. And knowledge collected by the take a look at are as per IRC: 115-2014.

Keywords: Rehabilitation, road pavement, FWD

INTRODUCTION

In economic growth and development of country Transportation infrastructure plays a lead role. The road transport is the oldest and most widely mode of transport of mankind. Pavements are the key elements of infrastructure of the

country, whose functions are to promote transport activities, economic activities and to improve the standard of living life. All structures fail at some point but the life of structure is extending by the maintenance and rehabilitation activities. The maintenance and rehabilitation activities of pavement structures become increasingly important as pavements deteriorate with time and traffic operation. (Das) The combined effects of traffic loading and the environment will cause every pavement, no matter how well-designed/constructed to deteriorate over time.

Structural evaluation of pavements involves application of a standard load to the pavement and measuring its response in terms of stress, strain or deflection. Benkelman beam has been among the earliest equipment used for measuring deflection and structural evaluation of pavements. In this technique, a static load is applied to the pavement surface and rebound deflections are measured at one or more locations. Measurement of deflection under a static load does not simulate the loading conditions produced in pavements by moving vehicle. The evaluation of pavements by such methods is labor-intensive and, in general, time consuming. (CSIR - Central Road Research, 2020) The existing guidelines for strengthening of flexible pavements using Benkelman beam technique are contained in IRC:81 and were developed based on the findings of the Research Scheme R-6 of Ministry of Road Transport and Highways carried out during 1984 to 1990 (Congress, Indian Road, 2014).

LITERATURE REVIEW

Falling weight deflectometer (FWD) testing is a valuable method for assessing the structural condition of existing pavement structures. For jointed plain concrete pavements (JPCPs), FWD testing is used to detect voids, monitor joints and crack performance, and back calculate the modulus of elasticity of the existing Portland cement concrete (PCC) and the k-value of all supporting layers. For asphalt concrete (AC) pavements, FWD testing is used to back calculate the stiffness of each layer and to estimate the amount of damage in the existing asphalt. This report summarizes the testing protocols and data analysis procedures recommended. The report consists of three primary sections. The first section describes the testing protocols recommended for FWD data collection. The second section defines the changes proposed to current PennDOT documents (including Publication 242, Publication 408, and the PennDOT Pavement ME Design Preliminary User Input Guide) based on the findings of this study. The third section is an appendix that is divided into four separate appendices: A-Scheduling and performing FWD testing; B-Data analysis guidelines; C-Research findings and D-Laboratory and field testing. Murillo Feo C.A. and Bejarano Urrego L.E, Research on Correlation between deflections measurements on flexible pavementsobtained under static and dynamic load techniques. Aim of this paper is Correlation between deflections measurements on flexible pavements obtained under static and dynamic load techniques. The techniques most used in Colombia to measure pavement deflections are the Falling Weight Deflectometer (FWD) and the Benkelman beam, the first one works under dynamic loading and the second device under static loading (Patil, 2018). different associations like the AASHTO do not recommend the use of deflectometers under static load, but in several countries, including Colombia which presents damage in the most of the road network, these devices are still in use especially the Benkelman beam, not only for structural evaluation but also for design of pavement structures; this is due especially to difficult acquisition, unfamiliarity and cost of falling weight deflectometer (Pittsburgh, 2018).Therefore, it is important to determine the degree of correlation between these two devices to be able to obtain FWD deflections as a function of Benkelman beam deflections. In this paper representative results of deflection basins are acquired in the study. The tendency of the deflection curves is deep and of short length, which means that the subgrade corresponds to a poor-quality soil and deficient pavement performance (Federal Highway Administration US Department of Transport, 2006). It was observed that the deflection basins obtained from the Benkelman beam are much deeper (12 to 232 mm^2) than those obtained using FWD (31, 29 to 164, 14 mm^2) giving more critical quality of the structure. The effective structural number (SNeff) was obtained using the methodology of the Hogg Model for BBD and FWD measurements.

METHODOLOGY AND ANALYSIS

The principle of Falling Weight Deflectometer
When a moving wheel load passes over the pavement it produces load pulses.
Major Applications of FWDs square measure within the following areas.

- Evaluation of the structural capability of in-service versatile, semi-rigid, and rigid pavements
- Quality management of subgrade and granular layers of pavements throughout the development stage
- Assessment of the requirement for and style of the thickness of overlays
- Determination of the speed of degradation of pavement structures
- Evaluation of the degree of bonding between pavement layers
- Assessment of equivalent moduli of concrete blocks in block pavements
- Evaluation of the load transfer capability within the joints of concrete pavements
- Detection of voids underneath rigid pavements

A Criterion for classification of pavement sections is given in Table

Pavement Evaluation Survey and Data Collection

Pavement Condition Survey

Deflection Measurement

Estimation of Sample Size

The following equation can be used for estimating the sample size (n).

$$n = (z * CV)^2 / (ME^2)$$

Where,
n = sample size
z = normalized normal deviate which can be obtained from standard statistical tables for a selected confidence level
CV = coefficient of variation of deflection (standard deviation/mean) expressed as percentage
ME = acceptable margin of error (as percentage of mean)
It is recommended that 90 percent confidence level and 10 percent margin of error (ME expressed as % of mean) may be considered in these guidelines for the purpose of estimation of sample size. The coefficient variability values for "good", "fair" and "poor".
Different measurement schemes can be adopted. These include
(i) Measurement along the most distressed wheel path of the carriageway
(ii) Measurement along inner as well as outer wheel paths of all the lanes
(iii) Measurement along both wheel paths of only the outer most lanes and
(iv) Measurement along the more distressed wheel paths of each of the lanes.
The guidelines given in Table below are recommended for selection of deflection measurement schemes for different types of carriageways.

Determination of Pavement Layer Thicknesses

Pavement layer thicknesses are essential inputs to the process of back calculation of layer moduli and, in turn, to the estimation of remaining life and overlay requirements of the in-service pavement. Hence, it is necessary that accurate information is collected about layer thicknesses from different sources. Layer thicknesses can be obtained from historical data, by coring bound layers and/or by excavating test pits (600x600x1000 mm) size and/or through the non-destructive technique of Ground Penetrating Radar (GPR) survey.

Analysis of Data

Identification of Homogeneous Sections

Since the assessment of the remaining life of in-service pavement and the strengthening requirement in terms of bituminous overlay will be done on the basis of the back calculated moduli of in-service pavement layers. It is prudent to identify homogeneous sections for the purpose of structural design primarily based on deflection bowl parameters and other relevant information i.e. pavement condition, peak deflections/peak deflection bowl parameters (SCI), Design Traffic (MSA), trail pits data (pavement layer type/composition, thickness), subgrade strength etc. Based on the above methods two homogeneous sections were identified throughout the project road.

Fatigue Model

Two fatigue equations were fitted, one in which the computed strains in 80 per cent of the actual data in the scatter plot were higher than the limiting strains predicted by the model (and termed as 80 per centreli ability level in these guidelines) and the other corresponding to 90 per cent reliability level. The two equations for the conventional bituminous mixes designed by Marshall Method are given below:

Nf= 2.21 * 10-04x [1/εt]3.89* [1/MR]0.854

Nf= 0.711 * 10-04x [1/εt]3.89* [1/MR]0.854

Where,

Nf = fatigue life in number of standard axles,

εt = Maximum Tensile strain at the bottom of the bituminous layer,

MR = resilient modulus of the bituminous layer.

Rutting Model

Rutting model also has been calibrated in the studies using the pavement performance data collected during the studies at 80per cent and 90 per cent reliability levels. The two equations are given below:

N = 4.1656 x 10-08 [1/εv] 4.5337

N = 1.41x 10-8x [1/εv] 4.5337

Resilient Modulus

The behavior of the sub grade is essentially elastic under the transient traffic loading with negligible permanent deformation in a single pass. Resilient modulus is the measure of its elastic behavior determined from recoverable deformation in the laboratory tests. The modulus is an important parameter for design and the performance of a pavement. The relation between resilient modulus and the effective CBR is given as:

MR (MPa) = 10 * CBR for CBR 5

MR (MPa) = 17.6 * (CBR)0.64 for CBR > 5

Where, MR = Resilient modulus of sub grade soil

MR_granular= 0.2* h0.45* MR sub grade

Where, h = thickness of granular sub-base and base, mm.

Design Traffic (MSA)

Project traffic is indicated in terms of million standard axles. In this project for flexible pavement design only commercial vehicles with gross weight above 3000kg are considered. Seven days 24hr traffic volume data has been collected and presented in terms of ADT

As per IRC 37 2012 the design traffic is calculated by using the formula below

Ns = the cumulative number of axles to be carried in the design period

Ns= 365*A[(1+r) ^x-a] *F*D/r

CONCLUSION

There are various equipment are available for non-destructive evaluation of structural health of pavement. Based on the working principles, these can be classified in two major groups, deflection based method and wave propagation based method. Static loading, steady state loading, impulsive loading etc. are different types of deflection based methods; stress wave, electromagnetic method etc. are different types of wave propagation method. FWD (impulsive loading equipment) can be efficiently used for estimation of in-situ stiffness values and thickness of the pavement layers. In this paper the case of NH-20 (Champus to Rimuli) was taken for study. From the above analysis for crust designs of flexible pavements FWD test results were analyzed using KGP back so that remaining life of the existing layers can be considered for the realistic and economical designs. Hence as per design Dense Bituminous macadam (DBM) of 80 mm &Bituminous Concrete (BC) of 40 mm Thickness was suggested for overlaying on the existing Carriageway which is economical as compared to the strengthening of the total road.

Nevertheless, it is a fact that road safety is a complex issue and is characterized by different sectors such as road engineering, human psychology, vehicle design etc. A systematic incorporation of engineering measures with planning and enforcement can improve better and safer road use.

RESULT AND DISCUSSION REPORTS

Table No.4 to 9

Design Traffic

Name of the work:- Strengthening To NH-20 From Km0/000 To 14/000 Km (ChampuaRimuli) And Link Road To NH 20 From 14/000 To 14/690 Km (At Parasala) And Connecting Road From Rimuli Square At 14/000 To 1/430 Of NH 520 For The Year Of 2019-20 In The State Of Odisha On EPC Mode

Type of Lane		=	**Double**
No. of commercial vehicle as per last count	(P)	=	**2460**
Initial traffic count in the year of complete	$A=P(1+r)^x$	=	2583.00
Growth rate per annum	(r)	=	0.05
Design Life	(n)	=	15
Vehicle Damage factor	(F)	=	5.0
No. of year between last count and the year of complete of construction period	(x)	=	1
Lane Distribution Factor	(D)	=	0.5
		=	N

Design Traffic

$$N = \frac{365x[(1+r)^n-1]}{r} xAxDxF$$

50860404.6

= **51.00** msa

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Table 1. A Criterion for classification of pavement sections

Type of Carriageway		Recommended Measurement Scheme		Maximum Spacing for Test points along selected wheel path for pavements of different classification		
				Poor	Fair	Good
Two-lane two-way single carriageway	Measure along both outer wheel paths	60	130	500		

Table 1. Pavement Condition Survey

Classification	Pavement Condition
Good	Isolated cracks of less than 3.0 mm width in less than 5% area of total paved surface AND average rut depth less than 10 mm
Fair	Isolated or interconnected cracks of less than 3.0 mm width in 5 to 20% area of total paved surface AND/OR average rut depth between 10 to 20 mm
Poor	Wide interconnected cracking of more than 3.0 mm width in 5 to 20% area (include area of patching and raveling in this) of paved area OR cracking of any type in more than 20% area of paved surface AND/OR average rut depth of more than 20 mm

Table 2. Deflection Measurement

Type of Carriageway	Recommended measurement scheme	Maximum Spacing (m) for test points along selected wheel path for pavements of different classification		
		Poor	Fair	Good
Single-lane two-way	i) measure along both outer wheel paths	60	130	500
Two-lane two-way single carriageway	i) measure along both outer wheel paths	60	130	500
Four lane Single carriage way	i) measure along outer wheel paths of outer carriageway lanes	30	65	250
	ii) measure along the outer wheel path of more distressed inner lane	60	130	500
	iii)measure along the centre line of paved shoulder (in case of widening projects)	120	260	500
	(i) measure along outer wheel paths of outer lanes	30	60	120

Four lane dual divided c/way	(ii) measure along the outer wheel path of inner lane	60	130	500
	(iii) measure along the centre line of paved shoulder (in case of widening projects)	120	260	500
Dual Carriageway having 3 or more lanes in each direction (measurement given in each carriageway)	(i) measure along outer wheel paths of each outermost lanes	30	65	250
	(ii) measure along outer wheel path of more distressed inner lane	60	130	500
	(iii) measure along the centre line of paved shoulder (in case of widening projects)	120	260	500

Table 4
Classified Traffic Volume Count Survey

Name of the Road				:	Strengthening To NH-20 From Km0/000 To 14/000 Km (ChampuaRimuli) And Link Road To NH 20 From 14/000 To 14/690 Km (At Parasala) And Connecting Road From Rimuli Square At 14/000 To 1/430 Of NH 520 For The Year Of 2019-20 In The State Of Odisha On EPC Mode									
PERIOD				Day	Car/Jeep/Taxi /Three wheeler auto	Two wheeler motor cycle / scooter	LCV	Bus	2 Axle Truck	Multy Axle Truck	Agriculture Tractor with Trailor	Cycle Rickshaw / other human powered	Bullock Cart	
FROM		TO												
DATE	HOUR	DATE	HOUR											
16-10-2019	6 A.M	17-10-2019	6 A.M	WED	782	2413	184	77	113	1901	109	264	0	
17-10-2019	6 A.M	18-10-2019	6 A.M	THU	815	2138	202	101	121	1915	151	240	0	
18-10-2019	6 A.M	19-10-2019	6 A.M	FRI	834	2187	211	117	81	1976	140	281	0	
19-10-2019	6 A.M	20-10-2019	6 A.M	SAT	767	2306	274	105	93	1869	122	256	0	
20-10-2019	6 A.M	21-10-2019	6 A.M	SUN	792	2297	156	114	77	1889	87	307	0	
21-10-2019	6 A.M	22-10-2019	6 A.M	MON	807	2437	189	96	90	1979	153	232	0	
22-10-2019	6 A.M	23-10-2019	6 A.M	TUE	789	2394	259	121	105	1956	89	273	0	
Total for 7 Days					5586	16172	1475	731	680	13485	851	1853	0	
Total Per Days					798	2310	**211**	**104**	**97**	**1926**	**122**	265	0	
Equivalency Factors					1	0.5	1.5	3	3	4.5	4.5	1.5	8	
Average PCU for the Week					798	1155	317	312	291	8667	549	398	0	
Average CVD for the Week					**2460**									

Table 3. Pavement Design

Design Traffic	:	51.00	MSA	
Design CBR	:	5 %		
	Referring IRC 37:2012			
	GSB	:	300	mm
	WMM	:	250	mm
	DBM	:	115	mm
	BC	:	40	mm
	Total	:	705	mm

Table 4. Existing Crust Details

Sl. No	Chainage	Side	SAND	GSB	WMM	DBM/BM	BC/SDBC	Total	Remark
1	000+050	RHS		300	200	75	25	600	
2	001+100	LHS		300	250	50	25	625	
3	002+000	RHS		300	300	50	50	700	
4	003+000	LHS		300	250	100	25	675	
5	004+000	RHS		250	250	75	25	600	
6	005+000	LHS		300	250	50	25	625	
7	006+000	RHS		300	300	50	50	700	
8	007+000	LHS	700	300	250	75	25	650	
9	008+000	RHS		300	150	75	25	550	
10	009+000	LHS		200	200	100	30	530	
11	010+000	RHS		250	220	55	25	550	
12	011+000	LHS	300	200	150	70	30	450	
13	012+200	RHS		200	150	50	25	425	
14	013+000	LHS		220	150	50	25	445	
15	014+000	RHS		280	200	50	25	555	
16	014+450	LHS		280	150	75	25	530	
17	014+600	RHS		300	200	75	25	600	
18	000+265	RHS		200	250	70	30	550	
19	000+835	RHS		300	250	100	25	675	
20	001+700	LHS		250	250	50	25	575	
					Average	67.25	28.25		
					Total Bituminous layer		96 mm	=	100 mm

Table 5

Loading plate diameter: 150 mm

Measurement normalized to:40 KN

Designed Traffic: 51 msa

Modulus of overlay layer: 3000MPa

	Elastic moduli(Mpa)			**Remaining Life(MSA)**			**After overlay(MSA)**	
	Surface	**Base**	**Sub grade**	**Fatigue life**	**Rutting Life**	**Overlay**	**Fatigue life**	**Rutting Life**
Section Ch. 0/000 km to 3/750 km.(LHS)								
Average	1399	257	82	7.96	126.14	87	53.93	726.85

minimum	661	73	62	0.51	8.51	45	51.37	572.16
maximum	1689	396	87	17.75	261.8	145	55.79	930.32
std. deviation	299	126	8	6.86	97.59	35	1.77	88.91
85% percent	**1156**	**112**	**74**	**1.16**	**23.62**	**127**	**51.67**	**668.84**
Median	1507	250	87	4.97	96.57	85	54.73	722.23
Section Ch. 4/250 km to 6/750 km.(LHS)								
Average	1484	166	85	2.56	206.52	109	54.73	2219.43
minimum	1282	93	77	0.97	72.94	80	52.55	2076.42
maximum	1725	256	87	5.99	413.1	130	57.61	2525.19
std. deviation	162	53	4	1.64	107.06	16	1.7	155.54
85% percent	**1301**	**120**	**86**	**1.17**	**122.27**	**126**	**52.67**	**2117.64**
Median	1491	165	87	2.34	199.37	105	54.74	2133.18
Section Ch. 7/250 km to 9/750 km.(LHS)								
Average	1248	161	79	2.72	52.98	117	55.13	837.21
minimum	625	73	51	0.45	8.56	60	53.13	265.51
maximum	1601	367	87	11.6	188.86	145	58.65	1303.32
std. deviation	306	91	12	3.56	56.8	27	1.62	326.22
85% percent	**1025**	**100**	**70**	**0.5**	**12.47**	**140**	**53.43**	**508.2**
Median	1331	127	87	1.19	34.83	125	55.2	885.21
Section Ch. 10/250 km to 13/750 km.(LHS)								
Average	1435	243	85	6.43	434.24	89	55.01	2154.04
minimum	829	73	67	0.33	29.1	50	52.3	1579.42
maximum	1782	396	87	16.34	1007.43	150	57.9	2601.06
std. deviation	279	98	6	5.31	316.53	28	1.77	278.2
85% percent	**1143**	**176**	**86**	**2.67**	**215.27**	**103**	**52.97**	**1933.06**
Median	1529	206	87	3.77	287.1	93	55.25	2147.15
Section Ch. 14/250 km to 14/690 km.(LHS)								
Average	1103	214	87	13.11	262.69	75	53.82	1275.13
minimum	460	83	87	1.76	85.48	10	51.69	678.31
maximum	1575	396	87	40.85	684.77	115	55.65	2064.11
std. deviation	405	125	0	16.15	246.8	41	1.41	543.66
85% percent	**767**	**97**	**87**	**2.13**	**89.73**	**111**	**52.69**	**766.74**
Median	1189	189	87	4.92	140.26	88	53.98	1179.05

Table 6

Loading plate diameter: 150 mm
Measurement normalized to:40 KN
Designed Traffic: 51 msa

Modulus of overlay layer: 3000MPa

	Elastic moduli(Mpa)			Remaining Life(MSA)			After overlay(MSA)	
	Surface	Base	Sub grade	Fatigue life	Rutting Life	Overlay	Fatigue life	Rutting Life
Section Ch. 0/000 km to 4/000 km.(RHS)								
Average	1193	150	75	3.52	60.14	122	54.63	767.27
minimum	242	73	37	0.25	1.77	45	51.24	192.52
maximum	1695	396	87	17.68	261.09	155	58.24	1236.51
std. deviation	402	119	15	6	88.26	38	2.55	304.93
85% percent	**956**	**73**	**64**	**0.3**	**9.72**	**150**	**51.51**	**443.72**
Median	1256	95	81	0.52	14.66	133	54.95	808.02
Section Ch. 4/000 km to 7/000 km.(RHS)								
Average	1292	125	80	1.64	137.96	124	53.8	2246.81
minimum	386	73	61	0.44	27.15	75	51.12	1161.5
maximum	1635	278	87	7.21	485.45	145	55.72	3461.05
std. deviation	394	70	9	2.28	145.18	23	1.36	867.37
85% percent	**1161**	**73**	**73**	**0.55**	**55.44**	**141**	**53.12**	**1228.4**
Median	1371	88	87	0.69	85.93	135	53.65	2188.69
Section Ch. 7/000 km to 10/000 km.(RHS)								
Average	1166	177	85	2.84	61.33	111	53.89	899.61
minimum	646	73	77	0.48	16.24	65	51.08	579.96
maximum	1717	356	87	10.18	169.93	145	57.14	1274.69
std. deviation	376	92	3	3.05	47.27	25	1.93	242.1
85% percent	**798**	**104**	**87**	**0.76**	**29.29**	**130**	**51.64**	**614.63**
Median	1134	130	87	1.63	42.28	115	53.69	940.29
Section Ch. 10/000 km to 14/000 km.(RHS)								
Average	1118	209	85	3.67	285.84	100	55.12	1990.64
minimum	586	73	72	0.48	43.53	55	52.17	1651.15
maximum	2123	396	87	12.56	790.67	145	57.07	2273.06
std. deviation	498	85	5	3.39	199.08	23	1.56	203.85
85% percent	**620**	**140**	**87**	**1.44**	**150.6**	**117**	**53.42**	**1754.99**
Median	1131	221	87	2.87	243.51	100	55.43	2038.76
Section Ch. 14/000 km to 14/690 km.(RHS)								
Average	1343	270	87	19.63	354.32	54	56.63	974.7
minimum	518	185	87	5.85	155.19	5	55.24	763.17
maximum	2022	396	87	50.57	787.77	85	57.47	1172.9
std. deviation	579	82	0	18.02	252.62	30	0.88	159.98
85% percent	**783**	**197**	**87**	**7.52**	**186.71**	**76**	**55.81**	**818.36**
Median	1415	250	87	11.05	237.15	63	56.91	981.36

Table-9: STATEMENT FOR OVERLAY FOR BITUMINOUS COURSE AS PER F.W.D. TEST ON N.H.20 FROM 0/0 TO 14/690 KM

		Overlay Thickness (in mm)		Average of LHS & RHS (in mm)
Sl. No	**Chainage**	**L.H.S.**	**R.H.S.**	
1	0/0 to 4/0 Km	127.00	150.00	138.50
2	4/0 to 7/0 Km	126.00	141.00	133.50
3	7/0 to 10/0 Km	140.00	130.00	135.00
4	10/0 to 14/0 km	103.00	117.00	110.00
5	14/0 to 14/690 Km	111.00	76.00	93.50
			Total:-	**610.50**
	Average overlay crust thickness		=	122.1 mm
Now it is proposed for Bituminous overlay for strengthening of the stretch				
	1) D.B.M Grade-II		=	80
	2) B.C Grade-II		=	40
				120 mm

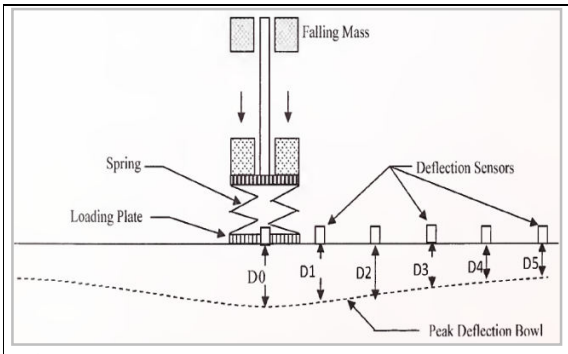

Figure 1. Instrument used for the Deflection Survey

Figure 2. FWD

Percentile	CBR
100.0	3.85
95.0	4.85
90.0	4.98
85.0	5.03
80.0	5.63
75.0	5.89
70.0	6.22
65.0	6.69
60.0	6.7
55.0	6.73
50.0	6.88
45.0	7.03
40.0	7.11
35.0	7.22
30.0	7.79
25.0	8.22
20.0	8.66
15.0	8.89
10.0	9.02
5.0	9.62

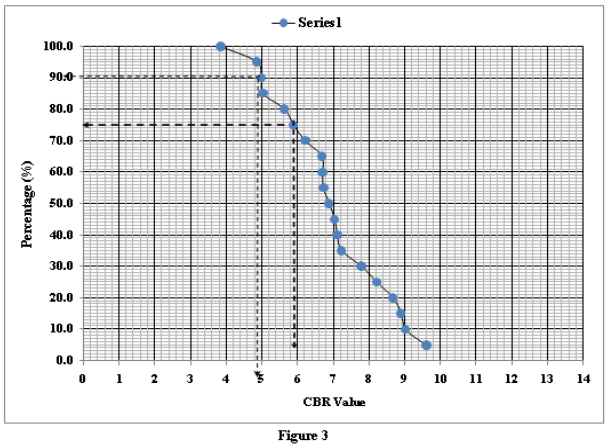

Figure 3

90th Percentile = 5.00% Equivalent to 5%

Acc to IRC:37:2018 Cl. No.6.2.2

Figure 3 : CBR Value

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REVIEW ARTICLE

Current Trends in: Epidemic Diseases

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ABSTRACT

The world has built up an expand worldwide wellbeing framework as a defense against known and obscure irresistible sickness dangers. The framework comprises of different formal and casual organizations of associations that serve various partners; have changing objectives, modalities, assets, and responsibility; work at various provincial levels and cut across people in general, private-for-benefit, and private-not-revenue driven areas. The advancing worldwide wellbeing framework has done a lot to ensure and advance human wellbeing. Nonetheless, the world keeps on being stood up to by longstanding, arising, and reappearing irresistible infection dangers. These dangers contrast generally regarding seriousness and likelihood. They likewise have differing ramifications for dreariness and mortality, just as for an unpredictable arrangement of social and financial results. To different degrees, they are additionally managable to elective reactions, going from clean water arrangement to guideline to biomedical counter measures. Regardless of whether the worldwide wellbeing framework as right now established can give powerful assurance against a unique exhibit of irresistible illness dangers has been raised doubt about by late flare-ups of Ebola, Middle East respiratory disorder, SARS, and flu and by the approaching danger of rising antimicrobial obstruction. The worry is amplified by quick populace development in regions with powerless wellbeing frameworks, urbanization, globalization, environmental change, common clash, and the changing idea of microbe transmission among human and creature populaces. This Council would fortify the worldwide wellbeing framework by improving cooperation and coordination across associations filling in information holes concerning (for instance) irresistible sickness reconnaissance, innovative work needs, financing models, production network co-ordinations, and the social and monetary effects of possible dangers; and making significant level, proof based proposals for overseeing worldwide dangers related with irresistible illness.

Keywords*:* worldwide wellbeing, worldwide wellbeing frameworks, irresistible sickness, symptoms, measure, WHO advices and reaction.

INTRODUCTION

An epidemic is the quick spread of irresistible disease to countless individuals in a given populace inside a brief timeframe. As per current ideas, an epidemic is characterized as the event locally or district of instances of an ailment or other wellbeing related occasions plainly in abundance of ordinary hope. The people group or locale, and the time span in which the cases happen are determined definitely. An epidemic disease isn't needed to be contagious, and the term has been applied to West Nile fever and the obesity epidemic (e.g. by the World Health Organization), among others. Consequently, epidemics allude to the "unordinary" event locally or area of disease, explicit wellbeing related conduct (e.g., smoking) or other wellbeing related occasions (e.g., car crashes) plainly in overabundance of "anticipated event". The quantity of cases differs as indicated by the disease-causing specialist, what's more, the size and sort of past and existing openness to the specialist [1,2].

Epidemics of infectious disease are generally caused by several factors including

Change in the biology of the host populace (for example expanded pressure or expansion in the thickness of vector animal groups)

1. Genetic change in the microorganism supply or the presentation of an arising microorganism to a host populace (by the development of microbe or have).
2. Generally, an epidemic happens when have insusceptibility to one or the other an set up microorganism or recently arising novel microbe is abruptly diminished beneath that found in the endemic balance and the transmission edge is surpassed.
3. The conditions which administer the episode of epidemics additionally incorporate tainted food supplies, for example, sullied drinking water and the movement of populaces of specific creatures, like rodents or mosquitoes, which can go about as disease vectors.
4. Certain epidemics happen at specific seasons. For instance, challenging hack happens in spring, while measles produces two epidemics, one in winter and one in March. Flu, the regular cold, and other diseases of the upper respiratory plot, like sore throat, happen transcendently in the colder time of year [3].
5. Disease flare-ups are generally brought about by a contamination, sent through individual to-individual contact, creature to-individual contact, or from the climate or other media.
6. Outbreaks may likewise happen following openness to synthetics or to radioactive materials. For instance, Minamata disease is brought about by openness to mercury.
7. Epidemics might be the outcome of debacles of another sort, for example, typhoons, floods, seismic tremors, dry spells, and so forth.
8. Occasionally the reason for an episode is obscure, even after intensive examination [4].

TYPES OF EPIDEMIC DISEASES[3]

COMMON-SOURCE EPIDEMICS

Normal source epidemics are habitually, yet not generally, due to openness to an irresistible agent. They can result from tainting of the climate (air, water, food, soil) by modern synthetics or pollutant. E.g., Bhopal gas misfortune in India and Minamata disease in Japan coming about because of utilization of fish containing a high centralization of methyl mercury.

Single Exposure Or "Point-Source" Epidemics

These are otherwise called "point-source" epidemics. The openness to the disease specialist is brief and basically synchronous, the resultant cases all create inside one brooding time of the disease. E.g., an epidemic of food harming. The principle highlights of a "point-source" epidemic are:

1. The epidemic bend rises and falls quickly, with no optional waves
2. The epidemic will in general be hazardous, there is a grouping of cases inside a restricted time period, and
3. More critically, every one of the cases create inside one brooding time of the disease.

Continuous or Multiple Exposure Epidemics

On the off chance that the epidemic proceeds over more than one hatching period, there are either a constant or numerous openings to a typical source or a proliferated spread. Sometimes the openness from a similar source might be delayed – consistent, rehashed or irregular – not really simultaneously or place. For model, a whore might be a typical source in a gonorrhea flare-up, however since she will taint her customers throughout some undefined time frame there might be no unstable ascent in the quantity of cases. A well of tainted water, or a broadly disseminated brand of antibody (for example polio immunization), or food, could result in comparative outbreaks. In these occurrences, the subsequent epidemics will in general be more broadened or irregular. The flare-up of respiratory ailment, the Legionnaire's disease, in the mid year of 1976 in Philadelphia (USA) was a typical source, ceaseless or rehashed openness outbreak. This flare-up, as in other outbreaks of this sort, proceeded past the scope of one hatching period. There was no proof of who had contact with sick people. auxiliary cases among people.

Propagated Epidemics [5]

An engendered epidemic is regularly of irresistible cause and results from individual to-individual transmission of an irresistible specialist (e.g., epidemics of hepatitis-A and polio). The epidemic as a rule shows a progressive ascent and tails off over an any longer time of time. Transmission proceeds until the quantity of susceptibles is exhausted or defenceless people are not, at this point presented to tainted people or delegate vectors. The speed of spread relies on group resistance, openings for contact and optional assault rate. Propagated epidemics are bound to happen where countless powerless are totaled, or where there is an ordinary inventory of new helpless people (e.g., birth, migrants) bringing down crowd invulnerability.

Mixed Epidemics [6]

A few epidemics have highlights of both basic source epidemics and proliferated epidemics. The example of a typical source flare-up followed by auxiliary individual to-individual spread isn't uncommon. These are called mixed epidemics.

2017 UGANDA MARBURG VIRUS OUTBREAK [7]

Marburg Hemorrhagic Fever is an uncommon, however genuine, zoonotic illness. Episodes are as often as possible set off by collaboration with African organic product bats. The viral contamination has a hatching time of 5 to 10 days and generally gives itself fever, chills, cerebral pain, and myalgia; the case casualty rate normally goes from 23% to 90%. The flare-up in Eastern Uganda, first affirmed on October 17, 2017, was even more disturbing in that it had a case casualty pace of 100%; as indicated by the most recent Weekly Bulletin on Outbreaks and Other Emergencies delivered by WHO, there were 3 affirmed cases, every one of whom kicked the bucket. At present, there are no antibodies accessible to ensure against the infection, and there is no particular treatment by the same token. Be that as it may, steady emergency clinic treatment may help increment the odds of endurance.

Marburg virus is filamentous enveloped, negative-sense, single-stranded RNA (ssRNA) viruses that belong to the family Filoviridae and can cause severe hemorrhagic fever in both humans and nonhuman primates. The virus is one of two members of the species Marburg Marburg virus, which is included in the genus Marburgvirus, family Filoviridae, orderMononegavirales. The name Marburg virus is derived from Marburg (the city in Hesse, Germany, where the virus was first discovered) and the taxonomic suffix virus.

SYMPTOMS [8]

The manifestations of Marburg infection disease normally please out of nowhere after a hatching time of around five to 10 days. Early side effects are as per the following:

- Fever
- Chills
- Headache
- Muscle throbs

Around five days after the side effects initially happen, different manifestations may happen as follows:

- A rash happens on the chest, back, and stomach in certain people.
- Nausea
- Vomiting
- Chest pain
- Sore throat
- Stomach pain
- Loose bowels may show up.

Side effects proceed and can get extreme; they incorporate the accompanying:

- Jaundice
- Pancreatic irritation
- Severe
- weight loss
- Delirium
- Liver disappointment
- Massive draining with organ disfunction

The case casualty rate (passing rate) goes from about 23%-90% of tainted people.
Large numbers of the side effects are like those of other irresistible infections like Ebola, intestinal sickness, typhoid fever, and others; so indicative tests are helpful to preclude different reasons for the manifestations. Individuals presented to the Marburg infection ordinarily give indications of contamination no later than around 14 days after openness, but since the clinical side effects look like Ebola infection illness, the vast majority are set in disconnection for 21 days.

TRANSMISSION [9]

At first, human MVD disease results from delayed openness to mines or gives in occupied by Rousettus bat settlements. Marburg spreads through human-to-human transmission by means of direct contact (through broken skin or mucous layers) with the blood, discharges, organs or other natural liquids of contaminated individuals, and with surfaces and materials (for example bedding, dressing) polluted with these liquids.

Medical services laborers have regularly been tainted while treating patients with suspected or affirmed MVD. This has happened through close contact with patients when contamination control safeguards are not carefully rehearsed. Transmission by means of defiled infusion hardware or through needle-stick wounds is related with more serious illness, quick crumbling, and, perhaps, a higher casualty rate. Entombment functions that include direct contact with the body of the perished can likewise contribute in the transmission of Marburg. Individuals stay irresistible as long as their blood contains the infection.

SEXUAL TRANSMISSION [10]

Marburg infection transmission by means of tainted semen has been archived as long as seven weeks after clinical recuperation. More observation information and exploration are required on the dangers of sexual transmission, and especially on the commonness of suitable and contagious infection in semen after some time. In the meantime, and dependent on present proof, WHO suggests that:

- All Marburg survivors and their sexual accomplices ought to get guiding to guarantee more secure sexual practices until their semen has twice tried negative for Marburg infection.
- Survivors ought to be given condoms.
- Male Marburg survivors ought to be selected semen testing programs when released (beginning with directing) and offered semen testing when intellectually and truly prepared, inside a quarter of a year of sickness beginning.
- Marburg survivors and their sexual accomplices ought to either: abstain from every single sexual practice, or observe more secure sexual practices through right and steady condom use until their semen has twice tried undetected (negative) for Marburg infection.
- Having tried undetected (negative), survivors can securely continue typical sexual practices with limited danger of Marburg infection transmission.
- Male overcomers of Marburg infection illness should rehearse more secure sexual practices and cleanliness for a year from beginning of indications or until their semen twice tests undetected (negative) for Marburg infection.
- Until such time as their semen has twice tried undetected (adverse) for Marburg, survivors should rehearse great hand and individual cleanliness by quickly and completely washing with cleanser and water after any actual contact with semen, including after masturbation. During this period utilized condoms ought to be taken care of securely, and securely discarded, in order to forestall contact with original liquids.
- All survivors, their accomplices and families ought to be shown regard, respect and sympathy.

DIAGNOSIS [11, 12]

It very well may be hard to clinically separate MVD from other irresistible sicknesses like jungle fever, typhoid fever, shigellosis, meningitis, and other viral hemorrhagic fevers.

Marburg infection disease is made utilizing the accompanying indicative techniques:

- Antibody-catch catalyst connected immunosorbent examine (ELISA)
- Antigen-catch recognition tests
- Serum balance test
- Reverse transcriptase-polymerase chain response (RT-PCR) measure
- Electron microscopy
- Virus disengagement by cell culture.

Tests gathered from patients are a limit biohazard hazard; lab testing on non-inactivated

Tests ought to be led under most extreme natural regulation conditions. All organic examples ought to be bundled utilizing the triple bundling framework when moved broadly and universally.

PREVENTION AND CONTROL MEASURES [12]

Great flare-up control depends on applying a bundle of intercessions, to be specific case the board, observation and contact following, a decent research facility administration, protected and noble internments, and social activation. Local area commitment is critical to effectively controlling episodes. Bringing issues to light of hazard factors for Marburg contamination and defensive estimates that people can take is a viable method to diminish human transmission. Hazard decrease informing should zero in on a few variables: Reducing the danger of bat-to-human transmission emerging from delayed openness to mines or surrenders occupied by natural product bat states.

During work or exploration exercises or vacationer visits in mines or surrenders possessed by natural product bat provinces, individuals should wear gloves and other proper defensive dress (counting covers). During flare-ups every single creature item (blood and meat) ought to be completely cooked before utilization. Diminishing the danger of human-to-human transmission locally emerging from immediate or close contact with tainted patients, especially with their body liquids. Close actual contact with Marburg patients ought to be kept away from. Gloves and proper individual defensive hardware ought to be worn when dealing with sick patients at home. Normal hand

washing ought to be performed subsequent to visiting wiped out family members in emergency clinic, just as in the wake of dealing with sick patients at home. Networks influenced by Marburg should put forth attempts to guarantee that the populace is very much educated, both about the idea of the actual sickness and about vital episode regulation measures.

Flare-up regulation measures incorporate brief and safe internment of the dead, distinguishing individuals who may have been in contact with somebody contaminated with Marburg and checking their wellbeing for 21 days, isolating the solid from the debilitated to forestall additionally spread, and keeping up great cleanliness and a spotless climate should be noticed. Decreasing the danger of conceivable sexual transmission. In light of additional examination of continuous exploration, WHO suggests that male over comers of Marburg infection illness practice safe sex and cleanliness for a year from beginning of indications or until their semen twice tests negative for Marburg infection. Contact with body liquids ought to be kept away from and washing with cleanser and water is suggested.

WHO PREVENTION AND CONTROL[13]

Great flare-up control depends on applying a bundle of mediations, in particular case the executives, reconnaissance and contact following, a decent research facility administration, protected and noble entombments, and social assembly. Local area commitment is vital to effectively controlling flare-ups. Bringing issues to light of hazard factors for Marburg contamination and defensive estimates that people can take is a powerful method to decrease human transmission.

Hazard decrease informing should zero in on a few factors [14, 15]

Reducing the danger of bat-to-human transmission emerging from delayed openness to mines or gives in occupied by natural product bat settlements. During work or examination exercises or traveler visits in mines or buckles possessed by natural product bat provinces, individuals should wear gloves and other fitting defensive dress (counting veils). During episodes every creature item (blood and meat) ought to be completely cooked before utilization. Reducing the danger of human-to-human transmission locally emerging from immediate or close contact with contaminated patients, especially with their body liquids. Close actual contact with Marburg patients ought to be kept away from. Gloves and proper individual defensive gear ought to be worn when dealing with sick patients at home. Standard hand washing ought to be performed in the wake of visiting debilitated family members in clinic, just as subsequent to dealing with sick patients at home. Communities influenced by Marburg should put forth attempts to guarantee that the populace is very much educated, both about the idea of the actual infection and about important flare-up regulation measures.

Outbreak control measures incorporate brief and safe internment of the dead, recognizing individuals who may have been in contact with somebody tainted with Marburg and checking their wellbeing for 21 days, isolating the solid from the wiped out to forestall additionally spread, and keeping up great cleanliness and a spotless climate should be noticed. Reducing the danger of conceivable sexual transmission. In view of additional examination of continuous exploration, WHO suggests that male overcomers of Marburg infection sickness practice safe sex and cleanliness for a year from beginning of side effects or until their semen twice tests negative for Marburg infection. Contact with body liquids ought to be dodged and washing with cleanser and water is suggested. WHO doesn't suggest segregation of male or female recovering patients whose blood has been tried negative for Marburg infection.

TREATMENT [16]

Like Ebola and numerous other viral illnesses, there is no particular treatment for Marburg infection sickness. Patients are given steady emergency clinic care by keeping up their liquid and electrolyte balance and different contemplations, like supplanting lost blood and keeping a decent oxygen supply. This strong consideration is most adequately done in a serious consideration emergency clinic unit. There are no home solutions for treat Marburg infection diseases.There is presently no powerful Marburg virus-explicit treatment for MVD. Treatment is principally steady in nature and incorporates limiting intrusive methodology, adjusting liquids and electrolytes to counter lack

of hydration, organization of anticoagulants right off the bat in contamination to forestall or control spread intravascular coagulation, organization of procoagulants late in disease to control discharging, keeping up oxygen levels, torment the executives, and organization of anti-toxins or anti-mycotics to treat auxiliary diseases Experimentally, recombinant vesicular stomatitis Indiana infection (VSIV) communicating the glycoprotein of MARV has been utilized effectively in nonhuman primate models as post-exposure prophylaxis. Experimental helpful regimens depending on antisense innovation have shown guarantee, with phosphorodiamidatemorpholino oligomers (PMOs) focusing on the MARV genome New treatments from Sarepta and Tekmira have been effectively utilized in people just as primates. silver

STEPS TAKEN [18]

The Ugandan Ministry of Health proceeds to proactively react to the flare-up with help from WHO and partners. Contact following is continuous, just as dynamic case search in wellbeing offices and at the local area level. Revealed passings are likewise researched for Marburg before internment and dubious passings agreed protected and honorable entombments. A confinement and treatment unit was set-up in Kapchorwa with strategic help from WHO (world wellbeing association), UNICEF (joined countries global youngsters secret stash), and MSF (drugs sans boondocks). A total emergency convention has been carried out.

Social assembly and hazard correspondence are continuous. With the help from Red Cross volunteers, UNICEF, and WHO correspondence specialists, more than 4,000 local area individuals have gotten data on MVD. Psychosocial support experts have been conveyed to Kween and directing meetings are being led for relatives of the perished Marburg cases, wellbeing laborers, and other local area individuals. Guided voyages through the Marburg treatment units in Kapchorwa and Kween were coordinated to disperse the dread of the treatment community and bits of gossip about wrong practices by medical services laborers that cause the passing of conceded patients.

A cross-line meeting among Uganda and Kenya wellbeing specialists is booked for seventh November 2017 in Kapchorwa, and cross-line observation exercises are progressing. Kenya Marburg infection illness episode alternate course of action and the general wellbeing EOC (crisis tasks focus) have been enacted and readiness measures have begun. 2000 Personal Protective Equipment sets have been dispatched by WHO and delivered to Trans Nzoia County, Kenya. Blood examples were gathered and have been dispatched to Nairobi's KEMRI Laboratory. A brief treatment place (Kaisang at Health focus) has been distinguished and the Kenya Red Cross Society is selecting and re-arranging attendants to deal with the MVD treatment center. UNICEF is helping with correspondence exercises and local area commitment. MSF-France has sent to help the setting up of treatment focuses in Uganda (Kapchorwa and Kaproron) and Kenya (Kaisangat).

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Table no-1: ABBREVIATION

SI.NO	ABBERVIATION	FULLFORM
1	WHO	WORLD HEALTH OEGANIZATION
2	USA	UNITED STATES OF AMERICA
3	ss RNA	SINGLE STANDARD RIBONUCLEIC ACID
4	MVD	MURBURG VIRUS DISEASE
5	ELISA	ENZYME LINKED IMMUNOSORBENT ASSAY
6	RT-PCR	REVERSE TRANSCRIPTASE-POLYMERASE CHAIN REACTION
7	UNICEF	UNITED NATIONS INTERNATIONAL CHILDREN FUND
8	MSF	MEDICINES SANS FRONTIERS
9	EOC	EMERGENCY OPERATION CENTRE
10	VSIV	VESICULAR STOMATITIS INDIANA VIRUS

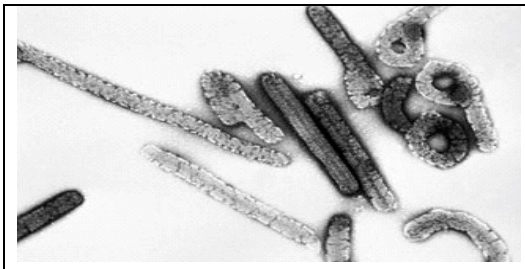

Fig. No.1: Marburg virus microscopic view

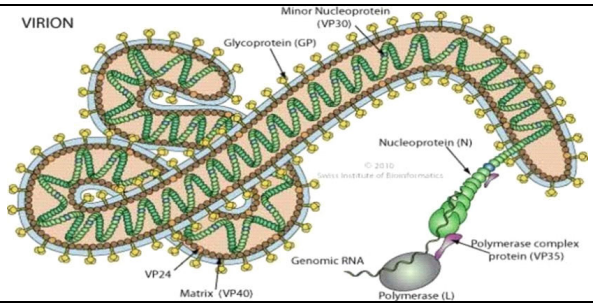

Fig. No. 2: Marburg virus structure

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REVIEW ARTICLE

A Brief Review of Bioethanol Sources

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ABSTRACT

Bioethanol is a green fossil fuel which is also oxygenated (35 percent oxygen thereby having the capacity for reducing automobile emissions. Bioethanol is ethanol generated through refining organic materials, including waste materials or crops cultivated especially for the needs of producing ethanol. Bioethanol might be generated from a variety of raw materials. Bioethanol is significantly generated by microbial fermentation of sugar or starch from various feedstocks, including cane sugar, corn, various grains, agriculture wastes, forestry wastes, municipal wastes, livestock manures, etc. Wheat is an important source of feedstock. Sugar beet may also be used as a feedstock containing sugar. Sweet Sorghum is cited as a promising production of biomass crop. Higher estimation is intended to produce the fermentable sugars for a process involving acid hydrolysis of straw, the lowest reliable energy ratio crop variety tends to be sugar beet. A high-octane, non-aqueous alcohol, also called as hydrated ethanol is then produced using distillation and dehydration. In this article we focus a few sources of bioethanol for replacing fossil fuels.

Keywords: Biofuels, Feedstocks, Bioethanol, Fossil, Stover.

INTRODUCTION

Bioethanol is the biofuel most commonly used for transportation worldwide.Biofuels are seen as sustainable sources for replacing fossil fuels [1], offering environmental benefits through protection of natural resources and reduction of greenhouse gases. About 95% of ethanol produced in the world is from agricultural products [2-6]. Bioethanol from corn and wheat is considering as the first-generation biofuel compared to other biofuel products, because only hexose sugar is used for fermentation. Using simplified steps before ferment with the yeast strain, high titer

ethanol can be obtained from corn and wheat. Bioethanol from corn and wheat was newly implemented in number of developed and developing nations on industrial scale to satisfy bioethanol demands. Fuel ethanol production is an power-efficient processes today, and further work is underway to boost its economic viability over the longer term. The ethanol component oxygenates fuel and reduces air pollution.

Some Common Sources of Bioethanol

Sugar beet

Beet sugar constitutes 30 percent of the sugar production in the world. For cultivated sugar beets, there are several other uses for sugar beets for the most significant application is for processed sugar, there are several other applications of sugar beets. The beets make up a strong, rum-like, alcoholic beverage in several countries. Unrefined beet syrup is the product of shredded beets, which were cooked for several hours and then pressed. These by-products are used not simply in the manufacturing of beer, industrial baking and in drugs as above [7]. Betaine and Uridine are also isolated from the sugar beet production by-products too. Sugar is a fuel for the human body, so United Kingdom sugar beet surpluses were used to manufacture biobutanol by BP. Sugar beet syrup is widely used for manufacturing of Sugar and Ethanol.

Stover and Straw

Stover consists of corn (maize), sorghum leaves and stalks left in a field after harvest. It can be grazed directly by the cattle or dried for fodder (forage) use. It is related to straw, the remainder leave for its seed after any grain of cereals or grass are harvested at maturity. Stover has gained some attention fermentation as a potentially substitute source of fuel and as biomass. Straw is an agriculture by-product, the dry stalk of a cereal plant, after removal of the nutrient grain or seed. Straw accounts for around half of the production of a cereal crop such as barley [8], oats, rice, rye or wheat. The use of straw as a carbon-neutral energy source, particularly for biobutanol, is rapidly increasing.

Potato and Sweet potato

Potato (*Solanum tuberosum*) is a evergreen plant of the Solanaceae family which is commonly cultivates for its starchy tuber. Potatoes are high in carbohydrates and contain starch, minerals (especially potassium) and vitamins. Freshly harvested potatoes hold more ascorbic acid than saved ones. Potatoes also contains starch, flour, sugar, dextrin, and feed for livestock. Sweet potato (*Ipomoea batatas*) is a crop whose starched, sweet-flavoring tuber roots are an essential vegetable of root origin. The tuberous starchy roots are by far the most significant product, although the leaves and shoots are edible too. In some tropical regions they are a staple food-crop. These are high in dietary fiber, retinol, ascorbic acid, and pyridoxine as well as starch. Both cultivars are sweet-flavored to more-or-less. Commercial applications include starch processing and commercial alcohol manufacturing. All plant parts are used to feed animals. In South America red sweet potato juice is combined with lime juice to make a cloth dye. Each color from pink to purple to black can be achieved by changing the proportions of the juices.

Corn and Whey

Corn is abridged form of Indian corn, that is to say Indian grain. Sweet corn is generally shorter than the varieties of field-corn. Maize among the world's most prominent foods in different world regions. Maize is alternatively used as a biomass fuel, such as ethanol [9]. Whey is the yellowish liquid making different cultured dairy products [10].Two varieties of whey are, Sweet whey and acid whey. It is also used as a lacto-fermented drink like limeades. Whey's main ingredient, lactose, is a milk derived sugar. Several research on the conversion of whey to usable value-added products, including ethanol [11-13] and citric acid have been performed. Nevertheless, genetically engineered strain of the homo-lactic fermentative bacterium, *Lactococcus lactis*, has been produced to be able to generate Et OH from whey effectively. Likewise, lactose can be assimilated but not processed by *Escherichia coli* and some recombinant.

CONCLUSION

Bioethanol represents a good option. It is much cleaner than normal fuels, as it reduces the emission of characteristics and ozone formation compared to normal fuels such as diesel by using bioethanol. Future Potential Improvements may be made in a number of ways to current generation techniques. Chief among these are creation of different strains of species for fermenting the sugars into ethanol, and a better integration of processes that would theoretically lead to higher energy ratios. There is a good potential for using 2nd generation manufacturing technologies, using lignocellulosic biomass as a feedstock. Although production costs of cane, beet, or corn are higher than those for bioethanol, most lignocellulose components are by-products of farming operations, factory wastes, or domestic waste. This provides enormous potential for large scale fuel ethanol production. Nevertheless, disposal of byproducts left by varied lignocellulosic feed stocks is likely to be much expensively than those from commonly used methods, since the products can differ in nature depending on the combination of feedstock being used at a given time.

ACKNOWLEDGEMENT

Nil

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RESEARCH ARTICLE

A Phenomenological Study to Explore the Lived in Experiences Among Menopause Women.

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ABSTRACT

Menopause / Climacteric stage is the Permanent cessation of Menstrual period which results in various symptoms such as hot flushes, sleep disturbances, mood swings, vaginal dryness, weight gain, etc.,. Menopause women suffer from these symptoms which affect their day to day activities and finally leads to decrease in quality of life. Therefore, it is very important to study the lived in experience of women during Menopause. The aim of this study is to explore the lived in experiences among menopause women. Twelve women were purposively selected who experienced menopause from the selected village Karaikal. Data was collected by semi-structured interviews. Data analysis was done by Colalizzi's analysis method. Six (06) themes emerged from the findings, they are; Intolerable discomforts in the body, Loss of physical strength, problems in family relationships, Memory problems, Emotional instability and urinary problems. Hot flushes, sweating, sleep disturbances, joint pain, back pain and vaginal dryness were the physical experiences. Further they also experience loss of physical strength such as lack of energy, feeling very tired, unable to do the work. Women also faces problems in family relationships due to family conflicts and less sexual activities. Difficulty in memorizing, difficulty in concentration and forgetting things and events are the memory problems. Women experiences emotional instability such as shouting at family members, difficulty in managing decisions, wanting to be alone. Majority of the women experience urinary problems such as increased frequency of urination and dribbling of urine during coughing or laughing. These findings revealed that women suffer from different experiences during menopause which has an impact on reducing their Quality of life.

Keywords: Menopause women, Lived in experience, discomfort, hot flushes, memory problems, emotional instability, urinary problems.

INTRODUCTION

The Climacteric or Menopause is an unavoidable stage of life of all the women[1,8]. Menarche, the first menstruation which is the beginning of Reproductive stage and Menopause, the last menstruation which is the end of reproductive stage are the turning point in the life of a women[2]. Menopause is also named as ' the change of life' as it is the symbol of end of woman's reproductive life[3]. As In this current generation life span and life expectancy of women has increased, women spend one – third of their lifetime after menopause period4,5. Menopause is influenced by changes in hormone levels. During fertile periods of women, the three reproductive hormones which facilitates production and release of egg is oestradiol, oestrone and oestriol which are collectively known as oestrogen. As women gets older, less oestrogen is produced and the process take several years[1,8]. This longer variable period of physiological termination of Menstruation, subjects women into a complex and Psychosocial change[6].

The most common symptom of the menopause is Hot flushes which occurs in three in every four menopausal women. Other common symptoms include night sweats, sleep disturbances, dryness in vagina, irritated skin, urinary incontinence, urinary tract Infections, mood swings and decreased interest in sex. During menopause, decreased production of estrogen is the main cause for all the common symptoms. oestrogen lack may affect many parts of the body which includes the brain, changes in emotional well- being and the skin, influencing its elasticity and thickness.[1,2,8], Menopausal period is positively correlated with non communicable disease such as hypertension, diabetes, cervical cancer, osteoporosis and breast cancer.7,8 The duration, severity and impact of these symptoms may vary from individual to individual, population to population. Some women may suffer from severe symptoms which greatly affects their personal and social functioning and also their quality of life [9]. In India the average age of Women is 47.5 years. But in India premature menopause occur due to a combination of environmental and genetic reasons [10].

Mohammed HA *et al., .,* (2014) reported that most severe symptoms in vasomotor, psychological, physical and sexual domains were, hot flushes, experiencing poor memory, being dissatisfied with their personal life, low backache and change in their sexual desire. The mean scores of each domain suggest that menopausal symptoms were associated with decrease in women quality of life [9].

Samarasiri.D.G.C.N*et al.,* (2017), conducted a phenomenological study to explore the women's experience of menopause. 20 women were purposively selected and data was conducted through semi – structured interviews. Four (04) themes emerged from the findings which are unbearable discomfort in the body, emotional instability and memory problems, problematic issues in family relationships and increased expenditure for the treatments. The findings revealed that women suffer from different experiences during menopause which reduce their quality of life [11].

Paquette, Shirley Ellen (1996) conducted a study on women's lived experience of natural menopause. Eight Newfoundland women were selected and data was collected through semi structured interviews. Thematic statements from the analysis were , Menopause is a normal change in a women's life; but problem with hot flushes is their unpredictability; the experience of menopause brings an increased consciousness of aging, receiving support during menopause can make the experience less traumactic. Becoming who they are was the essence of the lived experience [12].

Hoda L *et al.,* (2015) , reported on women's experience of menopause : a systematic review of qualitative evidence. The objective is to identify the best available evidence related to how women experience menopause worldwide.

From 24 included studies, 108 findings were extracted. These findings were aggregated into 17 categories and then into six synthesized findings. The findings are: the physical and emotional changes of menopause strongly affect the women, Resilience is improved at the time of menopause and coping strategies are adopted to enhance physical and emotional well being, etc., [13].

METHODOLOGY

Research Design

A qualitative phenomenological design was utilized in this study to explore women's lived in experience of menopause. This design is used to explore women's lived in experiences adequately and in – depth since here the people are allowed to talk freely.

Study Settings and Participants

The study was conducted in Kottucherry village, Karaikal district. Twelve women were purposively selected as participant for this study. They were in the age category 45 – 55 years and have experienced menopause for a period of one year. Their willingness to discuss experiences of menopause was also considered when selecting the participant. Women who had abnormal vaginal bleeding, hysterectomy, medical illness such as Diabetes Mellitus, Hypertension, cancer, renal disorders, thyroid disorders and mentally challenged women were excluded from the study.

Ethical Considerations

Ethical approval was obtained from Ethics Review Committee from our Institution and Deputy Director Immunization from Karaikal District. Prior conducting the study all the participant were fully informed about the purpose of the study. Informed consent was obtained from each and every participant before collecting the data and voluntary participation was encouraged. Confidentiality and Anonymity were assured to the participants.

Data Collection

Semi-structured interviews were used for data collection. The theme list was used to guide the interviews validated by referring appropriate literature and expert opinions. Probe questions were used to explore lived in experiences. The words such as " How, What, Why…" were used accordingly to encourage women to explain their lived in experiences in detail.

During the Interviews, the women were taken to an calm environment and separated from friends and family members to enhance free expression of their experiences without bias. The participants were treated in a respectful manner during data collection. The skills such as listening well, encouraging them by demonstrating positive affirmation of their view points, looking at the in an interested manner, nodding the head, etc., were used to collect the data. The researcher concentrated on their body language, non verbal clues such as facial expression, sighing which were used by the menopause women to express their experiences during interview process. Data was recorded on mobile phone. The duration of every interview is about 40 to 50 minutes on average.

Data Analysis

The data analysis was done using the Colaizzi's method. First, all the recordings were listened to carefully in order to obtain the clear sense of the whole content of the participants explanations and views. Then they were transcribed in to texts with several reviews. Then, important statements which were relevant to the phenomenon were extracted from them and recorded on separate sheets. The meaning of each phrase was described and defined. The formulated meanings were categorized in to sub themes and then themes and these categories were referred to initial protocols for confirming their validity. Then the fundamental structure of the phenomenon was described. The descriptions were reviewed to avoid ambiguity.

RESULTS AND DISCUSSION

Six themes were emerged from the findings, they are; Intolerable discomforts in the body, Loss of physical strength, problems in family relationships, Memory problems, Emotional instability and urinary problems. These are presented as model (Fig 1) which illustrates the women's experiences of menopause.

Intolerable Discomforts In the Body

During menopause, women experienced hot flashes, around their body (Fig 2). It lasts only for few minutes . During this time, they felt burning sensations around the whole body. Ms.D described her experiences on hot flushes.

"All of a sudden I feels very hot and burning sensations around my body especially around my face. But it last for only 2 to 3 minutes and sweats immediately". (Interview 04, Ms.D).

Women experienced excessive sweating during day time. They express that they sweats more than before. One such experience was recorded from Ms.B.

" Oh ..wof… intolerable it sweats a lot now-a-days. No such sweating before menopause. My blouse become completely wet and sweat excessively and now also u can see me how I sweats."Interiview-02, Ms.B

Women experienced less duration of sleep . Insomnia is a sleeping disorder due to menopause. Financial problems, increased frequency of urination creates sleep disturbances. They also said that their sleep was restful and falling asleep become very difficult .One such experience from Ms.C .

"Most of the night I don't sleep . It is very difficult to fall asleep . Many times I go to washroom which disturb my sleep too. Some time I keep thinking of my family problems, financial issues which really disturbs my sleep"(Interview-03,Mrs.C)

Women experience joint pain in knees , hips, and back. Joint pain is common symptom among menopausal women. They expresses that it affects their daily activities. Ms. E experienced about has joint pain as follows:

"Uh…knee pain is very severe .I am unable to sit down and if at all I sit, I am unable to get up immediately. I feel very difficult to climb to the staircase . Hip pain and low backache is also very severe. All this pain affects my daily activities .Its delays my work (Interview-05Ms.E)

Women reported dryness in vagina and decreases in sexual desire which creates a crucial and unpleasant experiences in face sexual activity becomes uncomfortable due to lack of lubrication. Vaginal dryness was the most emotionally disturbing menopausal symptoms since it reduces the frequency of engaging in sexual activities. One such experience is recorded from Ms.J.

"Mmm ..earlier …we had sex three or four times a week. But, now I feel very painful in my vaginal area, It is very discomforting experience for me .Acho…(with facial expression)it is very painful. (Interview – 10.,Ms.J)

The findings revealed that menopause is one of the stage of life, experienced in different ways. Hot flushes , sweating, sleep disturbances, joint pain , vaginal dryness were the strongest symptoms reported by women . The way in which the women approaches the changes either in positive or negative ways depends on their personal , family and socio- cultural background.

Loss of Physical Strength

During menopause , menopause women experiences decreases in their physical strength (Fig. 3). They feel that their energy level is very less and unable to do any activities as before. They feel very tired often even after a small work. The experience was described by Ms.F.

"sshh… No energy at all ma. Now-a-days. I become very tired often. Before I used to do all the household activities continuously. But now , after small work I become very tied and I need to take some rest and then continue my work .(Interview.06.Ms.F)

Problems in Family Relationship (Fig.4)

Menopause women experiences decreases in sexual desire, due to low estrogen level. Vaginal dryness is also another symptom faced by menopause women. Sexual activities becomes very discomfort and painful due to loss of libido and vaginal dryness. Ms. I described her experience as follows.

"Mmm ..earlier …we had sex three or four times a week .But ,now I don't have any feelings , now-a-days .I feel difficulties. When we are having sex I feel very painful in my vaginal area. Now we have a schedule for a month, when that day comes I feel like running somewhere and I am worried why that day comes. He doesn't understand my age and my difficulties during sex" (Interview.09, Ms.I)

Conflicts is common in many families. Conflicts occurs due to financial issues and some women reported that conflicts occurs due to un co-operation in sexual activities. Ms. A described her experience as follows.

"Happa..da he gets very angry when I don't co-operate for sexual activities. Conflicts occurs between us and he will not Speak for days"… (Interview – 01.,Ms.A)

Memory Problems (Fig.5.)

As a result of menopause many women noticed that , they have difficulty in concentration and memorizing . This makes them worried and can have significant impact on all aspects of daily life . Women reported that sleep disturbances also leads to difficulty in concentration and confusion in their life .They also experience changes in their cognitive function as well .Ms. C describes it as follows:

"Mmm… Now-a-days I have difficulty in concentrating things .In kitchen too, while cooking I have less concentration. Once before I used to cook mutton kulumbhu very tastily. But now I am Unable to concentrate in correct proportion of ingredients and taste also becomes less . My son scolds and tells me don't go to kitchen for cooking " (Interview-03.,Ms.C)

Majority of participants have described that they experience some level of forgetfulness associated with menopause. Due to this they face difficulties in their job and day-to- day activities. One such experiences is recorded from Ms.G.

"ha… ha… sometimes I used to Keep the money secretly without knowing to my husband. But I will forget where I have kept the purse and keep on searching for it". (Interview.07.,Ms.G.)

Emotional Instability (Fig.6.)

Menopause women experience mood swings and anger. They experience sudden intense anger. Sometimes they become irritable due to emotional instability. Ms. B describes her experience as follows.

"Mmmm… sometimes I keep on shouting at family members especially towards my children .Recently only I behave like this .I don't know why I am shouting often. Her children reported that madam, kindly advice our mom not to shout at us often .Now-a-days she is keep on changing her mood.."(Interview.02.,Ms.B.)

Some of the menopause women reported that they wanted to be alone sometimes. They experience this due to increase commitments at home and restless activities .They express that they may take rest when they are alone at home . It is described by an Ms. H as follows.

"oh.. I like to be alone sometimes and not always. All the time no rest at home..Continuous work makes me tired very often. Now-a-days my energy level also decrease. If I am alone I can take some rest "…(Interview.08.,Ms.H.)

Some women said that sometimes they felt frustrated when they are unable to make some decisions. Sleep disturbances , difficulties in concentration, poor memory are the main causes for difficulties in making decisions. One such experiences is reported by Ms. J.

"Mmm… After menopause , I feel experience difficulties in concentration . It leads to many confusion and it has many impact in my daily activities too. Problematic issues in family relationship also prevent me in taking some decisions ." (Interview.10 Ms.J)

Urinary Problems (Fig.7.)

Almost all participants have described that they experience frequency of urination . They express that they have difficulties in situations like long travelling, or in any ceremonies. Some women expresses that have dribbling of urine when laughing or coughing. They feel it as unpleasant situation . Frequency of urination disturbs their sleep too. Sleep disturbances make their tired and interrupts in their daily activities . It is described by on Interviewer Ms.D.

"Mmm.. I often go to washroom to pass urine .It is very difficult for me especially at night .It disturbes my sleep too. This disturbed sleep makes me very tired next day and I am unable to concentrate in things .Sometimes when I cough, automatically urine dribbles in my inskirt and becomes wet and it is an unpleasant situation for me"(Interview.04.,Ms.D).

CONCLUSION

Menopause had brought a series of challenging experiences which varies from individual to individual. Six themes related to menopause were emerged from this study, they are: Intolerable discomforts in the body, Loss of physical strength, problems in family relationships, Memory problems, Emotional instability and urinary problems. This study has proved that menopause has poorly affected their quality of life. But many studies have proved that awareness program or counseling regarding menopause symptoms and self help tips will help in improving the Quality of Life among menopause women.

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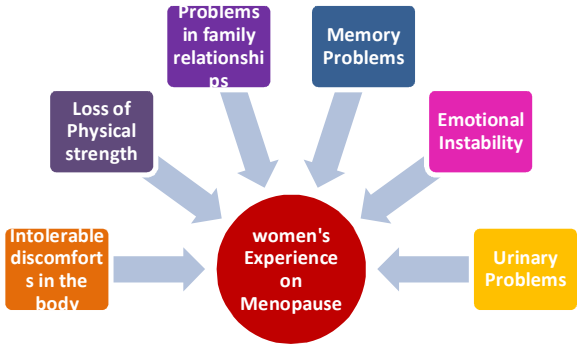

Fig.1 .Women's Experience of Menopause

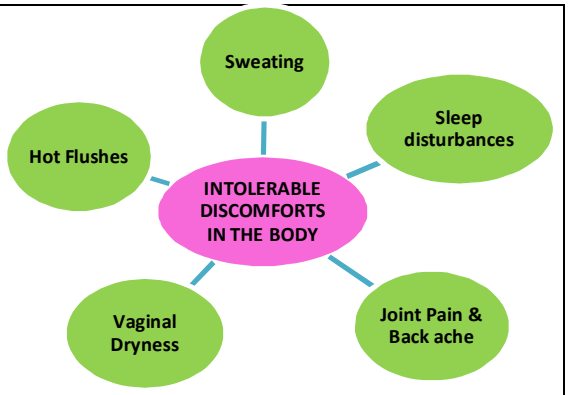

Fig.2. Women's Experience of Intolerable Discomforts in the body during Menopause

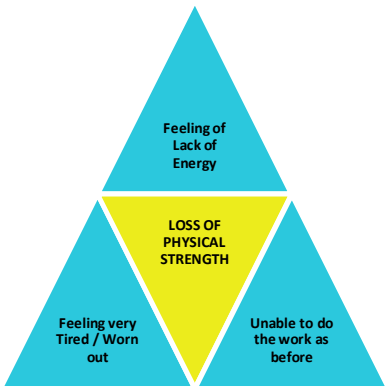

Fig.3. Women's Experience of Loss of Physical Strength during Menopause

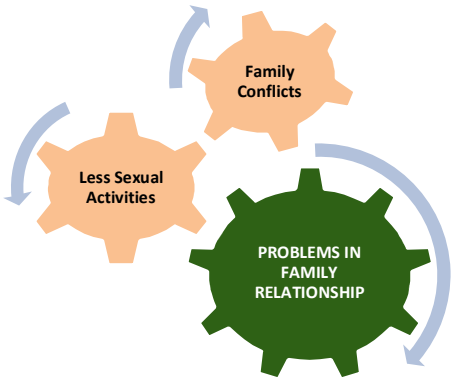

Fig.4. Women's Experience of Problems in Family Relationship during Menopause

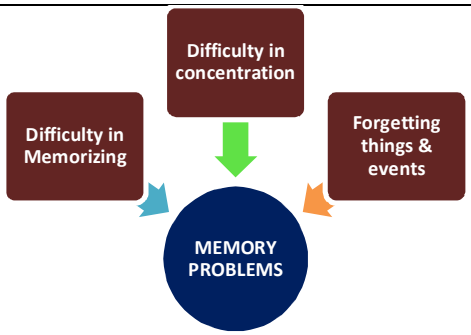

Fig.5. Women's Experience of Memory Problems during Menopause

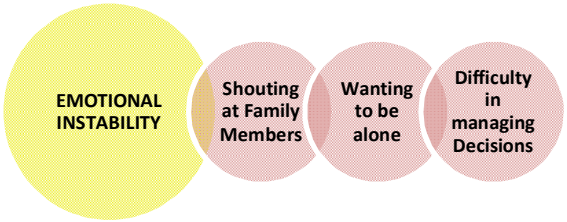

Fig.6. Women's Experience of Emotional Instability during Menopause

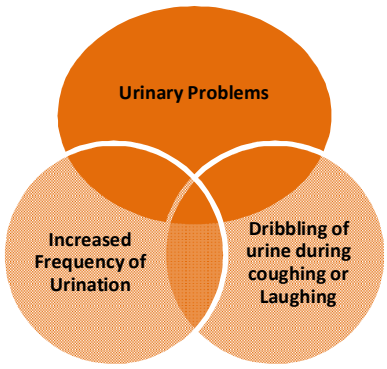

Fig.7. Women's Experience of Urinary Problems during Menopause

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RESEARCH ARTICLE

Molecular Docking of Luteolin from the Sprouts of *Cocos nucifera* L. against Hp-QAPRTase of *Helicobacter pylori*

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ABSTRACT

Significant contribution from Bioinformatics is the development of novel drugs through the identification of lead molecules against macromolecule targets. In the present scenario, researchers focus on the development of novel drugs from natural products enriched with secondary metabolites with minimal impact on the environment, economically viable without any side effects. Luteolin or 3',4',5,7-Tetrahydroxyflavone or digitoflavone or flacitran or flavopurpol, a potent flavone was isolated from the sprouts or haustorium of *Cocos nucifera* L. The objective of the present study is to analyze, validate and confirm the functional role of luteolin through *in silico* docking against the target protein molecule, Hp-QAPRTase (2B7N) of *Helicobacter pylori* which was retrieved from Protein Data Bank. Stereo chemical quality of the target protein was validated by Ramachandran plot which has indicated the presence of 90.1 per cent residues in most favoured regions. Computation of the non-bonded interactions between the atoms of the target protein molecule was carried out through ERRAT analysis which has revealed an overall quality factor of 96.966. Target protein and the ligand molecules were prepared in Autodock 4.2.6, MGL tools. Chain A of 2B7N with maximum number of residues in favoured regions was retained and 5 active torsions were set in the ligand molecule for docking. This was followed by the preparation of grid maps and launching of auto grid4. Molecular docking using Auto dock 4.2.6 with rigid docking method of genetic algorithm (GA) was followed with a population size of 150. Maximum binding affinity was

observed as –5.95 Kcal mol^{-1} in the second GA run and estimated inhibition constant (Ki) was found to be 43.63 uM. The docking results were analyzed and visualized using several leading visualization web tools such as Protein-Ligand Interaction Profiler, Proteins Plus (DoG Site Scorer) and BIOVIA Discovery Studio 2020 Visualizer. Aromatic edges and faces, charges, hydrogen bonds, hydrophobic interactions and ionizability were analyzed and these interactions confirmed the functional role of luteolin as a lead molecule for the first time from *Cocos nucifera* L. sprouts against Hp-QAPRTase of *Helicobacter pylori*.

Keywords: Molecular docking, luteolin, coconut sprouts, Hp-QAPRTase, *Helicobacter pylori*, peptic ulcer.

INTRODUCTION

Conventional health therapies are under practice for several years. The significance of different plant parts of medicinal plants, tree species and plant-derived food products are well-known for the discovery of natural drugs as these are cost-effective, toxic-free which can act as promising therapeutic agents [1].

Cellular endosperm of *Cocos nucifera* L. (Family: Arecaceae) is enriched with phytoconstituents having medicinal and pharmaceutical properties [2, 3]. It is reported that it has been used as folklore medicine in the treatment of different diseases such as cancers, diarrhea, diabetes, ulcers and many more [4]. Once the coconut germinates, the embryo's basal part embedded in the solid endosperm enlarges and produces a cotyledonary structure known as 'sprout' or 'haustorium'. Coconut sprouts were reported to possess cardio protective effect particularly during myocardial infarction [5]. Squalene, a triterpenoid from coconut sprouts, was reported from Gas-Chromatography- Mass Spectrometry (GC-MS) analysis and its anti-ulcer property was confirmed through *in silico* docking [6]. Wine with potent antioxidant activity was produced from the sprouts of *Cocos nucifera* L. using yeast strain, *Saccharomyces cerevisiae* [7]. Luteolin, a potent flavone belonging to the group of flavonoids was isolated for the first time from the coconut sprouts and its bioactive potential especially anti-ulcer activity was analyzed [8]. However, there is no study related to the identification of a promising lead molecule from the sprouts of *Cocos nucifera* L. enriched with several pharmaceutical properties and its functional role through *in silico* molecular docking.

The present scenario has been focused on developing alternative medicine using potential bioactive secondary metabolites from the natural products which can function against life threatening human diseases. In the current scenario, one such commonly occurring disease is peptic ulcer which is caused either because of non-steroidal anti-inflammatory drugs or due to the infection by *Helicobacter pylori* or due to excess acid peptic hyper secretion in Zollinger-Ellison syndrome [9]. *H. pylori* is a gram-negative pathogenic bacillus, flagellate, micro aerophilic bacteria. It is reported that the type-I strain of *H. pylori* possess maximum pathogenic activity which is due to the presence of cytotoxin-associated gene (cagA) resulting in the infiltration of polymorph nuclear leucocytes, monocytes, plasma cells in lamina propria and neutrophil infiltration [6]. The HP1355 gene from *H. pylori* (nadc) generally encodes *Hp*-QAPRTase, a type II quinolinic acid phosphoribosyl-transferase. It is a crucial enzyme in NAD^+ biosynthetic pathway. A step catalyzed by *Hp*- QAPRTase is vital in the biosynthesis of NAD and the survival of prokaryotic cells. Hence, *Hp*- QAPRTase acts as a captivating target for antibacterial secondary metabolites or drugs [10].

Various tools and software have several applications and aid in the evaluation of proteins, enzymes, nucleic acids, vitamins and several other lead molecules. It helps in the characterization of protein families and it is a preface for molecular evolutionary analysis [11]. Luteolin (3',4',5,7-Tetrahydroxyflavone) is an important bioactive dietary flavone occurring in different fruits, vegetables, medicinal plants and plant-derived food products with utmost medicinal value. It is also known as digitoflavone or flacitran or flavopurpol [8]. Luteolin is abundantly present in carrot, pepper, broccoli, olive oil, celery, thyme, oregano, rosemary, pomegranate, lettuce, turnip, cucumber, peppermint, perilla leaves, buckwheat sprouts, green tea, lemon, spinach, horseradish, fennel, cauliflower, cabbage,

parsley, kohlrabi and found in *Terminalia chebula* bark and leaves which are used as a traditional medicine. Luteolin glycosides, luteolin pyranosides, luteolin rutinoside are some of the derivatives of luteolin [12]. Luteolin is reported to possess anti-inflammatory, antioxidant, antiviral, diuretic, anti-ulcer, anti-microbial, anticancer, antispasmodic, anti-histaminic, anti-allergic, anti-secretory, bacteriostatic, anti-angiogenic, anti-proliferative, neuroprotective and several other bioactivities [8].

Coconut sprouts is a boon to the pharmaceutical industries for the development of novel drugs as it has potential primary and secondary metabolites. Since not much research work has been explored in the sprouts of *Cocos nucifera* L., the present study was focused with an objective to analyze the functional role of a predominant lead molecule, luteolin through *in silico* docking which has not been validated earlier. Hence, the rationale and novelty is to study the secondary metabolite, luteolin as a lead molecule for the anti-ulcer property against the target protein molecule, Hp-QAPRTase of *Helicobacter pylori*.

MATERIALS AND METHODS

Input Files- Target Protein and Ligand Molecule

X-ray crystal structure of phosphoribosyl transferase in complex with quinolinic acid of *Helicobacter pylori* was used as the target protein retrieved from Protein Data Bank (PDB ID: 2B7N; Resolution 2.30 Å; DOI: 10.2210/PDB2B7N/pdb; https://www.rcsb.org/structure/2B7N). The ligand molecule, luteolin which was identified and characterized from the sprouts of *Cocos nucifera* L. was drawn using the software, Chem Draw Ultra version 12.0 [8] (Fig.1)

Ramachandran Plot

Stereochemical quality of the target protein molecule was analyzed through residue-by-residue geometry and overall structure geometry using PROCHECK server (https://www.ebi.ac.uk/thornton-srv/software/PROCHECK/). The target protein molecule (2B7N) was validated with Ramachandran plot [13].

ERRAT Analysis

ERRAT analysis (https://saves.mbi.ucla.edu/) was carried out in order to compute the non-bonded interactions between the atoms of the target protein molecule (2B7N) [14].

Softwares Used

Different softwares such as Autodock 4.2.6, MGL tools and Open Babel were downloaded, installed and used for performing *in silico* analysis to analyze the protein-ligand interactions.

Preparation of Target Protein Molecule

The target protein was first prepared using Autodock 4.2.6, MGL tools [15]. Water molecules and hetero atoms in 2B7N were removed. 2B7N possess three identical chains namely, chain A, B and C. Based on the Ramachandran plot validation, chain A of 2B7N was retained whereas chain B and C were removed. It was followed by the addition of polar hydrogens to the target molecule. Further, Kollman and Gasteiger charges were computed [16].

Preparation of Ligand

The ligand molecule, luteolin, was drawn using Chem Draw Ultra version 12.0 and converted to PDB format using Open Babel. Ligand molecule was prepared using Autodock 4.2.6, MGL tools. Root was detected in the ligand, Gasteiger charges were added, non-polar hydrogens were merged and aromatic carbons were detected. Ligand with three different types of bonds namely, rotatable, non-rotatable and unrotatable bonds were analyzed of which

rotatable bonds are necessary for docking. Further, the active torsions were set and the ligand was finally saved (.pdbqt) for molecular docking [16].

Auto Grid Calculation and Launching Auto Grid 4

Active binding site in the target protein molecule was detected based on the literature and a grid was placed in equal number of points (40 × 40 × 40) in XYZ dimensions with 0.500 spacing in angstrom. Further, coordinates of central grid point of maps were set (-10.644, 180.307, -3.183) at x, y and z centers respectively. Minimum coordinates (-20.644, 170.307, -13.183) and maximum coordinates in grid (-0.644, 190.307, 6.817) were maintained and the file was saved (grid.txt). Further, the output was saved as Grid Parameter File (.gpf). Generally, the current total grid points per map was 64,000. The program path name (autogrid4.exe), the parameter file name (.gpf file) and the log file name (.glg file) were set and auto grid 4 was launched and the grid maps were generated respectively [16].

Molecular Docking

Molecular docking using Auto dock 4.2.6 was carried out with rigid docking method of genetic algorithm with a population size of 150. Further, the maximum number of energy evaluations were set as 2500000 and maximum number of generations were 27,000 respectively. Moreover, the number of GA runs were 10. The program path name (autodock4.exe), the parameter file name (.dpf file) and the log file name (.dlg file) were set and auto dock 4 was launched. Out of 10, the GA run indicating maximum negative value was an indication of promising binding affinity and was considered as the best run. Molecular docking results in several interactions between the target protein and ligand [6, 16].

Analysis and Visualization of Autodock 4 Results

Protein-ligand interactions were analyzed and visualized using several leading visualization web tools such as Protein-Ligand Interaction Profiler (https://plip-tool.biotec.tu-dresden.de/plip-web/plip/index) [17], Proteins Plus (DoG Site Scorer) (https://proteins.plus/) [18] and BIOVIA Discovery Studio 2020 Visualizer (https://discover.3ds.com/discovery-studio-visualizer-download).

RESULTS

Hp-QAPRTase of *Helicobacter pylori* (2B7N) was used as the target protein molecule and luteolin was used as the ligand molecule to study its functional role.

Ramachandran Plot

Validation of the target protein molecule was carried out through Ramachandran plot which has indicated the presence of 90.1 per cent residues in most favoured regions [A, B, L], 9.1 per cent residues were found to be in additional allowed regions [a, b ,l, p] and 0.8 per cent residues were located in generously allowed regions [a, b, l, p]. No residues were present in disallowed regions (Fig. 2).

ERRAT Analysis

Non-bonded interaction between various atoms in 2B7N which were computed by ERRAT analysis revealed an overall quality factor of 96.966 (Fig. 3).

Preparation of Target Protein Molecule

The target protein molecule, 2B7N was prepared and saved in such a way that it can be docked with the selected ligand molecule, luteolin. Chain A with maximum number of residues (96 per cent) located in favoured regions was retained whereas B and C were removed in order to reduce the computation time (Fig. 4).

Preparation of Ligand

In the ligand, Gasteiger charges were thoroughly computed, 6 non-polar hydrogens were merged, 15 aromatic carbons and 5 rotatable bonds were detected with 5 active torsions (Fig. 5).

Auto Grid Calculation and Launching Auto Grid 4

Auto Grid is a pre calculation program resulting in grid maps of the interaction energies and it is an important step in docking. Grid maps are used by docking calculations in order to determine the total interaction energy for luteolin with the target protein (Fig. 6).

Molecular Docking

Luteolin docked against the target protein molecule showed maximum binding affinity of –5.95 Kcal mol^{-1} in the second GA run (Table. 1 and 2). It's Cluster RMSD (Root Mean Square Difference) and Reference RMSD values were found to be 0.00 and 0.82 A which indicated the promising binding affinity in the target-protein complex. Further, three multi-member conformational clusters were observed out of ten runs.

Analysis and Visualization of Autodock 4 Results

The docking results were first analyzed and visualized in Protein-Ligand Interaction Profiler (PLIP) which indicated promising hydrophobic and hydrogen bond interactions between the various amino acid residues. In Proteins Plus visualizer, DoG Site Scorer accurately detected and visualized the binding site in the protein-ligand interaction complex and was split into sub-pockets. Higher the drugg ability score (between 0-1) in the DoGSiteScorer resulted in the confirmation of the presence of potential binding pockets. Protein-ligand interaction revealed a maximum druggability score of 0.83 thereby revealing that the detected binding pocket is more druggable and accurate (Fig. 7). In BIOVIA Discovery Studio Visualizer, Protein-ligand docked complex interactions, ligand interactions, receptor-ligand interactions such as aromatic edges and faces, interpolated charges, hydrogen bonds, hydrophobicity and ionizability were analyzed and visualized (Fig. 8 and 9). 2 dimensional diagram of the protein-ligand interactions was accurately generated in BIOVIA Discovery Studio Visualizer (Fig. 10).

DISCUSSION

Molecular docking not only accelerate the identification of drugs in addition, it predicts their resistance and characterize the side effects [19]. Identification of lead molecules from natural products without any side effects is the need of the hour. There are different softwares available namely Autodock tools, Mcule, Patch dock and many more [20, 21]. X-ray crystal structure of phosphoribosyl transferase in complex with quinolinic acid of *Helicobacter pylori* was used as the target protein and luteolin was used as the ligand molecule to confirm its functional role related to anti-ulcer activity. Single subunit of Hp-QAPRTase has a molecular weight (30.8 kDa) followed by 11 α helices and 12 β strands in two different domains (N and C terminal) [10].

Three backbone torsion angles (Φ, ψ, ω) were reported to be the determinants of a protein fold. Allowed range of co-angles are usually restrictive and hence the variations in these angles will not be giving variety of conformations. This led to the development of Ramachandran plots which are the 2 dimensional scatter plots Φ, ψ pairs, comparing these to a predicted distribution [11]. It is essential to validate the target protein before performing *in silico* analysis. Earlier study has reported that a good quality model would be expected to have over 90 per cent in the most favoured regions [13]. Similar findings were observed in 2B7N, where 90.1 per cent residues was observed in most favoured regions which indicated that the selected target protein is a good quality model and suitable for *in silico* docking.

ERRAT is an online program to verify the structure of proteins usually determined by crystallography method. It is reported that the regions at the 95 per cent confidence level can be rejected (yellow) and it is expected that 5 per cent

of a good protein structure should have an error value above this level. At 99 per cent level regions appearing in red can be rejected [14]. However, in the present study, there were no red regions in 2B7N. The observed results coincides with the underlying principle of ERRAT analysis and makes 2B7N a verified protein structure for *in silico* docking with the selected ligand.

Preparation of target protein and the ligand molecules are considered to be an important refinement process. There is no accurate web tool or software till date which can predict how the water molecules are going to interfere with the ligand in an active binding site. When a crystal structure is produced, it is always done in a solution state where some of the water molecules enter the binding site. Hence, it is essential to remove the water molecules before docking. All the hetero atoms were removed in 2B7N in order to avoid any kind of hindrance or error [16]. Chain A of 2B7N was used for docking as 96 per cent of its residues were present in the favoured regions in Ramachandran plot. There are different types of interactions that may happen in the protein-ligand complex such as hydrogen bond interactions, hydrophobic interactions or pi-pi stacking. Hence it is essential to add hydrogens to the target protein. A study showed polar hydrogens were best suited for 2B7N, hence these were added and target protein was prepared. Kollman charges were added which are the template values for every single amino acid which was derived from corresponding electrostatic potential using quantum mechanics. However, Gasteiger charges are computed on the concept of electronegativity equilibration. Hence, addition of charges is essential because in the absence of charges, the electrostatic interactions between the ligand-protein will be absent [22].

The present findings revealed that luteolin had three different bonds namely rotatable, non-rotatable and unrotatable bonds of which five rotatable bonds played a potent role in making the ligand molecule appropriate for docking. Number of torsions in the ligand is related to its flexibility and is incorporated as an essential variable in the thermodynamic function of binding free energy [23]. In this study, luteolin was prepared with 5 active torsions to get a maximum binding affinity which is correlated to the earlier study.

AutoGrid is a program which usually pre-calculates grid maps of interaction energies for different types of atoms namely aliphatic and aromatic carbons, hydrogen bonding and many more with a macromolecule. Grid map plays a crucial role in the determination of total interaction energy in protein-ligand interaction [15]. In the present study, grid maps were accurately generated for molecular docking.

Autodock is a computational program which is based on empirical free energy force field and Lamarckian genetic algorithm [24]. Binding energy of a ligand-protein molecule is a combination of hydrogen bonds, electrostatic, torsion free energy, dispersion, repulsion and total intermolecular energy. Cluster RMSD is Root Mean Square Difference in coordinate between the docking conformation and cluster reference. Reference RMSD is Root Mean Square Difference between the docked complex and the input structure. Inhibition constant is correlated to half of maximal inhibitory constant at which 50 per cent of the protein is inhibited. This quantity measure indicated the amount of specific drugs or substances needed to inhibit the biological process. Promising binding affinity was revealed which depicts that luteolin can act as a potent anti-ulcer agent. Different energy values and RMSD of the protein-ligand complex depicted the ability of luteolin to suppress *H. pylori* infection. The obtained inhibition constant (Ki) value of 43.63 uM is an evidence that the target protein is inhibited.

Molecular visualization is an important aspect concerned with *in silico* analysis. It is essential to study the different interactions of amino acid residues, bond interactions and many more in addition to promising binding affinity (protein-ligand complex). Hence, visualization plays a major role in these aspects. PLIP (Protein-Ligand Interaction Profiler) is a visualization web tool which allows to identify non-covalent interactions in the protein-ligand complex. It provides atom-level information on the characteristics of binding and its visualization [17]. The present findings revealed that the presence of strong hydrogen bonds and hydrophobic interactions in the protein-ligand complex might be responsible for the maximum binding affinity resulting in the inhibition of the target protein. Proteins Plus visualizer focuses on the protein-ligand interactions, in which DoGSiteScorer (grid-based method) is predominantly

used. It depicts potential binding pockets based on protein's 3D structure by splitting them into sub-pockets as reported in earlier studies. In default, there is a druggability score for each sub-pocket based on the hydrophobicity, volume and enclosure. Moreover, a subset of descriptors are present in this web tool to predict sub-pocket druggability score. Maximum the score indicates that the pocket is more druggable [25]. Maximum druggability score (0.83) observed in the present study is a clear evidence that the binding pocket of the target protein is more druggable which may be the reason for binding of the ligand molecule at the accurate site. BIOVIA Discovery Studio 2020 Visualizer is a graphics visualization tool for viewing, analyzing, optimizing the protein-ligand interactions and generating models using the data. Aromatic edges and faces, interpolated charges, hydrogen bonds, hydrophobic interactions and ionizability of the protein-ligand interactions were visualized. These interactions are responsible for the inhibitory potential of the ligand molecule, luteolin. Thus, visualized structures are clear evidence that the luteolin can act against Hp-QAPRTase of *Helicobacter pylori.*

Novelty and significant findings of the present study includes,
(i) Identification of the functional role of luteolin, a flavone reported for the first time from the *Cocos nucifera* L. sprouts or haustorium through *in silico* docking,
(ii) Coconut sprouts with luteolin can be used as a nutrient or dietary supplement without any side effects for peptic ulcer problems,
(iii) Coconut sprouts being an anti-ulcer agent can be further used for the prevention and management of peptic ulcer as it is enriched with potential secondary metabolites.

CONCLUSION

The functional role of luteolin from the sprouts of *Cocos nucifera* L. against Hp-QAPRTase of *Helicobacter pylori* was confirmed through *in silico* molecular docking. Luteolin is a bioactive flavone with numerous pharmaceutical properties. This study emphasizes the role of luteolin in the promotion of nutraceuticals from the coconut sprouts. Drug development and large scale commercial production with quality check and clinical trials are in progress.

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Conflicts of Interests

The authors declared that they had no conflicts of interests.

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Author's Contribution

Abiraami Valli. S, Ph.D. Research Scholar performed the experiments, drafted the manuscript, analysed and interpreted the data. Dr. S. Uma Gowrie, Associate Professor and Dean of Research (Aided) proposed the concept and designed the experiments, supervised, analysed, interpreted the data, technically supported, critically revised and finally approved the manuscript.

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Table. 1: Docking results of the protein-ligand interactions

Rank	Sub- Rank	GA Run	Binding energy (Kcal mol^{-1})
1	1	2	–5.95
1	2	4	–5.42
1	3	9	–5.33
2	1	8	–5.09
3	1	7	–4.98
4	1	3	–4.85
4	2	1	–4.67
4	3	6	–4.56
5	1	5	–4.75
5	2	10	–4.75

Table. 2: Docking results of the GA run with maximum binding affinity

Estimated Free Energy of Binding (Kcal mol^{-1})	Estimated Inhibition Constant (Ki)	Final Intermolecular Energy, vdW + Hbond + desolv energy, Electrostatic Energy (Kcal mol^{-1})	Final Total Internal Energy (Kcal mol^{-1})	Torsional Free Energy (Kcal mol^{-1})	Unbound System's Energy (Kcal mol^{-1})
–5.95	43.63 uM	–7.44, –6.72, –0.72	–1.82	+1.49	–1.82

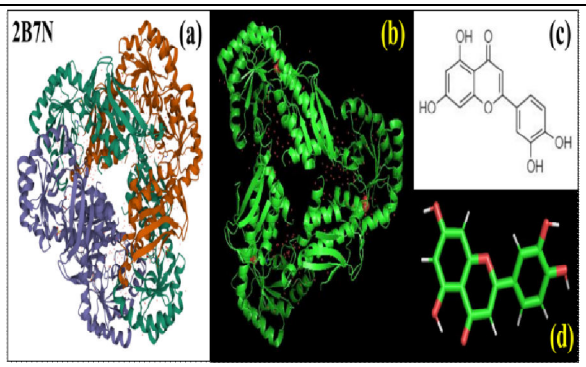

Fig. 1: (a) 3-D structure of target protein from PDB (b) 2B7N visualized in PyMOL (c) Luteolin drawn using ChemDraw (d) Luteolin visualized in PyMOL

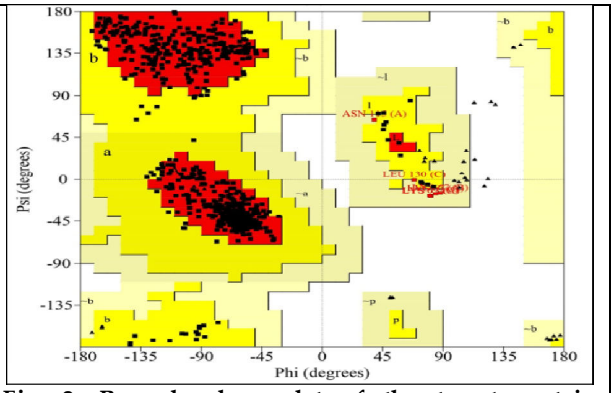

Fig. 2: Ramachandran plot of the target protein molecule, 2B7N

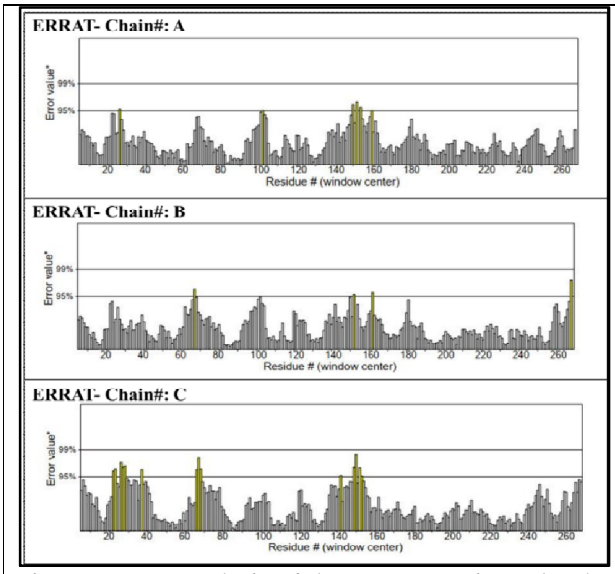

Fig. 3: ERRAT analysis of the target protein molecule, 2B7N

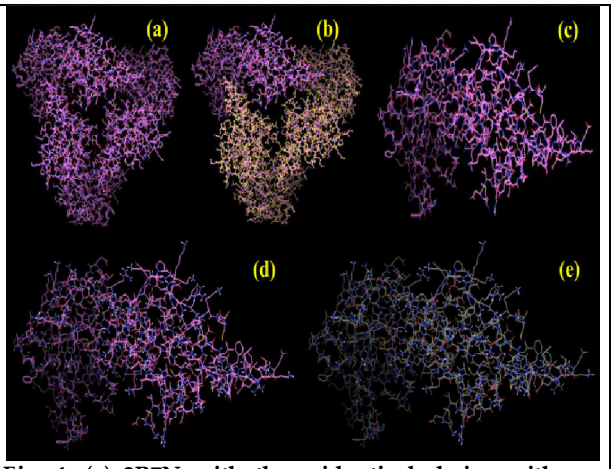

Fig. 4: (a) 2B7N with three identical chains with no water molecules and hetero atoms (b) Chain A (purple) highlighted in 2B7N (c) Retained Chain A of 2B7N (d) Addition of polar hydrogen atoms, Kollman, Gasteiger charges and atoms edited with Assign AD4 type (e) Prepared target protein molecule

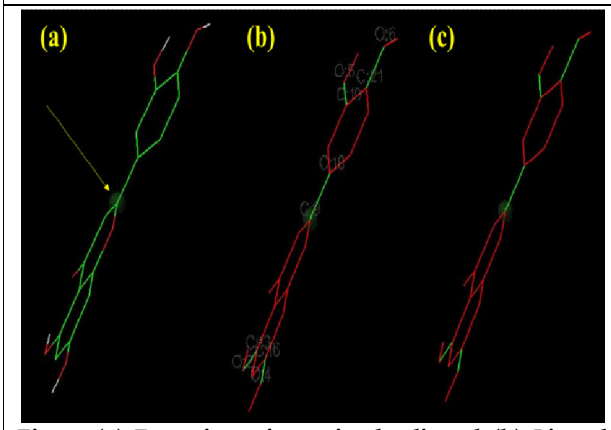

Fig. 5: (a) Detection of root in the ligand (b) Ligand indicating rotatable (green), non-rotatable (magenta) and unrotatable (red) bonds (c) Prepared ligand with 5 rotatable bonds and active torsions for docking

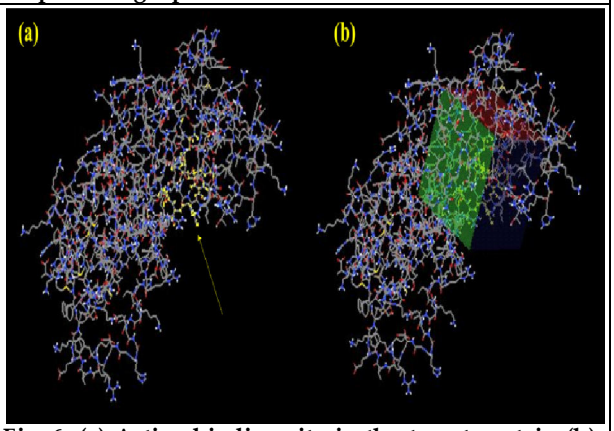

Fig. 6: (a) Active binding site in the target protein (b) Illustration of grid map

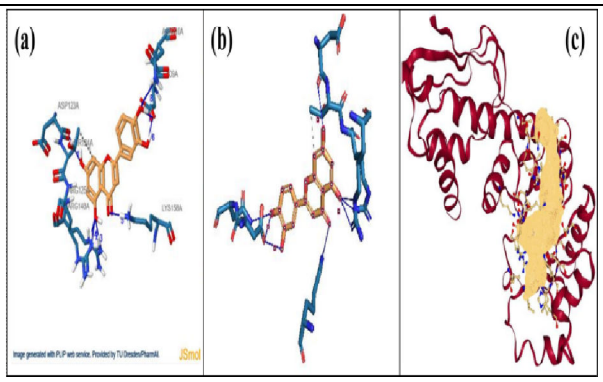

Fig. 7: (a) Protein-Ligand complex visualized in PLIP (b) Generated PLIP structure visualized in PyMOL (c) DoG Site Scorer pose with maximum druggability score in Proteins Plus

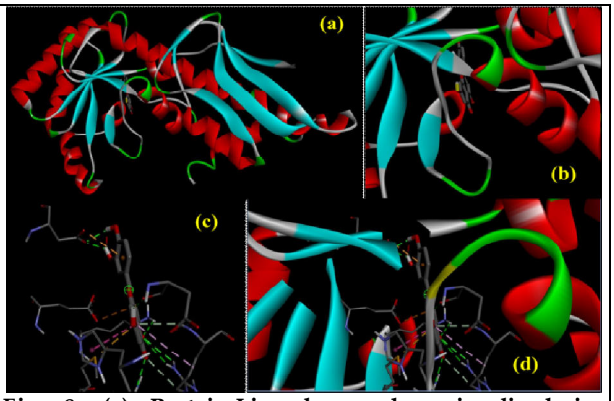

Fig. 8: (a) Protein-Ligand complex visualized in BIOVIA Discovery Studio 2020 Visualizer (b) Ligand interacting with receptor (c) Visualization of ligand interactions (d) Target-Ligand interactions

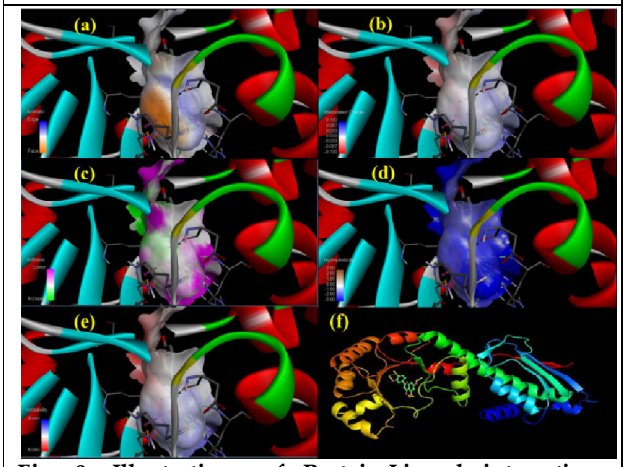

Fig. 9: Illustrations of Protein-Ligand interactions visualized in BIOVIA Discovery Studio 2020 Visualizer (a) Aromatic edge and faces (b) Charges (c) H-Bonds (d) Hydrophobicity (e) Ionizability (f) Ball and stick visualization of protein-ligand interactions in PyMOL

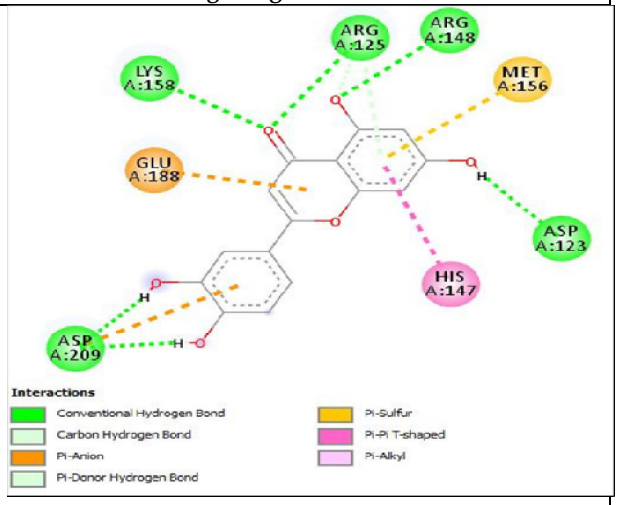

Fig. 10: 2D diagram of protein-Ligand interactions generated in BIOVIA Discovery Studio 2020 Visualizer

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REVIEW ARTICLE

A Review on Controlled Release Drug Delivery System

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ABSTRACT

Controlled drug delivery is one which delivers the drug at a predetermined rate, for locally or systemically, for a specified period of time. Continuous oral delivery of drugs at expectable and reproducible kinetics for pre determined period through the course of GIT. Controlled release drug delivery employs drug-encapsulating devices from which therapeutic agents may be released at controlled rates for long periods of time, oscillating from days to months. Such systems offer numerous advantages over traditional methods of drug delivery, including tailoring of drug release rates, protection of fragile drugs and improved patient comfort and compliance. Controlled drug delivery system is to make sure safety and to improve efficiency of the drug as well as patient acquiescence. A controlled release system includes any delivery system that grasps slow release of the drug over an prolonged period of time. This is achieved by better control of plasma drug level and less frequents dosing. The rationalization for the developing of controlled release drug delivery system of drug is to improvement its therapeutic aids. Minimalizing its side effect even as improving the management of the disease condition. It is the purpose of this piece of writing to comprehensively analysis drug delivery system design for control release by conversing the recent parents available.

Keywords: controlled drug delivery system, drug release mechanism, modified release, uses of controlled release drug delivery system, advantages, disadvantages..

INTRODUCTION [1-5]

Top consideration is focused on the expansion of ongoing or regulated drug delivery programs. Oral drug administration has always been the most common and preferred method of delivery for most medical agents. A

well-controlled drug delivery system is one that delivers the drug at a predetermined rate, locally or systematically, at a specific time. A different standard for immediate release, the rate of drug exposure in the body within such a system is not controlled by the absorption process. The concentration of the drug in the body should be kept above the active level and below the toxic level. However when the drug is given to a patient, the initial concentration of the drug in the body is above the level of toxicity before it decreases and often reaches an ineffective level due to excretion. Decreased fluid retention will cause tissue absorption and transport to the bloodstream. The peaceful drug delivery system should deliver the drug at a rate determined by the body's needs during treatment that is, it should supply the desired concentration of plasma to the plasma and keep it stable throughout the course of treatment.

There are several reasons for the attraction of these scale forms. It is widely known that in many disease regions, a large number of active chemicals are already present in the functioning of these drugs, however, they are often limited by side effects or the need to treat the compound in a clinical setting. Polymers have been very effective in the development of solid, liquid, and dosage forms and are particularly useful in the development of modified drug delivery systems. Both synthetic and natural polymers have been extensively investigated for this purpose. However, the use of natural polymers in pharmaceuticals is attractive because they are economical, readily available, non-toxic, and chemically modified, which can be easily borrowed and sparingly, and with the growing effect is the fact that plant resources are renewable and if refined or harvested in a sustainable way. always of raw material.

POLYMER USING DRUG DELIVERY PROGRAM [6-9]

Polymers can be used as film coating to hide the unpleasant taste of the drug, to strengthen the stability of the drug and to change the characteristics of the drug release. The review focused on the importance of the pharmaceutical polymer for controlled drug delivery applications. Sixty patients benefit from high-quality drug delivery programs today, obtaining the safe and effective doses of drugs they need to fight various human diseases, including cancer. Controlled Drug Delivery (CDD) occurs when a polymer, either natural or synthetic, is cleverly combined with a drug or other active agent in such a way that the active agent is extracted from the contents in the manner previously prescribed. Active agent release may occur over a long period of time, may be cyclic for a long time, or may be caused by natural or other external events. In any case, the goal behind drug delivery control is to implement effective treatment options while eliminating the potential for less and more overdose.

CONTROL USE RELEASES DRUG DISPLAY PROGRAM: [10,11]

Polymers are becoming increasingly important in the field of drug delivery. The use of pharmaceutical polymers from its use as additives to tablets to control agents and flow controls for liquids, suspensions and emulsions. Polymers can be used as film coating to hide the unpleasant taste of the drug, to strengthen the stability of the drug and to change the characteristics of the drug release. The review focused on the importance of the pharmaceutical polymer for controlled drug delivery applications. Sixty patients benefit from high-quality drug delivery programs today, receiving the safe and effective doses of drugs they need to fight various human diseases, including cancer. Controlled Drug Delivery (CDD) occurs when a polymer, either natural or synthetic, is cleverly combined with a drug or other active agent in such a way that the active agent is extracted from the contents in the manner previously prescribed. Active agent release may occur over a long period of time, may be cyclic for a long time, or may be caused by natural or other external events. In any case, the goal behind drug delivery control is to implement effective treatment options while eliminating the potential for less and more overdose.

CRDDS CANDLES: [12-14]

All medications cannot be administered as regulated dosage forms. The drug should have the following characteristics of the structure of the controlled release dosage forms.

- A short life span
- Longer life expectancy
- Minor treatment index
- Absorption rate

- How to suck
- First pass result

FACTOR INFLUENCING DESIGN AND PERFORMANCE OF CONTROLLED DRUG DELIVERY SYSTEM :[15-20]

➢ Bio Features of Medicinal Drugs
- Weight of drug cells
- Liquid solubility of the tree
- The apparent coefficient of separation
- Drug stability
- Management route

➢ Pharmacokinetic properties of the drug
- Absorption rate
- Elimination of part of life
- Physical level
- Scale from the index

➢ Pharmacodynamic properties of the drug
- Level of Treatment
- Indication for treatmen
- Plasma accountability relationships

The formulation is based on the physiological characteristics of the drug and the pharmacokinetic behavior of the drug. With the standard dosage, the dose-limiting dose is usually absorbed by the bio-membrane when incorporated into a controlled drug administration step to reduce the rate of drug release in dosage form.

Classification of Controlled Release Drug Delivery Systems[21-23]
Depending on the drug release mode, these programs are categorized as follows;
1 program
- Two types of pool device distribution system and matrix devices.
- The three types of matrix system of dispersion are hydrophobic, hydrophilic and fat-wax matrix system.

2. Ongoing disintegration of systems
- Soluble solidification systems are a soluble pool, a soluble matrix and a continuous reinforced delivery system.

3. Methods of applying osmotic pressure
- One osmotic pump chamber
- Pump Elementary Osmotic Pump (EOP)
- Multi-room osmotic pump
- Pump Push pull osmotic pump.
- Pump Osmotic Pump with second expandable cable
- Certain types

The most widely used systems for osmotic diversity; controlled osmotic porosity pump, monolithic osmotic systems, osmotic bursting osmotic pump, OROS-CT, Multi-Particulate Delayed Release Systems (MPDRS) and Liquid Oral Osmotic System (L-OROS).

4. Porcelain Matrix system based on porosity

Mineral matrix is based on porosity systems such as macro porous, micro porous and non-porous system.

5. Mixed Matrix system

Various matrix systems are combined with bio-mucoadhesive, floating, critical pH formation and decay

Patented Pharmaceutical Controlled Release System [24]

Existing viewing sites are interested in more controlled or sustainable copyright technology based on modern patents and provides a framework for a variety of copyrighted copyright technology. International patent data Patent Analysis Software Cobalt IP 2012, Patent Free online, WIPO, Patent Scope, United States Patent Office And (USPTO) and Google patents were hired to collect copyright and patent applications.

hydrophilic matrix system, (3) Hydrophobic matrix system, (4) Porous matrix system, (5) Enteric coatedmatrix system, (6) Floating matrix system

The controlled output system is divided into the following main categories according to the output pattern.

i. Evaluate the pre-planned drug delivery system
ii. The drug delivery system used
iii. Response controlled by a drug delivery system
iv. A plan directing the delivery of drugs to the area

Evaluate the pre-planned drug delivery system [25]

In this case, the release of the drug molecule in the delivery system is prearranged with a specific profile of the drug flow rate. The system controls the proliferation of drug particles within or across a central obstacle or within the delivery system.

Polymer membrane permeation system controlled

In this system, the drug is placed in whole or in part in a water storage area with a drug reservoir covered by a flow rate that controls the polymeric membrane. In a drug source, a drug can be solid or dispersed in solid drug particles or a drug solution centered in a liquid or in a solid dispersal form. The polymeric membrane may be made of a synthetic form of skin such as porous or a non-porous or thin layer of space-filled membrane.

Polymer-controlled matrix system

In this tree, the pond is prepared by particles of the drug dispersed evenly in a ratio that controls the hydrophilic or lipophilic polymer matrix. The resulting medicated polymer effect provides a honeycomb disk with a defined surface and a controlled size.

Micro pool partition control system

Drug reservoirs the suspension of solid particles in an aqueous solution of a water-soluble polymer. Micro-dispersing isolation system is controlled using high scattering techniques. Near the pond and the distribution of the matrix forms a small dam

Ways to Achieve Controlled Drug Delivery [26]

The purpose of designing an ER measurement form is to develop a reliable structure that has all the advantages of an immediate release volume form but without volume disposal. Various techniques have been used in the design of ER products. Generally, the extended structure can be divided into different categories depending on the drug release mechanism.

- Removable Controlled Release
- Diffusion Controlled Release

- Release of Ion Exchange Resins
- Swelling Controlled Release

Controlled Release Disposal [27]

This type of controlled emission involves two processes, the separation of drug molecules from the surface of its solid structure to the visible local connector, followed by its diffusion from the visible connector to the contents of the liquid mass. The level of dissolution and the amount dissolved per unit time in this system can be calculated using the Noyes-Whitney calculation relating to the degree of dissolving solids in solid and dissolved material structures, as well as the relationships

Diffusion Controlled Release [28]

In this type of controlled release system, the active ingredient varies by polymeric condition. These are mainly classified as repositories and matrix systems.

Water Storage System [29]

Cellulose-based products are often used in pool systems. It has a spine (pond) and a covering membrane (distribution barrier). The active ingredient varies in the pool using a coating layer. In a pool system where a drug depot is surrounded by a layer of polymeric hydrogel, Fick's first distribution law can be used to describe drug extraction by membrane.

Matrix system

In this review article the emphasis is on the matrix controlled output of the design of extended expansion tablets. The matrix system consists of active and inactive ingredients that are dispersed evenly and mixed into a simulation form. It is the most widely used oral technology and the popularity of matrix systems can be due to several factors. The exclusion from matrix type construction is governed by Fick's first distribution rule.

Release of Ion Exchange Resins[29]

Ion exchange structures are insoluble polymers connected to water carrying the invisible active groups. The ingredients have been used in a variety of pharmaceutical programs, especially to hide taste and controlled extraction systems. In tablet formation, ion exchange structures have been used as composites, due to their inflammatory potential. It forms an irreversible complex with ionizable drugs when long-term exposure to a drug in resin. The resin-bound drug is removed when the appropriate ion contacts the ion exchange groups. The area and length of diffusion pathway, and the amount of cross-linked polymer in the resin moiety governs the rate of drug release.

Swelling Controlled Release[30]

Swelling controlled systems are based upon swelling of ER polymer. Due to the viscoelastic properties of the polymers, which are enhanced by the presence of cross-linked network, anomalous penetrate transport can be observed. This behavior is bound by pure Fickian diffusion and case II transport. Therefore, transport can be reduced to three driving forces. The penetrate concentration gradient, polymer concentration gradient and osmotic force behavior are observed as a result of polymer network. Appropriate polymer can counterbalance normal Fickian diffusion by hindering the release of embedded drug, leading to an extended period of drug delivery, and possibly zero-order releaseDrug release from swellable matrix tablets can be affected by glassy-rubbery transition of polymer (as a result of water penetration into the matrix where interaction among water, polymer and drug or fillers is considered as the Primary factor for release control) and the various formulation variables, such as polymer grade and type, drug to polymer ratios, drug solubility, drug and polymer particle sizes, compaction pressure and presence of additives or excipients in the final formulation.

Advantages of Matrix System[31]
Unlike reservoir and osmotic systems, products based on matrix design can be manufactured using conventional processes and equipments. Secondly, development cost and time associated with the matrix system generally are viewed as variables, and no additional capital investment is required. Lastly, a matrix system is capable of accommodating both low and high drug loading and active ingredients with a wide range of physical and chemical properties.

Limitations of Matrix System[32]
As with any technology, matrix systems come with certain limitations. First, matrix systems lack flexibility in adjusting to constantly changing dosage levels as required by clinical study outcome. When new dosage strength is deemed necessary, more often than not a new formulation and thus additional resources are expected. Furthermore, for some products that require unique release profiles (dual release or delayed plus extended release), more complex matrix based technologies such as layered tablets are required.

Matrix System Types
The matrix system can be divided into two categories depending on the type of delaying agents or polymeric materials.
1) Hydrophobic matrix system
2) Hydrophilic matrix system

Hydrophobic Matrix system. [33,34]
This is the only system in which the use of polymer is not necessary to provide controlled drug release, despite the use of unresolved polymers. As the name suggests, the main control measures for the hydrophobic matrix of water do not dissolve naturally. These ingredients include waxes, glycerides, fatty acids, and polymeric substances such as ethyl cellulose, methyl cellulose and acrylate copolymer. To measure drug release, it can help to incorporate soluble ingredients such as lactose into the formulation. The presence of an unresolved ingredient in the formulation helps to maintain the body size of the hydrophobic matrix during drug release. Therefore, the distribution of an active ingredient from the system is an extraction method, and the corresponding extraction factor can be defined by the Higuchi equation known as the square root of the kinetic discharge time. The square root of the time release profile is expected with a porol monolith, where the release in this system is similar to a drug load. In addition, hydrophobic matrix systems are generally not suitable for an unresolved drug because the concentration gradient is too low to provide adequate drug release. As such, depending on the actual ingredients or composition of the composition, incomplete drug release during bowel movement is extremely dangerous and needs to be clarified during construction. With the growing demand for best practice, matrix systems provide the most cost-effective delivery systems. Permanent level delivery has been one of the main objectives of a controlled release program especially for a drug with minimal therapeutic indications.

Hydrophilic matrix system[35]
The first ingredients that limit hydrophilic matrix ingredients are polymers that can swell when they come in contact with water solution and form a gel layer on the surface of the system. When the extraction site (e.g. water) is combined with a polymer, the solvent enters the free spaces between the macromolecular chains. The polymer may undergo a relaxing process, due to the pressure of the solvent penetrating, so that the polymer chains become flexible and the matrix swells. This allows the prescribed tree to spread more quickly outside the matrix. On the other hand, it may take longer for the drugs to spread out from the matrix as inflammation of the matrix increases the distribution process. It is widely known that inflammation and proliferation are not the only factors that determine the rate of drug release.

For a non-removable polymer matrix, polymer dissolving is another important method that can measure the rate of drug delivery. Although swelling or melting may be a prominent feature of certain types of polymers, in most cases drug extraction kinetics is the result of a combination of these two methods.

Matrix programs

In matrix systems polymer: drug solution or dispersion is infused with connecting materials to form pellets or sprayed on pellets to achieve increased drug release. The drug is evenly distributed inside the polymer and is dispersed, dispersed or dispensed and dispersed. These plans outline several benefits in the following

Easy to do and low cost (1 step process)

- Less risk of dose loss (if accidental cover is torn) too
- Opportunity for the development of the melting of strong drugs

Drug-polymer interactions may also bring benefits depending on mechanical features such as the plasticizing effect. The main disadvantages include quick initial and incomplete releases in the specified time. The latter can be avoided by covering the sugar cores with a different polymer: drug concentrations, in which the drug was concentrated in the deeper parts of the matrix and therefore opposed the increasing path of distribution. In addition, matrix systems have been found to regulate the release of highly soluble drug drugs.

Matrix solutions, matrix distribution and drug withdrawal methods

In matrix systems, the drug and the polymer are dissolved or dispersed in a standard solvent despite solvent evaporation, solid solution (drug dissolved in polymer) or solid dispersion (drug dispersed in polymer) or a combination of both is available. If the concentration of the original drug is less than the solubility of the drug in the polymer, the drug dissolves and the drug release mainly expands the drug differentiation in the polymer.

Integrated Dam Programs

The pool-bound system consists of a drug-coated line surrounded by polymer. The main advantages of this system depend on the fact that very high drug loads can be used and different drug release profiles can be obtained, depending on the type of polymeric membrane

DESIGN AND ACTION TO RELEASE PRODUCTION PRODUCTS: [36-39]

Body structures

1. **Aqueous Solubility's:** Most active pharmaceutical areas (APIs) are extremely weak or fundamental in nature that affect the water melting of the API. Weak water drugs are difficult to design for the performance of a controlled control. Excessive exposure to liquid extracts followed by rapid increase in plasma drug concentration. These types of drugs are a good member of CRDDS. Melting of pH depends on creating a problem in the formation of CRDDS. BCS class-III & IV drugs are not the right choice for this type of formulation.
2. **Separation coefficient (P value):** P value refers to the fraction of a drug in oil and the liquid phase which is an important factor affecting the spread of the drug throughout the biological membrane. Drugs have a high or low P value not suitable for CR, they should be soluble in both phases.
3. **Drug pKa:** pKa is a factor that determines the ionization of a drug at body pH in GIT. In general, high ionized drugs are poor people in CRDDS. The absorption of compound drug occurs faster compared to ionized drugs from the biological membrane. The pKa concentration of an acidic drug that ionization depends on pH is 3.0 to 7.5 and in the basic drug it sets between 7 and 11.
4. **Drug stability:** Drugs based on acid / base, enzymatic degradation, and other gastrointestinal fluids are most suitable for CRDDS. If the drug is lowered into the stomach and small intestine, it should not be administered under controlled control as it will decrease the availability of anti-depressant medication.

5. **Cell size & molecular weight:** Cell size & cell weight are two important factors that affect cell differentiation throughout the biological membrane. Cells of cells less than 400D are easily dispersed but larger than 400D create a problem for drug proliferation.
6. **Binding proteins:** A complex protein drug acts as a plasma pool of a drug. Drugs that show the binding of high plasma proteins are not the right group for CRDDS because protein binding prolongs half-life. There is therefore no need to fund drug withdrawal.

Biological factors: [40-43]

1. **Absorption:** The similarity in the level and quantity of absorption is an important factor in building CRDDS. However, a step-by-step measure is extracted with a drug in the rating form. The absorption rate should be accelerated and dosage to prevent dose loss. Various factors such as water solubility, log P, acid hydrolysis, affecting drug absorption.
2. **Half Life expectancy (t1 / 2):** A drug usually has a short life span that requires constant measurement and proper appointment of a controlled dosing program. A drug with a long shelf life needs to be prescribed after a long period of time. Ideally, drugs with t1 / 2 2-3 hrs are an appropriate component of CRDDS. The drugs have t1 / 2 over 7-8 hours not used in a controlled release system.
3. **Dose Size:** CRDDS is designed to eliminate duplication, so it should contain a volume larger than the standard dosage form. However the standard used standard measurement provides an indication of the volume to be used in CRDDS. Continuous dose capacity should be large as it falls under acceptance procedures.
4. **Treatment window:** Drugs with minimal treatment indications are not suitable for CRDDS. If the delivery system fails to control the discharge, it can cause dose loss and severe toxicity.
5. **Sucking Window:** Drugs that show absorption from a particular segment of GIT, are a bad member of CRDDS. Drugs absorbed throughout the GIT are people who are ready for a controlled release.
6. **Patient physiology:** The patient's physical condition such as abdominal discharge, duration, and GI disorders influence the release of the drug in direct or indirect dosage form.

Standard Sucking Method [44 - 50]

In order for a drug to be a flexible candidate for each oral CRDDS, its absorption method must be distributed throughout the GI tract. The term spread here refers to both the absorption pathway by separating the lipid membrane (in all cells) or through water-filled cavities (between cells). It is also important that absorption occurs in all parts of the GI tract which may depend on the pKa of the drug, the pH in the component, the binding of the drug in the compost, the rate of blood flow, etc. The absorption process appears to be highly dependent on hydrodynamics in the GI lumen. Although that initial order and the square root of the release period can lead to more efficient drug delivery systems it is widely believed that the main purpose of the zero order release profile. Zero in vitro release will produce zero order in vivo release and zero order in vivo absorption only if;

(1) The entire GI tract behaves as a single room model, i.e. the different components throughout the GI tract are similar in terms of absorption, and
(2) Drug release rate is a measure that reduces the rate of absorption process. With the issuance of the first order on the other hand, smaller and smaller amounts are issued per unit of time and increasing time. If you consider that the absorption rate is slower than the small intestine due to increased viscosity, decreased mixing, and decreased intestinal area, the drug is reduced less. In any case, drug withdrawal from CRDDS should not be influenced by pH changes within the GI tract, by enzymes present in lumen, peristalsis, etc. For all practical use, an open one-room model is ideal for CRDDS multi-drug design.

Advantages of Control Release drug delivery system:[55-59]

- Reduce the frequency of drug administration
- Compliance with patient development
- Reducing drug levels in the blood
- Reducing total drug use compared to conventional treatment
- Reduction of drug accumulation and chronic treatment
- Reduction of drug toxicity (local / formal)
- Strengthening medical condition (due to similar drug levels)
- Improving the availability of certain medicines due to local control
- Savings for health care and patient care providers

Trade / Industrial Benefits

- New / technical leadership diagram
- Extended product life cycle
- Product classification
- Market expansion

Disadvantages of CRDDS

- Initial delay of drug activity
- The possibility of dosing in the event of a malformed plan
- Potential increase in initial food approval
- Significant dependence on the GI duration of the scale form
- Presence of inaccurate dose adjustment in some cases
- The cost per unit is higher compared to standard doses
- Not all drugs should be formulated into ER measurement form

Drugs SHOULD NOT BE DESIGNED

- Minor treatment index
- Poor absorption
- Significant omissions
- A short life span
- Low water solubility
- Extension of major initial approval.

Applications for a controlled drug delivery system

- In the water storage system The substance of the drug is separated from living organisms by a water-soluble membrane. For example the polymers used in the pond system are ethyl cellulose, poly ethylene vinyl acetate, silicone.

CONCLUSION

Finally, the Controlled Drug Control Program greatly helps to increase dose effectiveness, dose safety and patient adherence. The regulated drug delivery system aims to deliver the drug in the required doses over time to maintain the quality of treatment in the blood. in content.

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Table 1. Pharmacokinetic parameters consider during the drug selection listed as follow:[51-54]

Parameter	Comment
Biological or elimination half-life	Should be between 2 to 6 hrs
Elimination rate constant(KE)	Required for design
Total clearance(CLT)	dose independent
Intrinsic absorption rate	should be greater than the release rate
Apparent volume of distribution (Vd)	Vd effect the required amount of the Drug
Absolute bioavailability	Should be 75% or more
Steady state concentration (Css)	lower Css and smaller Vd
Toxic concentration	The therapeutic window should be Broader

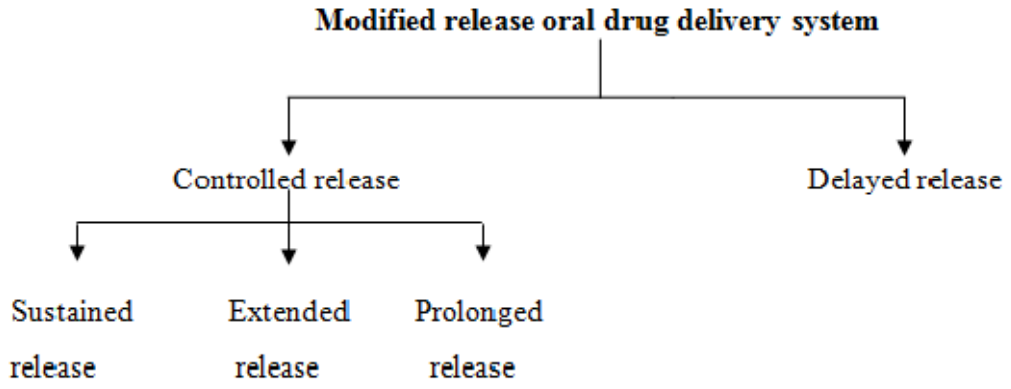

Fig 1: Modified Release Oral Drug Delivery System

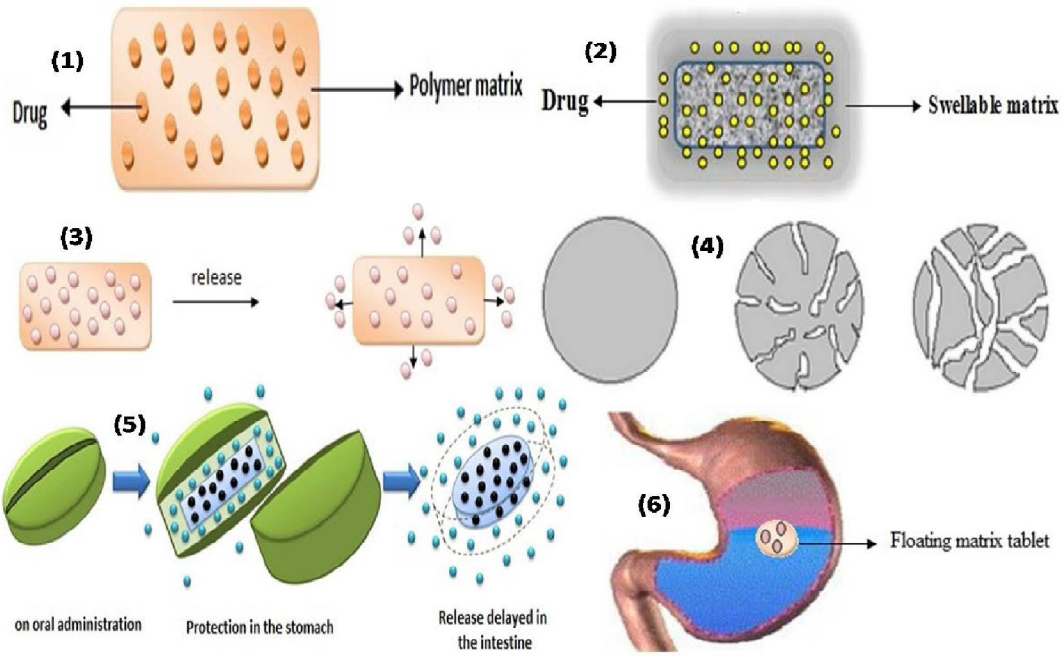

Fig. 2: Schematic representation of (1) Prototype matrix system, (2) Gel forming hydrophilic matrix system, (3) Hydrophobic matrix system, (4) Porous matrix system, (5) Enteric coatedmatrix system, (6) Floating matrix system

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RESEARCH ARTICLE

The Causal Agent of Leaf and Stem Rot in Tuberose is Identified as *Rhizopus oryzae*

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ABSTRACT

Tuberose (*Polianthes tuberosa* L.) is an important ornamental bulbous flowering plant belongs to *Asparagaceae* family widely cultivating for cut and loose flowers and flower oil trade. Severe leaf and stem rot was observed in tuberose crop at Enuguvaripalle village, Kadapa district, Andhra Pradesh (AP). We have suspected the disease as fungal infection and hence, its pure culture was isolated from the infected plant material by potato dextrose agar (PDA) plating method. After 3 to 5 days of incubation, white and cottony mycelia with a net like structure was grown on PDA plates. To confirm the pathogen, mycelium was observed initially under scanning electron microscope (SEM) and later its 28S rRNA gene was amplified and sequenced with LROR and LR7 primers. Based on the colony morphology, microscopic observations of mycelium and NCBI-BLAST analysis of 28S rRNA gene sequence confirmed that *Rhizopus oryzae* is the causal agent of the present studying disease of tuberose.

Keywords: Tuberose, *Rhizopus oryzae (R.oryzae)*, Internal transcribed spacer (ITS), Polymerase chain reaction (PCR), Scanning electron microscope (SEM).

INTRODUCTION

Tuberose (*Polianthes tuberosa* L.) is an important ornamental bulbous flowering plant majorly grown in tropical and subtropical areas (Biswas *et al.*,2002). It was spread from Mexico to different parts of the world and suspected to be brought into India via Europe. In India, it is an economically important flower crop majorly grown in states like West Bengal, Karnataka, Maharastra, Tamil Nadu, Haryana, Punjab, Gujarat, Rajasthan, Andhra Pradesh and Assam for cut and loose flowers and flower oil trade (Biswas *et al.*,2002; Khan and Pal, 2001). According to National Horticulture Board (NHB,2016), total area of tuberose cultivation is 16.19 000 hectares with production of loose and

cut were 107.91000 MT and 89.29000 MT, respectively. Out of which, in AP area of cultivation is 1.6 000 Ha with tuberose loose of 18.53000 MT. Tuberose plant is long with bright green leaves which are grouped at the base of the plant. It grown in longer spikes of size 30 to 45 cm in length which produce clusters of aromatic waxy white flowers to blossom from the bottom to the top of the spike which are star shaped and arranged loosely on spikes. In Andhra Pradesh, major tuberose producing areas are East Godavari, Guntur, Chitoor, Krishna districts (Jadav and Gurav, 2018). Mostly in India and Bangladesh people are commonly used in making flower garlands for wedding ornaments and for worshipping.

Tuberose crop is affected by many pests and pathogens and account for severe crop yield loss. The pests such as aphids, thrips, grass hoppers, bud borer, nematodes, weevils, red spider mites and rodents feed and damage young leaves, flower buds, flowers, shoot and root of the plants. Similarly, extensive crop damage has been reported from fungal pathogens. The major fungal pathogens are *Sclerotium rolfsii*, *Botrytis elliptica* and *Alternaria polyantha* causes stem rot (Collar-rot or sclerotial wilt), leaf spot and blight, Alternaria leaf spot diseases on tuberose, respectively (Das,1961; Priyadharshini *et al.*,2019; Mazumder *et al.*,2016).The fungal pathogen *Fusarium oxysporum* causes serious disease in tuberose and account for severe yield loss (Muthukumar *et al.*,2006). In the present study, we have identified the tuberose plants were severely infected and expressed brown lesions on the leaves and stem rot. Based on the symptomatology, we have suspected the disease to be a fungal infection. Based on the colony morphology, microscopic observations of mycelium, 28s rRNA gene amplification and sequence analysis identified *Rhyzopus oryzae* is the causal agent for the disease in tuberose at Enuguvaripalle.

MATERIALS AND METHODS

Sample Collection and Isolation of Fungal Pathogen

During the field inspection, we observed severe leaf and stem rot across the tuberose crop at Enuguvaripalle village, Kadapa district, AP. Suspecting as fungal infection, the selected symptomatic leaves and stem parts were randomly collected from Enuguvaripalle to the laboratory and were initially surface sterilized with 70 % alcohol and thrice washed with sterile distilled water and allowed for air dry in the laminar air flow chamber. Subsequently, the symptomatic leaf bits of 1x1 cm were placed onto potato dextrose agar (PDA) petriplates and incubated at 28 °C for 3-5 days. The grown fungal colonies were subcultured until the development of pure cultures and further microscopic observations.

Microscopic Observation

For SEM observations, the mycelium containing the formulations from PDA was mounted on aluminium stubs with double-sided carbon adhesive tape and observed under SEM.

Genomic DNA Isolation

A loopful of white cottony mycelium was inoculated into Potato dextrose broth (PDB) by using sterile inoculated loop and incubated at 28^{0}C in a shaking incubator for 3 days. The grown mycelium was drained and dried on a sterile filter paper. The filtered mycelium was ground with mortar and pestle with 1ml of extraction buffer solution (50 mM EDTA and 0.2 % SDS, pH 8.5) and transferred into a sterile eppendorf tube and incubated at 65 ^{0}C for 30 min and cooled to room temperature. Sample was centrifuged at 12000 rpm for 15 min and to the supernatant RNase A (50mg/ml) was added and incubated at 30 ^{0}C for 1 hr and again centrifuged at 10000 rpm for 15 min. To the supernatant, added 1/10th vol. of 5M potassium acetate (pH 5.2) and incubated on ice for 1 hr and centrifuged at 13000 rpm for 15 min and collected the supernatant. Supernatant was extracted twice with equal volume of phenol:chloroform: isoamylalcohol (49:49:2 v/v) and centrifuged at 13,000 rpm for 10 min. The final supernatant was transferred into a new eppendorf tube and precipitated the DNA with 2 vol. of ethanol and incubated at -20 ^{0}C for 30 min. The nucleic acid was recovered by centrifugation at 13,000 rpm for 15 min. The pellet was collected and washed

with 80 % cold ethanol and dried for 5 min at room temperature. Finally, the isolated DNA was resuspended in 100 µl of sterile distilled water and stored at –20 ^{0}C for further use.

PCR and sequencing of 28S rRNA Gene

PCR (Effendorf) amplification was done by using LR7 and LROR primers (specific to the large subunit 28S rRNA gene). Reaction of 25 µl containing 1 µg of DNA, 10 X Taq buffer, 10 mM dNTPs, 2 mM $MgCl_2$, 1.25 U of Taq polymerase (Thermo Scientific) and 1.5 µl of forward primer (LR7: 5' TAC TAC CAC CAA GAT CT 3') and reverse primer (LROR: 5' ACC CGC TGA ACT TAA GC 3') each. Reaction thermal cycling conditions for 30cycles: 94^{0}C for 45 sec, 51^{0}C for 30 sec, 72^{0}C for 2 min, followed by final extension at 72^{0}C for 10 min and kept hold at 4^{0}C. Further, the PCR product was sequenced by commercial sequencing facility (Eurofins, Bangalore) and analysed by NCBI-BLAST tool. The properly edited and analysed sequence was deposited in GenBank. Multiple sequence analysis and phylogenetic tree construction were made by ClustalW (BioEdit) and MEGA 5, respectively.

RESULTS AND DISCUSSION

In the year 2018, we have visited the tuberose fields (about 10 acres) at *Enuguvaripalle* (Kadapa, AP), where it was noticed that the crop plants were severely infected. The infected plants have shown stem rot and brown lesion on the leaves (Fig.1). As it was suspected to be a fungal infection, pure culture of the fungus was isolated from the symptomatic parts of leaf and stem of the infected plants on PDA plating method. Initially we have noticed whitish cottony mycelium with a net like structure and after 3-5 days later, it was turned into grayish black *at* 25 ^{0}C (Fig.2). Microsopic (SEM) observations of the fungal culture revealed that globose sporangia, globose to sub-globose columellum, numerous sub-globose or oval sporangiospores, straight non-septate sporangiophore (Fig.3).These mycological characteristics are similar R.oryzae causes Rhizopus soft rot on lily, soft rot on apple, Rhizopus rot on seedlings of grafted cucumber on pumpkin rootstock, leaf rot on pak choy (*Brassica campestris ssp.chinensis*), soft rot on storage roots of sweet potato, fruit rot on *Citrus medica* and brown rot on tomato (Hahm *et al.,* 2014; Kwon *et al.,* 2011; Kwon *et al.,* 2014; Arif *et al.,* 2019; Wang *et al.,* 2017; Hakim *et al.,* 2015; *Liaquat et al., 2019*). As part of *molecular* confirmation of fungal pathogens, many of the studies have used ITS1 and ITS4 (Internal transcribed spacer region) primers for the amplification and sequencing of 5.8S rRNA gene. PCR amplification and sequencing of ITS region have confirmed that the *Rhyzopus oryzae* was the pathogen for soft rot of apple, sweet potato, lily in Korea, China and Korea, respectively *(*Kwon *et al.,* 2011; Wang *et al.,*2017; Hahm *et al.,* 2014*).* In few studies along with ITS elongation factor 1 alpha (TEF) gene was also amplified to confirm *Rhyzopus oryzae (*Wang *et al.,*2017;Ganesh *et al.,*2020*).* In this study we have amplified the nuclear large subunit (nuc-lsu*)* 28S rRNA gene of isolated fungal pathogen with LR7 and LROR primers and subsequently sequenced. The obtained sequence was deposited in genbank (MK558195). NCBI-BLAST analysis revealed that the sequence has very close similarity with *R. oryza*. Multiple sequence comparison of the present study sequence with sequences of *R.oryzae strain FSU (JN939136), Rhizopus stolonifer* isolate AFTOL (DQ273817), *R.oryzae* isolate A9 (MG812522), *Bradysia coprophila (XR_005086075),* Mucor sp. H13(KU140634), *Mucor variisporus* CBS (NG_057972*)* showed more than 95 percent sequence similarity. It was identified that 100% sequence similarity with *R.oryzae strains* (FSU and A9). In the phylogenetic tree also it is grouped with *R. oryzae strains* (Fig.4). Based on these studies it was confirmed that the studing pathogen is *Rhyzopus oryzae.*

R.oryzae is a world wide distributed soil pathogen commonly causes post-harvested diseases on vegetables, fruits and ornamental plants (Kwon et al.,2011 & Cui et al.,2019). The majour reasons for occurance of the disease are improper storage like incorrect temperature, stored for extended period of time or mechanical failure during storage or transport etc., (Agrios et al.,2005). *Rhyzopus* soft rot by *R. oryzae* is now distributed world wide as a post harvested disease and effects on quality and quantity of the stored crops materials. It was reported on stored apple, banana, watermelon, sweet potato and other hosts in Korea (Kwon et al., 2000,2010,2011,2012a,2012b,2014). Similarly, *R.oryza* was the causal agent for soft rot and leaf rot on sweet potato and pak choy in china, respectively (Wang et al.,2017 ;

Arif *et al.,2019)*. However, natural infection by *R.oryzae* also noticed on some of the hosts. For example, *Rhizopus soft* rot of lily *(Lilium longiflorum)* by *Rhyzopus oryzae* was observed in the experimental field in Taean Lily Experiment station in Korea,2012 (Hahm et al.,2014). Similarly, it was reported that *R. oryzae* was associated with Melanagromyza splendida and stem disease of sunflowers in California (Mathew et al.,2015). In September 2016, a disease outbreak in potato confirmed as Rhizopus soft rot occurred in two fields in Guyuan County, Zhangjiakou City, Hebei Province of China (Cui et al. 2019). The boll rot of cotton caused by *R. oryzae* is new record in Bangladesh (Shamsi *et al.,*2014).The infected saplings showed soft-rot symptoms on the cortical tissues of the roots, resulting in the failure of grafting. As a causal agent of Rhizopus rot, *R. oryzae* produces enzyme Polygalacturonase (Pg) for maceration of infected mulberry roots essential for fungal pathogenicity (Yoshida et al. 2003). Also, in China, Rhizopus rot by *R. oryzae* was reported to infect roots of mulberry (Fang et al. 2011) and sugar beet (Hanson 2010). Recently Multi gene phylogenetic analyses revealed that *R. oryzae* is the natural pathogen or root rot of mulberry in India (Ganesh *et al.,*2020). It suggests that *R. oryzae* also a causal agent for natural infection in certain susceptible host plats.

CONCLUSION

The leaf and stem rot was noticed as a natural infection on tuberose crop at Enuguvaripalle in AP. Based on the mycological characteristics and molecular study (PCR amplification and sequencing of 28S rRNA gene), it was confirmed that the *R. oryzae* is the causal agent for stem rot of tuberose.

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Fig.1. Naturally infected tuberose crop; A) stem rot and B) ***dark brown lesions on the leaf.***

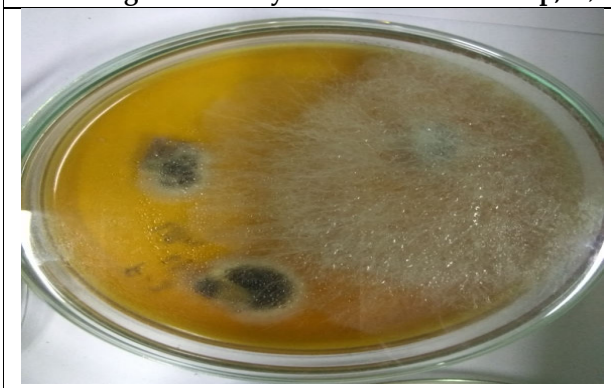

Fig.2. Characteristic whitish cottony mycelium of R. oryzae on PDA plate

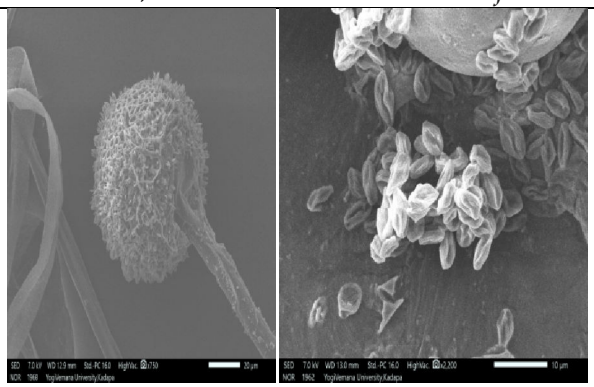

Fig.3.SEM showing long ***filamentous stalk sporangia with Sporangiophores.***

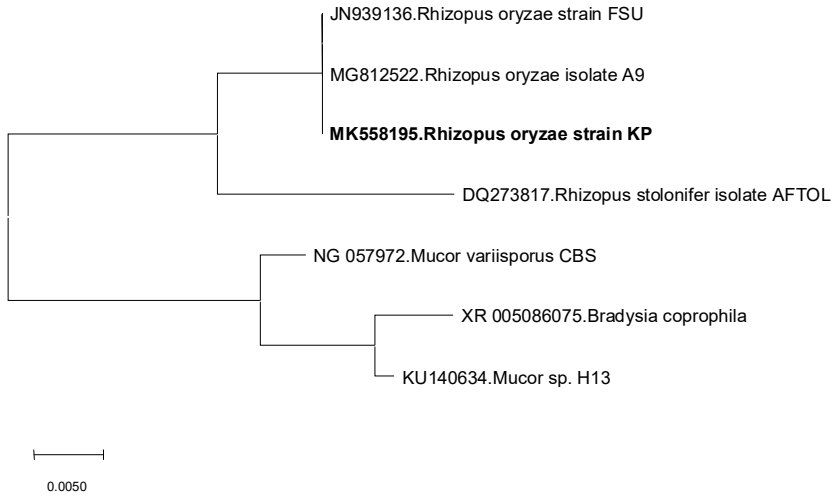

Fig.4 The phylogram was established with the **28S rRNA gene** *of R. oryzae*

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RESEARCH ARTICLE

Growth Performance of Broilers (*Gallus gallus domesticus* Linn.) Supplemented with Fermented Fish Hydrolysate (Milagrow®)

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ABSTRACT

In this study, the growth performance of broilers supplemented with different levels of Fermented Fish Hydrolysate from day 15 to day 35 was evaluated. Eighty (80) female-day old chicks were subjected to four treatments with four replications per treatment arranged in Completely Randomized Design (CRD). Birds at control T_0 were given pure water;T_1, 2.5 ml Fermented Fish Hydrolysate; T_2, 5 ml Fermented Fish Hydrolysate; and T_3, 7.5 ml Fermented Fish Hydrolysate/gallon of water, respectively. The average water consumption, feed consumed, feed conversion efficiency, final weight and economic returns were gathered and analyzed by Analysis of Variance (ANOVA) in CRD. Findings revealed that birds in all treatments have comparable water and feed consumption. Birds that were given 7.5 ml/gallon of water had the highest average final weight, lowest average feed conversion efficiency and gained the highest average economic returns. The highest dosage level of Fermented Fish Hydrolysate (Milagrow®) which is at 7.5ml increased the growth performance of broilers.

Keywords: Fermented fish hydrolysate; supplement; milagrow

INTRODUCTION

Broiler production is extremely important for the production of meats because it is one of the most valuable sources of protein for human diet. Thus, prospective growers should consider several factors such as providing proper nutrition because it is an important aspect that plays a vital role on the broiler's growth performance. Among all nutrients, protein is a very essential substance that animals should receive during their early stages of life because of its role in many vital processes. A major source of protein in feed formulation for broiler diets is fish meal, an approved feed ingredient, but due to its high prices because of the very expensive production process and its periodic scarcity have encouraged researchers to look for alternative protein feedstuffs [1]. As an answer to this,

large amounts of protein-rich by-products from the seafood industry are discarded or processed into fish meal [2]. Chemical, enzymatic, or microbial hydrolysis of proteins in animal by-products is an attractive means of generating high-quality small or large peptides that have both nutritional and physiological or regulatory functions in livestock and poultry. Enzymatic hydrolysis of fish protein has shown to be an effective way to recover potent bioactive peptides from waste material and numerous peptides derived from hydrolyzed food protein which have potential for nutritional or pharmaceutical applications [3]. As such, some peptides have been recognized for bioactivities and gained increasing attention as functional foods and/or dietary supplements. The hydrolysis of proteins by cell free-protease, microorganisms, acids or bases, results in the production of protein hydrolysates providing a high quality protein source for animal feeding [4].

Fermented Fish hydrolysate is safe and traceable, coming from the waste of fish by-products that undergoes fermentation and can meet the requirements of poultry. It is produced from sustainable fish waste products such as head, skin, trimmings, fins, frames, viscera and roes [5]. Fermented fish hydrolysate supplement contain predigested amino acids, vitamins A, D, E and B complex, fatty acids, omega 3 and 6 and minerals. Predigested amino acids can promote optimum growth performance in poultry. Studies regarding the exact dosage level of fermented fish hydrolysate (Milagrow®) in the water that can promote the optimum growth performance of broiler is not yet available. So this study aims to determine dosage levels as nutritive supplement on broilers in the growth performance of birds from brooding to finishing stage.

MATERIALS AND METHODS

IACUC Protocol

Before the conduct of the study, the proposal was submitted for approval of the Institutional Animal Care and Use Committee (IACUC) of the Southwestern University, Phinma.

Experimental Design and Treatments

The experiment was laid out in Completely Randomized Design (CRD) with four treatments replicated four times. The treatments were the following:T_0 – Plain Water,T_1 – 2.5 ml Fermented Fish Hydrolysate (Milagrow®),T_2 – 5 ml Fermented Fish Hydrolysate (Milagrow®),T_3 – 7.5 ml Fermented Fish Hydrolysate (Milagrow®).

Preparation of Rearing House

The experimental house was prepared one month before the experimental birds arrived. There were two houses designed for the study. The first house was for brooding where all chicks were raised for two weeks. The experimental birds were then transferred to the second house where the birds started to receive the different treatments after two weeks of brooding. Supplementation started from starting to finishing stage. The house has 16 cages, arranged in single deck with eighth cages on opposite sides. Each cage measured 1 m x 0.5m x 0.8m. The house was properly disinfected prior to the study. The brooder house was installed with electric bulbs to provide artificial heat to the experimental birds during the brooding period. Old newspapers were used as litter materials throughout the duration of brooding period. Individual feeder and waterer of the same sizes were provided from starting to finishing period.

Selection and Stocking of Experimental Birds

A total of eighty (80) female heads of a day old chick's broiler, apparently healthy and free from any defects were used in the study. The day old chicks were purchased from the local a grivet market and brooded for 14 days. The day old chicks were given with antibiotics and dewormer for three (3) days and multivitamins for four days, then plain water was provided for the rest of the brooding period. After brooding, the birds were transferred and randomly assigned to each treatment which was replicated four times. Each treatment consisted of five chicks. The drawing lots method was used to randomly assign the birds to their different treatments.

Application of Fermented Fish Hydrolysate

The experimental birds in each treatment received different levels of Fermented Fish Hydrolysate (Milagrow®) in water as supplement from day 15 to day 35. Birds in T_0 - pure water in 1 gallon of water was given, T_1- 2.5 ml (Milagrow®) added to 1 gallon of water , T_2 – 5 ml (Milagrow®) added to 1 gallon of water, T_3 - 7.5 ml (Milagrow®) added to 1 gallon of water. Application of water with varying dosage levels of fermented fish hydrolysate was done early in the morning together during feeding time. The water consumed was measured every day.

Feeds and Feeding Management

Each treatment received the same amount of feeds twice a day according to their age, from one to seven days old, broiler booster mash was given; seven to twenty days old, broiler starter crumble was given, at twenty-one to twenty-eight days old broiler grower crumble was given and at twenty-nine to thirty-five days old, broiler finisher crumble was fed to the birds. Ad libitum feeding was done. The feed given and feed refused were carefully recorded every day.

Health Management

Health care such as vaccination and sanitation management was strictly implemented to prevent the occurrence of any possible diseases throughout the duration of the study. At 21 day old, B1 Lasota was given to the broilers.

Harvesting

Harvesting time was done on the 36 days of age. Proper care was observed to minimize mortality case.

Gathering of the Data

Before the treatment started, the initial weights were taken before they were distributed to their respective treatments. The body weights of broiler were gathered weekly. The amount of water consumed was measured by getting the amount of water given minus the amount of water that was left the next day, at morning time. The amount of feed consumed was measured by getting the total amount of feed given minus the total amount of feed left on the next day, at morning time. Both feed and water consumed were measured every day.

Data Gathered

1. Average water consumption (birds/ml)

$$AWC = \frac{\text{total amount of water given – total amount of water consumed}}{\text{Total number of birds / treatment}}$$

2. Average final weight (g/bird)

$$AFW = \frac{\text{Weight of birds at harvest}}{\text{Total number of birds/ treatment}}$$

3. Average feed consumption (g/bird)

$$AFC = \frac{\text{Total feed given – Total left over feeds}}{\text{Total number of birds/ treatment}}$$

4. Average feed conversion efficiency (%)

$$AFCE = \frac{\text{Average weight gain}}{\text{Average feed consumption}}$$

5. Average economic return (peso/bird)

$$AER = \frac{\text{Gross Income - Total cost of the production}}{\text{Total number of birds/ treatment}}$$

Statistical Analysis

Data gathered were computed using the analysis of Variance (ANOVA) in a Completely Randomized Design (CRD). Treatment means that result in a highly significant difference was subjected further to Least Square Difference (LSD) test to validate the relations among them.

RESULTS AND DISCUSSION

Average Water Consumption

The importance of optimizing water intake for poultry has to be a very important consideration for a profitable enterprise. Feed intake correlates very closely with water intake up to a level which maximizes performance. Hence, any factor restricting water intake below optimum levels will result in reduced performance. Table 1 showed the performance of broilers in water consumption as mixed with the different levels of fermented Fish Hydrolysate ((Milagrow®) as supplement. During the 3rd week of the study, Analysis of Variance (ANOVA) showed that there was significant difference of water consumption as affected by the different levels of FFH (Milagrow®**)**. Treatment three (3) applied with 7.5 ml of FFH (Milagrow®**)** in 1 gallon of water had the highest water consumption of 858 ml, followed by treatment 2 (5 ml FFH (Milagrow®**)** 833 ml, treatment 0 (pure water) 818ml , then treatment 1 (2.5 ml FFH (Milagrow®) 783ml**.** Although each treatment gained different levels of water consumption, the data showed that each treatment was comparable to water alone.

On the 4th week of the study, Analysis of Variance (ANOVA) showed that there was significant difference of water consumption as affected by the different levels FFH (Milagrow®**)**. Treatment 0 applied with pure water had highest water consumption of 1780 ml, followed by treatment 3 (7.5 ml of FFH (Milagrow®) 1534.75 ml, treatment 2 (5 ml of FFH (Milagrow®) 1212.75 ml, and treatment 1 (2.5 ml of FFH (Milagrow®) 1113.5 ml. On the last week of the study, 5th week, Analysis of Variance (ANOVA) showed that there was significant difference of water consumption as affected by the different levels FFH (Milagrow®**)**. Treatment 3 (7.5 ml of FFH (Milagrow®) had the highest water consumption of 1155 ml, followed by Treatment 0 (pure water) 1113.75 ml, treatment 2 (5 ml of FFH (Milagrow®) 1012.5 ml, and treatment 1 (2.5 ml of FFH (Milagrow®) 1007. 75 ml. However, the highest level of supplementation was comparable to water alone.

The results of water consumption from weeks 3, 4 and 5 implies that the different levels of FFH (Milagrow®**)** as supplement do not affect the water consumption of broilers and it was comparable to water alone.

Average Feed Consumption

Increase feed intake can increase the growth performance of broilers. However, several factors must be considered to increase feed consumption. The palatability, texture of feeds, weather conditions and supplements contributes the greatest impact on feed consumption. The effect of water supplementation of different levels of Fermented Fish Hydrolysate on the average feed consumption of broilers is shown in Table 2. The result of Analysis of Variance (ANOVA) from 3rd week, 4th week and 5th week of the study showed that there were no significant differences found among all treatments. This implies that in terms of feed consumption, all birds in each treatment are comparable to the control birds. This is similar to the findings reported by [6] who included up to 30% offal silage in broilers diet and significant effect on feed intake was not found.

Average Feed Conversion Efficiency

Feed is typically the most costly expense in broiler production. As a result, feed efficiency is typically the primary tool by which a flock is evaluated. Feed efficiency is calculated by dividing feed intake by weight gain, thus the lower the number (referred to as Feed Conversion Ratio – FCR) the more efficient the flock was in using the feed supplied. The effect of water supplementation of different levels of Fermented Fish Hydrolysate on the average feed conversion efficiency of broilers is shown in Table 3. Analysis of Variance (ANOVA) showed that during 3rd week

and 4th week of the study each treatment had no significant difference on the feed conversion of broiler as affected by the different levels of FFH (Milagrow®) as supplements.

However, Analysis of Variance (ANOVA) during 5th week of the study revealed that broilers in treatment 3 supplemented with 7.5 ml FFH (Milagrow®) per 1 gallon of water had the lowest recorded feed consumption, but gained the highest weight. Comparable feed conversion efficiency was observed in treatment 2, treatment 1, and treatment 0. This means that the application of 7.5 ml FFH can be a good supplement to the dietary requirement of the broilers because it increased the body weight of the broilers without increasing the feed consumption. Increased levels of fermented fish hydrolysate supplementation also increased the amount of amino acid, multivitamins and minerals that increase growth of animals. Findings of [7] also stated that including fish silage (5%) and fish oil (0.8%) in the diet promote better weight gain of the broilers.

Average Final Weight (g)

The factors affecting the body weight of broilers are associated with the environment, the quality of feeds and the content of the diet applied. The effect of different levels of fermented fish hydrolysate (Milagrow®) as supplement to the weight of broilers is shown in Table 4. Analysis of Variance (ANOVA) showed that during the third week and fourth week of the study, the (Milagrow®) as supplement did not increased the average weight of broilers. However, on the fifth week of the study, Analysis of Variance (ANOVA) revealed that treatment three applied with 7.5 .ml of Fermented Fish Hydrolysate (Milagrow®) was significantly different from treatment 0, treatment 1, and treatment 2. There were no significant difference found between treatment 0, treatment 1 and treatment 2.

This implies that broilers supplemented with 7.5 ml FFH /gallon of water has gained the heaviest weight. Treatment 1 and T2 have a comparable effect with treatment 0. The higher level of supplementation was supported by Bourre (2015) that fermented fish hydrolysate has high protein content and good protein quality that can promote optimum growth performance in poultry. Fermented fish hydrolysate is natural source of vitamin A, D, E, B-complex and minerals that promote good health and normal growth, protects cell membrane, improves energy metabolism, and utilizes calcium and phosphorus which is essential in meat production.

Average Economic Return (peso/bird)

Poultry production is a short cycle, with good profitability that makes it successful as an industry. Table 5 below showed that supplementation of different levels of Fermented Fish Hydrolysate (Milagrow®) improved the performance of broilers and resulted economic benefits. The average economic return was obtained by getting the cost of the production minus the gross income earned after the birds were sold. The average economic return showed that birds in treatment 3 had the highest average economic returns, followed by treatment 2, treatment 1 respectively, with the least at treatment 0. The results of Analysis of Variance (ANOVA) revealed that there was a significant difference observed. Treatment 3 was significantly different from treatment 2, treatment 1 and treatment 0. This showed that birds that were supplemented with 7.5 ml FFH gained the highest average economic returns. Treatment 1 and treatment 2 had a comparable effect with treatment 0 in terms of average economic returns. This implies that the application of 7.5 ml FFH has the highest average economic return among all treatments due to its higher body weight.

CONCLUSION

Experimental birds that were given 2.5 and 5 ml / gallon of fermented Fish hydrolysate had a comparable effect on the average water consumption, average feed consumed and average economic return. Birds that were given 7.5 ml / gallon of water had the highest average final weight, lowest average feed conversion efficiency and gained the highest average economic returns. This proved that the highest dosage level of Fermented Fish Hydrolysate (Milagrow®) which is at 7.5ml could increase the growth performance of broilers.

Conflicts of Interest

The authors declare that they have no conflicts of interest to report regarding the present study.

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Table 1: Average Water Consumption of Broilers as Supplemented with different Levels of Fermented Fish Hydrolysate (Milagrow®).

Treatments	Average Water Consumption in Broilers (ml)		
	Week 3 (21 days)	Week 4 (28 days)	Week 5 (35 days)
T_0 – pure water	818 ^{ab}	1780 ^{a}	1113.75 ^{a}
T_1- 2.5 ml FFH (Milagrow®)	783 ^{b}	1113.5 ^{d}	1007.75 ^{b}
T_2- 5 ml FFH (Milagrow®)	833 ^{a}	1212.75 ^{c}	1012.5 ^{b}
T_3- 7.5 ml FFH (Milagrow®)	858 ^{a}	1534.75 ^{b}	1155.25 ^{a}
CV %	3.44	1410. 25	7.71
P-value	0.0187	0.0000	0.0133

* Means with the same letter are not significantly different.

Table 2: Average Feed Consumption of Broilers as Supplemented with different Levels of Fermented Fish Hydrolysate (Milagrow®).

Treatments	Average Feed Consumption of Broilers (g)		
	Week 3 (21 days)	Week 4 (28 days)	Week 5 (35 days)
T_0- pure water	1426	2246	2467
T_1- 2.5 ml FFH (Milagrow®)	1540	2039	2641
T_2- 5 ml FFH (Milagrow®)	1399	2005	2415
T_3- 7.5 ml FFH (Milagrow®)	1420	2117	2634
CV %	8.11	7.12	5.66
P –value	0.3617	0.1621	0.1032

Table 3: Average Feed Conversion Efficiency of Broilers as Supplemented with Different Levels of Fermented Fish Hydrolysate (Milagrow®).

Treatments	Average Feed Conversion Efficiency of Broilers (g)		
	Week 3 (21 days)	Week 4 (28 days)	Week 5 (35 days)
T_0 – pure water	3.14	2.77	2.52$_a$
T_1- 2.5 ml FFH (Milagrow®)	3.39	2.51	2.62$_a$
T_2- 5 ml FFH (Milagrow®)	3.00	2.21	2.38$_a$
T_3- 7.5 ml FFH (Milagrow®)	3.07	2.36	1.96$_b$

* Means with the same letter are not significantly different.

Table 4: Average Final Weight of Broilers as Supplemented with different Levels of Fermented Fish Hydrolysate (Milagrow®).

Treatments	Average Final Weight of Broilers (g)		
	Week 3 (21 days)	Week 4 (28 days	Week 5 (35 days)
T_o - pure water	450.00	817.50	991. 00 $_b$
T_1- 2.5 ml FFH(Milagrow®)	455.00	815. 00	1008.00 $_b$
T_2- 5 ml FFH (Milagrow®)	467. 50	917. 50	1040. 25 $_b$
T_3- 7.5 ml FFH (Milagrow®)	465. 00	905	1351. 50 $_a$
CV %	4.59	8.89	4.55
P-value	0.7651	0.1593	0.000

* Means with the same letter are not significantly different

Table 5: Average Economic Return of Broilers as Supplemented with different Levels of Fermented Fish Hydrolysate (Milagrow®).

Treatments	Average Economic Return of Broilers (Peso/birds)				
	Replication 1	Replication 2	Replication 3	Replication 4	Mean
T_0 – pure water	7.3	8.01	7. 36	8.9	7.21 b
T_1- 2.5 ml FFH (Milagrow®)	8	7.7	8.24	9	8.415 b
T_2- 5 ml FFH (Milagrow®)	11.05	11.89	8.8	10.9	9.935 b
T_3- 7.5 ml FFH (Milagrow®)	14.2	13.5	12. 5	13.4	13.4 a
CV %					22.684%
P- value					0.001

* Means with the same letter are not significantly different.

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REVIEW ARTICLE

Review of Health Monitoring Systems

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ABSTRACT

Now a days, fitness monitoring system gets the most popularity. Heart disease, lung failure and heart connected disorder are expanding at an alarming rate. Monitoring physical state of senior citizens and patients with critical condition at home or hospital requires urgent medical attention. Internet of things (IoT) technology and its increasing utilization makes it possible for real-time health monitoring. IoT based health monitoring aims to empower human being to live in a much better life with wearing linked gadgets. The latest development of smart sensors, wireless, communication and information network technology has transformed the health monitoring system. This paper presents a brief review of recent development of health monitoring system using IoT.

Keywords: Internet of things, health monitoring system, wearable sensor devices, mobile health monitoring device and microcontroller.

INTRODUCTION

Recent advancement in internet of things and smart sensors have transformed the health care systems. Real-time health monitoring systems have been developed with the help of IoT technology. IoT based health monitoring system contains different wearable patient monitoring devices (glucose, blood pressure, heart rate and activity monitoring, etc.) [1] that are connected online though internet. The main goal of this system is focused on monitoring of the patient's health remotely. By using the system, an expert can do monitoring, counselling and diagnosis of the patient and inform their family members before arrival in an emergency. Details medical information of the patient are stored in the internet server and can be accessed online by the authorised persons only. A study was conducted by the NCBI to determine the efficacy and effectiveness of various kinds of health maintenance transport to monitor the development of health management facilities as well as foundation of data processing to fitness awareness window. Studies have shown that patient's information available are not well maintained and are hand-held leading to patient data retrieval and data inconsistencies. The advance methods along with the support of IoT technology further support to retain the required data and patient details [14]. IoT systems use smart sensors to gather data of sufferers and show using liquid-crystal-display and save to personal computers (PC) as well as in the cloud for

further processing. The IoT, as describe by its name, is a 'interconnection of things 'rather in a specific factors 'interconnection of devices' (to have several ability) linked at a same time to attain some extra ordinary virtue in doing everything in system [13].

Health Monitoring Systems

The health monitoring system offers many options for changing traditional treatment of patients. In addition, there is also a solution which lowers the price of health management and support for the health care to upgrade the process of treatment and also provides a remote based health monitoring system. Over the centuries, people have been killed mainly because of conflicts, outbreaks, cheap living qualities, and the same cheap standard in the of medical management. Though, as times have changed and at present chronic illness is a major threat to longevity. Technological advancement is not a major factor in longevity. As we are aware the technology can't work as a magic in the treatment of chronic illness. Though, advances in technology can considerably assist patients in health management and also in the task of physicians. Modern technology has enough power to help doctors as well as patients to simplify medical protection when it happens to the monitoring and treatment of chronic diseases [4], [15]. The Health Monitoring System (HMS) is a complex and alternative technology for the conventional treatment as well as the health of the patient. Mobile health care is the integration of a portable computer with health monitoring system. Portable computer technology is used to improve communication between patients, physicians and other health professionals. Since, mobile devices have become an integral part of our life we can incorporate them into health care in our daily lives. This enables the delivery of accurate medical information anytime anywhere using mobile phones. Security and privacy are most important obstacles to cell phone health monitoring. Fig. 1 shows the classification of health monitoring systems. For the most part the system uses the same configuration for different software variants as well as Technology.

This section focuses on the various methods used in Health monitoring. Various ways are there to improve health management system considering the different variables. Smart health monitoring programs have also pros and cons that need to be considered. Patient monitoring program is divided into three standard categories: a patient monitoring device, a large financial device and software. Generally, a patient monitoring device contains a sensor for capturing important patient information (e.g., heart rate) and connectivity solution (e.g., PCBs, connectors, cables, etc.) that can transmit data to large objects. As the patient monitoring device itself collects important patient information, that data is sent (sometimes offline) to the main equipment where it is processed, stored, and displayed. The health monitoring program looks at the heart rate or pulse rate and other vital body signal details of the patient. In this paper [14] heart rate has been measured with the help of photolethysmograph. A unit for the reception of data is installed in the room of the doctor. This unit accepts and determines the details as well as continues to be displayed on the user interface that appears on pc or laptop. So, the monitoring of various patients can be done at a time. This also continues to monitor data and in the event of a defect, file for patient status, alarm connected to the system provides visual and gives the warning about the patient in emergency of every separate room. A GSM modem is attached with the system which transmits the messages for all staff members of the hospital [14].

This paper informs more about the imperfections of current hospital instruction system and suggest a location, recognition and communication system that is capable to defeat some of the weak points of current system and specially improve the regulation and throughput of the various portion of the hospital setup. This system totally based on RFID and wireless sensor. This system is also come up with a continuous visual simulation and survey platform to elegant functions. In this paper RFID and wireless sensor network-based location and guidance and the accompanying technology plan that would allow hospital assets, staff and patients to be chase in real-time for the reason of optimizing operations in every aspects of the everyday activities of hospitals. This proposed system has an RFID based tracking network that conforms to the DASH7 Mode-2 and open tag [2].

A system for the soldiers of Indian army which can be attached with their body has been proposed [3]. GPS is used in this system for the actual location of soldiers and it is set up in their body. It will do monitoring of the body every

time. By this low-cost system some precious human beings can be protected, number of deaths can be reduced by real monitoring of the soldiers, because it will identify the internal injuries of their body and action can be taken according to the situation. This paper also talks about other technologies like Zigbee, GSM etc. and discusses about few problems such as high cost of installation, signal loss and various other factors. Researchers have designed a portable and low-cost system as well as real time monitoring of the body. IoT plays a vital role in the transmission of health status to the control room. The health parameters are collected with the help of microcontroller, the GSM is used to move the data in base unit and cloud is used for collection and storage of information [3].

Connected devices help people to live a healthier life. The IoT technology is very useful in monitoring of health. In this paper [8], a health monitoring system has been developed for the peoples who have no time to visit the doctors regularly. The developed system stores medical data of person in every time like as heartbeat rate, pulse rate, blood pressure, ECG and body temperature. It is not easy to find out the abnormalities in the beat rate of the heart of a patient. It is a real-time monitoring of health. The processing of the PHS (Personalized Health Care System) is done by ARM7LPC 2138 processor and graphical user interface is used for displaying the data. Sensors and technologies used in these kinds of IoT devices are RFID, NFC, Bluetooth and Zigbee etc according to the application as shown in Fig. 2. The authors also discussed about the problems such as shortage of accurate and low-cost medical sensors. Here, the concept of IoT is reflecting connectivity of anyone, anytime and any kind of network. It reduces number of bed days in hospital and clinic visits. The stored data further can be used for analysis and consultation. Mainly this case study is focused on monitoring of heart rate and burnt calories per day [5].

According to this paper, nowadays surveys show that the diseases like lung failures and heart related diseases are increasing very rapidly. The IoT technology is not only useful in marketing or software businesses but it can also play a big role in health monitoring [12]. The IoT based health monitoring system consist various physical devices like as sensors for glucose, blood pressure and heart rate etc, these all connect to the internet and the conversion of physical information to digital information takes place. It also discusses about the five different layers of IoT namely perception layer, network layer, middle ware layer, application layer and business layer. The conventional health monitoring is a pen and paper system. It may create some errors in diagnosis process, missed perception and errors by human beings. Mainly this system involves three major functions namely tracking an object or patient, data identification and authentication, sensing and collection of Data. The main feature of the task is to provide technological support to make reliable health care systems easier and faster. Fig. 3, shows architecture of health monitoring system where the devices used are Raspberry pi, temperature sensor, pulse rate sensor, ECG sensor, pulse rate sensor and the basic protocol of IoT means MQTT is used by the author[7], [9].

Fig. 4. Shows a three-tier architecture used to monitor the patient's health parameters like as heartbeat, temperature of the body and the body position etc. Here, Raspberry pi is used which operates on 5V and it is also small in size (credit-card), mainly it is operated on IoT. Additionally, it provides a warning to the doctor and information is stored on web server. It also provides authentication of data for the user. It takes the various sample of health parameters and extraction of information takes place with the help of these samples. Tier 1 wired sensor network is of the patient which contains heartbeat sensor (SEN-11574), temperature sensor (DS18B20) and accelerometer (ADXL134). Tier 2 and Tier 3 have also their networks as on Tier 1. Here, two controllers have been used, one is for normal health status and other is for emergency health condition. These two controllers are present in decision making model. Tier2 is responsible for the processing of data [6].

A24/7 monitoring system for patient's body has been developed using IoT. Now days, patient monitoring system is gaining popularity on a patient researcher and caregiver. This program contains the ability to monitor physical signs in a patient's body every 15 seconds. This program is responsible for collecting heart rate, body temperature etc. from patient's body and send data to IoT Cloud platform via the WIFI-module and patient health status stored in the cloud. It empowers a medical professional or authorized person to monitor the health condition of the patient on the cloud server. The proposed result of this research provides appropriate and effective health facilities to patients [6].

Main reason for the development of any country is its advance health care system. To facilitate the remote monitoring of patient IoT is used when the doctors have access to the information of the patients [10]. This IoT based system can automatically monitor the patient's healthcare condition and at the same time store the data in its database. It also informs the doctor about the critical condition of the patient [11]. The main approach used in this paper is to make the system affordable, easy to use and efficient for everyone. This device will reduce the chances of ever that occurs by manually inspection by keeping the doctor updated about the patient's health condition and further improvements. If any emergency occurs this system plays a major role by generating an alert signal and informing both doctors and patients family about the deterioration in the condition. This will eventually lead to increase in rate of the recovery of the patient and doctors can save more life than before. Thus, it will prove to be most important device in health care sector.

CONCLUSIONS

This paper reviews developments in the healthcare system that is good for their use mainly in the field of medical science. The research is focused on wireless and autonomous heath management system. Methodology emphasizes the productiveness of the hospital system and the local environment. Many researchers are growing up online or web monitoring programs that play an important role in monitoring a patient in a variety of ways that produce high quality and accurate data. Most major system monitoring and sending remote channel such as local server, computer or Laptop for which can further process the data. Zigbee, Wi-Fi and Bluetooth these Distinct communication protocols are used for intelligent health tracking. A diverse health monitoring programme is validated by a variety of clinical and clinical trials. With the verification process, anyone can comfortably realize the correctness, accuracy measure etc of many approaches in detail.

Future Directions

It is not easy to examine and regulate the health status of patients in lonely three boundaries. Therefore, the insertion of a large quantity of sensors is a must as well as a positive feature sensor to call. On the other side, sensory exactness is a key element of this work. Individual senses and ways of the measurement of health care variables establish various outcomes. Although, the lacking in system accuracy can be reduced by using more precise sensors and good quality sensors. It is possible it can be used in a variety of ways and with several comparisons can be made, where the closest to the closest the correct result will also be used for the product. Future activities can be extended for consideration and analysis of wide range of health care variables and suggested appropriate precautionary measures in the event of an emergency.

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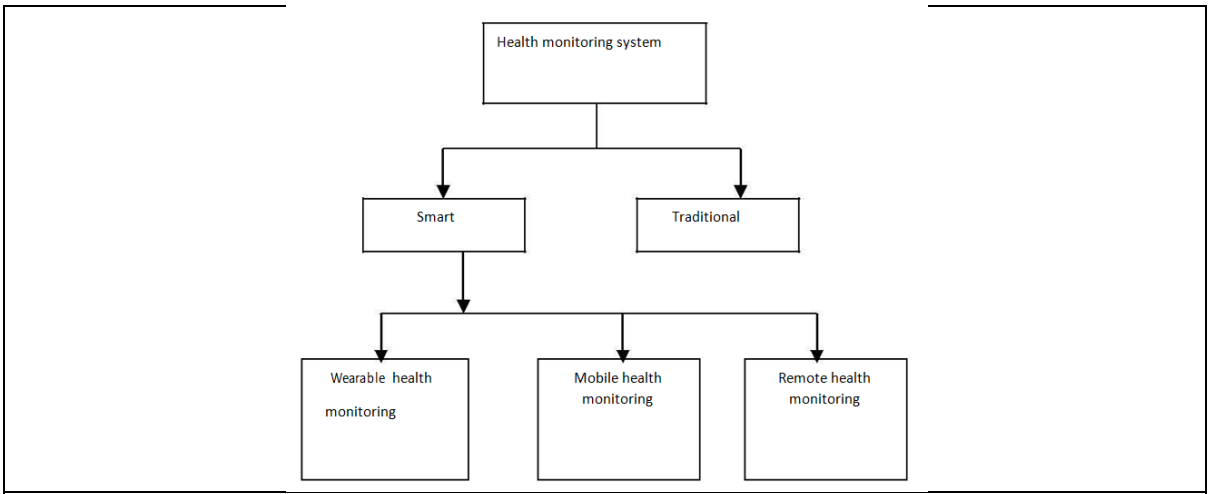

Fig. 1 Classification of health monitoring systems

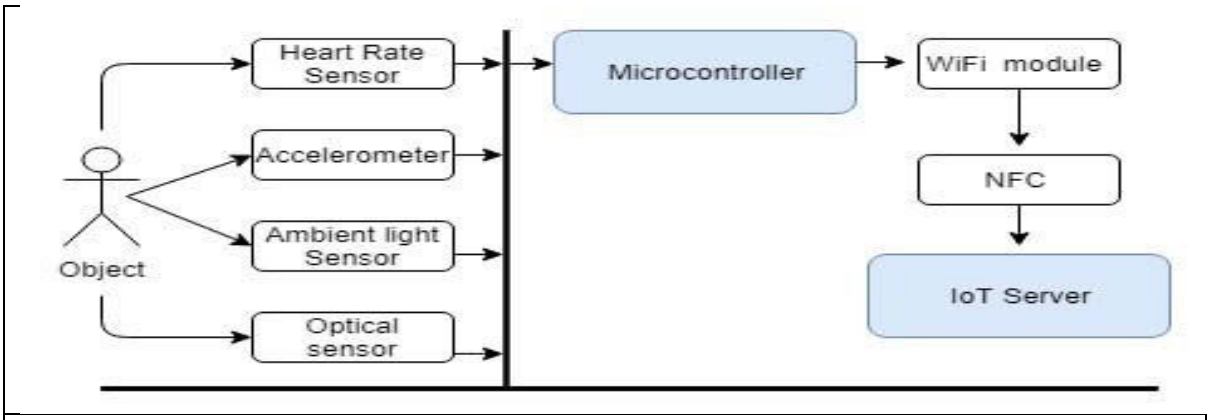

Fig 2.Block diagram of Health Monitoring System

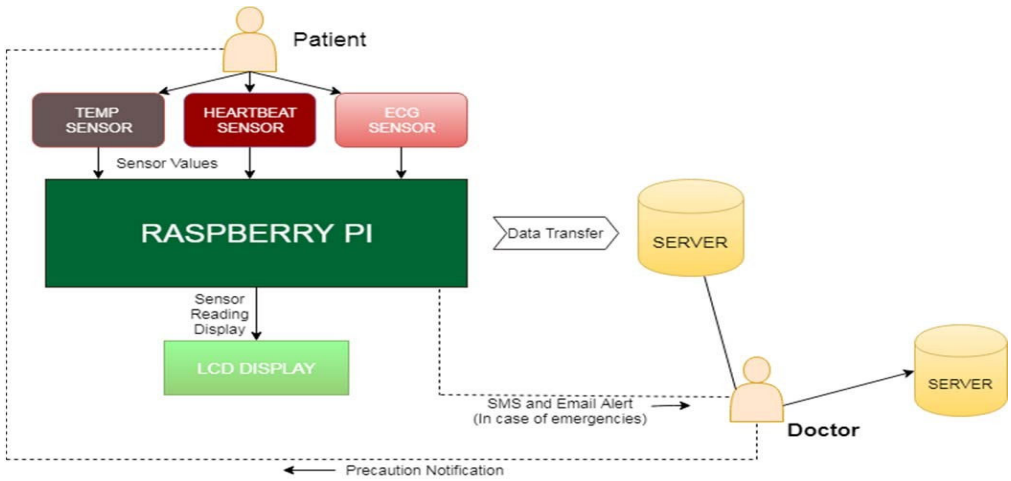

Fig. 3 Architecture of health monitoring system

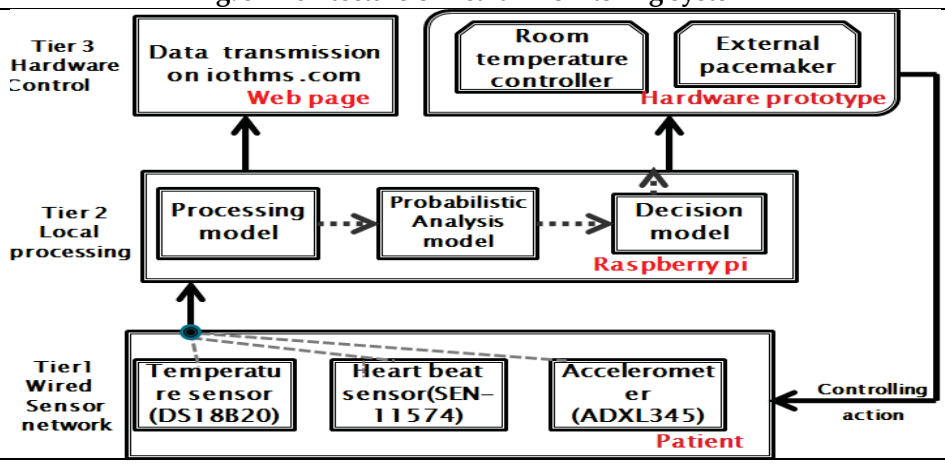

Fig. 4 Three Tier Architecture of proposed system

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REVIEW ARTICLE

A Review: Pandemic Diseases

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ABSTRACT

The world has built up an expand worldwide wellbeing framework as a defense against known and obscure irresistible sickness dangers. The framework comprises of different formal and casual organizations of associations that serve various partners; have changing objectives, modalities, assets, and responsibility; work at various provincial levels and cut across people in general, private-for-benefit, and private-not-revenue driven areas. The advancing worldwide wellbeing framework has done a lot to ensure and advance human wellbeing. Nonetheless, the world keeps on being stood up to by longstanding, arising, and reappearing irresistible infection dangers. These dangers contrast generally regarding seriousness and likelihood. They likewise have differing ramifications for dreariness and mortality, just as for an unpredictable arrangement of social and financial results. To different degrees, they are additionally managable to elective reactions, going from clean water arrangement to guideline to biomedical counter measures. Regardless of whether the worldwide wellbeing framework as right now established can give powerful assurance against a unique exhibit of irresistible illness dangers has been raised doubt about by late flare-ups of Ebola, Middle East respiratory disorder, SARS, and flu and by the approaching danger of rising antimicrobial obstruction. The worry is amplified by quick populace development in regions with powerless wellbeing frameworks, urbanization, globalization, environmental change, common clash, and the changing idea of microbe transmission among human and creature populaces. This Council would fortify the worldwide wellbeing framework by improving cooperation and coordination across associations filling in information holes concerning (for instance) irresistible sickness reconnaissance, innovative work needs, financing models, production network co-ordinations, and the social and monetary effects of possible dangers; and making significant level, proof based proposals for overseeing worldwide dangers related with irresistible illness.

Key words: worldwide wellbeing, worldwide wellbeing frameworks, irresistible sickness, symptoms, measure, WHO advices and reaction.

INTRODUCTION

An epidemic is the quick spread of irresistible disease to countless individuals in a given populace inside a brief timeframe. As per current ideas, an epidemic is characterized as the event locally or district of instances of an ailment or other wellbeing related occasions plainly in abundance of ordinary hope. The people group or locale, and the time span in which the cases happen are determined definitely. An epidemic disease isn't needed to be contagious, and the term has been applied to West Nile fever and the obesity epidemic (e.g. by the World Health Organization), among others [1]. Consequently, epidemics allude to the "unordinary" event locally or area of disease, explicit wellbeing related conduct (e.g., smoking) or other wellbeing related occasions (e.g., car crashes) plainly in overabundance of "anticipated event". The quantity of cases differs as indicated by the disease-causing specialist, what's more, the size and sort of past and existing openness to the specialist [2].

Epidemics of infectious disease are generally caused by several factors including

- Change in the biology of the host populace (for example expanded pressure or expansion in the thickness of vector animal groups).
- Genetic change in the microorganism supply or the presentation of an arising microorganism to a host populace (by the development of microbe or have).
- Generally, an epidemic happens when have insusceptibility to one or the other an set up microorganism or recently arising novel microbe is abruptly diminished beneath that found in the endemic balance and the transmission edge is surpassed.
- The conditions which administer the episode of epidemics additionally incorporate tainted food supplies, for example, sullied drinking water and the movement of populaces of specific creatures, like rodents or mosquitoes, which can go about as disease vectors [3].
- Certain epidemics happen at specific seasons. For instance, challenging hack happens in spring, while measles produces two epidemics, one in winter and one in March. Flu, the regular cold, and other diseases of the upper respiratory plot, like sore throat, happen transcendently in the colder time of year.
- Disease flare-ups are generally brought about by a contamination, sent through individual to-individual contact, creature to-individual contact, or from the climate or other media.
- Outbreaks may likewise happen following openness to synthetics or to radioactive materials. For instance, Minamata disease is brought about by openness to mercury.
- Epidemics might be the outcome of debacles of another sort, for example, typhoons, floods, seismic tremors, dry spells, and so forth.
- Occasionally the reason for an episode is obscure, even after intensive examination [4].

Types of epidemic diseases

- **Common-Source Epidemics**

Normal source epidemics are habitually, yet not generally, due to openness to an irresistible agent. They can result from tainting of the climate (air, water, food, soil) by modern synthetics or pollutant. Eg, Bhopal gas misfortune in India and Minamata disease in Japan coming about because of utilization of fish containing a high centralization of methyl mercury[3].

Single exposure or "point-source" epidemics

These are otherwise called "point-source" epidemics. The openness to the disease specialist is brief and basically synchronous, the resultant cases all create inside one brooding time of the disease. E.g. an epidemic of food harming. The principle highlights of a "point-source" epidemic are:

- ✓ The epidemic bend rises and falls quickly, with no optional waves.
- ✓ The epidemic will in general be hazardous, there is a grouping of cases inside a restricted time period, and
- ✓ More critically, every one of the cases create inside one brooding time of the disease [3].

Continuous or multiple exposure epidemics

On the off chance that the epidemic proceeds over more than one hatching period, there are either a constant or numerous openings to a typical source or a proliferated spread. Sometimes the openness from a similar source might be delayed – consistent, rehashed or irregular – not really simultaneously or place. For model, a whore might be a typical source in a gonorrhea flare-up, however since she will taint her customers throughout some undefined time frame there might be no unstable ascent in the quantity of cases. A well of tainted water, or a broadly disseminated brand of antibody (for example polio immunization), or food, could result in comparative outbreaks. In these occurrences, the subsequent epidemics will in general be more broadened or irregular. The flare-up of respiratory ailment, the Legionnaire's disease, in the midyear of 1976 in Philadelphia (USA) was a typical source, ceaseless or rehashed openness outbreak. This flare-up, as in other outbreaks of this sort, proceeded past the scope of one hatching period. There was no proof of who had contact with sick people. auxiliary cases among people[3].

Propagated Epidemics

An engendered epidemic is regularly of irresistible cause and results from individual to-individual transmission of an irresistible specialist (e.g., epidemics of hepatitis an and polio). The epidemic as a rule shows a progressive ascent and tails off over an any longer time of time. Transmission proceeds until the quantity of susceptibles is exhausted or defenseless people are not, at this point presented to tainted people or delegate vectors. The speed of spread relies on group resistance, openings for contact and optional assault rate. Propagated epidemics are bound to happen where countless powerless are totaled, or where there is an ordinary inventory of new helpless people (e.g., birth, migrants) bringing down crowd invulnerability[5].

Mixed Epidemics

A few epidemics have highlights of both basic source epidemics and proliferated epidemics. The example of a typical source flare-up followed by auxiliary individual to-individual spread isn't uncommon. These are called mixed epidemics [6].

MAJOR EPIDEMIC DISEASES IN 2002-2010

2002 - 2003

SARS Emerges in China

The Severe Acute Respiratory Syndrome (SARS) Covid, part of a group of infections that normally cause respiratory side effects like hacking what's more, windedness, is first recognized in late 2002 in southern China. SARS spreads to in excess of two dozen nations across four landmasses, tainting in excess of 8,000 individuals. In March 2003, the WHO triggers its Global Outbreak Alert and Response Organization (GOARN) to facilitate research by groups of worldwide specialists and the sending of provisions and wellbeing laborers to influenced nations. Wellbeing specialists forcefully reprimand Beijing for concealing the underlying spread of the infection. SARS murders near 800, most inside China and Hong Kong, by the time the episode is subdued in mid-2003. The infection is thought to have been sent to people through contact with civet felines[7].

SYMPTOMS

- ✓ Fever over 100.4°F
- ✓ Dry cough
- ✓ Sore throat
- ✓ Problems breathing, including shortness of breath
- ✓ Headache
- ✓ Body aches
- ✓ Loss of appetite
- ✓ Night sweats and chills
- ✓ Confusion
- ✓ Rash

TREATMENT[8]

There is no affirmed treatment that works for each individual who has SARS. Antiviral meds and steroids are now and again given to diminish lung growing, however aren't successful for everybody. Supplemental oxygen or a ventilator might be endorsed if important. In serious cases, blood plasma from somebody who has effectively recuperated from SARS may likewise be regulated. Be that as it may, there isn't yet sufficient proof to demonstrate that these medicines are viable.

STEPS TAKEN[9]

MARCH

March 12: The World Health Organization (WHO) gives a worldwide alarm for a extreme type of pneumonia of obscure beginning in people from China, Vietnam, also, Hong Kong.

March14: CDC (Centers for infectious prevention and avoidance) actuated its Crisis Operations Center (EOC).

March 15: CDC (Centers for infectious prevention and counteraction) gives first wellbeing alarm and has media tele-preparation about an abnormal pneumonia that has been named Severe Acute Respiratory Syndrome (SARS). CDC issues between time rules for state and nearby wellbeing divisions on SARS. CDC gives a "Wellbeing Alert Notice" for voyagers to the United States from Hong Kong, Guangdong Province (China).

March 20: CDC (Centers for infectious prevention and anticipation) issues disease control safeguards for airborne producing systems on patients who are associated with having SARS.

March 22: CDC (Centers for infectious prevention and anticipation) issues break lab biosafety rules for dealing with and handling examples related with SARS.

March 24: CDC (Centers for infectious prevention and counteraction) lab investigation proposes another Covid might be the reason for SARS. In the United States, 39 speculate cases (until this point) had been distinguished. Of those cases, 32 of 39 had headed out to nations were SARS was accounted for.

March 27: CDC (Centers for infectious prevention and anticipation) issues between time homegrown rules for the board of openings to SARS for medical care and other institutional settings.

March 28: The SARs episode is more far reaching. CDC starts using pandemic making arrangements for SARS.

March 29: CDC broadened its tourism warning for SARS to incorporate all of terrain China and added Singapore. CDC isolate staff started meeting planes, load ships and journey ships coming either straightforwardly or by implication to the US from China, Singapore and Vietnam and furthermore starts distributing health alert cards to voyagers.

APRIL

April 4: The number of suspected U.S. SARS cases was 115; announced from 29 states. There were no passings among these presume instances of SARS in the United States.

April 5: CDC (Centers for infectious prevention and avoidance) builds up local area outreach group to address demonization related with SARS.

April 10: CDC (Centers for infectious prevention and anticipation) gave explicit direction for understudies presented to SARS.
April 14: CDC distributes a succession of the infection accepted to be answerable for the worldwide pestilence of SARS. Recognizing the hereditary arrangement of another infection is essential to treatment and anticipation endeavors. The outcomes came only 12 days after a group of researchers and professionals started working nonstop to develop cells taken from the throat culture of a SARS patient.
April 22: CDC issues a wellbeing alert for voyagers to Toronto, Ontario (Canada).

MAY
May 6: In the United States, no new plausible cases were accounted for in the last 24 hours, and there was no proof of continuous transmission past the underlying case reports in voyagers for over 20 days. The regulation in the United States has been fruitful.
May 20: CDC lifted the movement alert on Toronto since over 30 days (or three SARS brooding periods) had slipped by since the date of beginning of side effects for the last detailed case.
May 23: CDC reestablished travel alert for Toronto on the grounds that on May 22, Canadian wellbeing authorities revealed a bunch of five new likely SARS cases.

JUNE
June 4: CDC eliminated the movement alert for Singapore and minimized the explorer warning for Hong Kong from a tourism warning to a movement alert.

JULY
July 3: CDC eliminated the movement alert for terrain China.
July 5: WHO declared that the worldwide SARS flare-up was contained.
July 10: CDC eliminated the movement alert for Hong Kong and Toronto.
July 15: CDC eliminated the movement alert for Taiwan.
July 17: CDC (Centers for infectious prevention and anticipation) refreshed the SARS case definition which decreased the quantity of U.S. cases considerably. The change comes about because of barring cases in which blood examples that were gathered more than 21 days after the beginning of ailment test negative.

DECEMBER
December 31: Globally, WHO got reports of SARS from 29 nations and locales; 8,096 people with plausible SARS bringing about 774 passings. In the US, eight SARS diseases were recorded by lab testing what's more, an extra 19 likely SARS diseases were accounted for.

2004
Afghanistan leishmaniasis epidemic[10]
Leishmaniasis is a parasitic infection that is found in pieces of the jungles, subtropics, and southern Europe. It is named a disregarded tropical sickness (NTD). Leishmaniasis is brought about by contamination with Leishmania parasites, which are spread by the nibble of phlebotomine sand flies. There are a few unique types of leishmaniasis in individuals. The most widely recognized structures are cutaneous leishmaniasis, which causes skin injuries, and instinctive leishmaniasis, which influences a few inward organs (generally spleen, liver, and bone marrow).

Experience explorers, bird watchers, evangelists, armed force faculty, development laborers, and analysts on evening time tasks are at higher hazard of being presented to sandflies. Enormous plagues of leishmaniasis can happen among individuals dislodged into swarmed metropolitan territories through war or relocation, or when high paces of unhealthiness debilitate individuals in influenced locales. By and large, canines and rodents are the repository for most species of Leishmania. In neediness stricken, thickly populated territories, people may turn into the essential ‘‘reservoir’’ and wellspring of repetitive disease with leishmaniasis, especially with *L.donovani*. This is

''anthroponotic''; transmission. Leishmaniasis is brought about by a protozoa parasite from over 20 Leishmania species. More than 90 sand fly species are known to transmit Leishmania parasites. There are 3 fundamental types of the infection:

- **Visceral leishmaniasis (VL):** otherwise called kala-azar is lethal assuming left untreated in more than 95% of cases. It is described by sporadic episodes of fever, weight reduction, growth of the spleen and liver, and iron deficiency. Most cases happen in Brazil, East Africa and in India. An expected 50,000 to 90,000 new instances of VL happen overall every year, with just between 25 to 45% answered to WHO. It stays one of the top parasitic illnesses with episode and mortality potential. In 2018, over 95% of new cases answered to WHO happened in 10 nations: Brazil, China, Ethiopia, India, Iraq, Kenya, Nepal, Somalia, South Sudan and Sudan.
- **Cutaneous leishmaniasis (CL):** is the most widely recognized type of leishmaniasis and causes skin injuries, principally ulcers, on uncovered pieces of the body, leaving long lasting scars and genuine handicap or disgrace. About 95% of CL cases happen in the Americas, the Mediterranean bowl, the Center East and Central Asia. In 2018 more than 85% of new CL cases happened in 10 nations: Afghanistan, Algeria, Bolivia, Brazil, Colombia, Iran (Islamic Republic of), Iraq, Pakistan, the Syrian Arab Republic and Tunisia. It is assessed that between 600, 000 to 1 million new cases happen overall every year.
- Mucocutaneous leishmaniasis leads to halfway or add up to obliteration of mucous layers of the nose, mouth and throat. More than 90% of mucocutaneous leishmaniasis cases happen in Bolivia(the Plurinational Territory of), Brazil, Ethiopia and Peru.

SYMPTOMS

- Prolonged fever
- Enlarged spleen and liver
- Substantial weight loss
- Progressive anaemia
- Usually fatal if untreated

Diagnosis and treatment [11]

In instinctive leishmaniasis, finding is made by joining clinical signs with parasitological, or serological tests (like quick symptomatic tests). In cutaneous and mucocutaneous leishmaniasis serological tests have restricted worth furthermore, clinical indication with parasitological tests affirms the finding. The treatment of leishmaniasis relies upon a few components including type of sickness, accompanying pathologies, parasite species and geographic area. Leishmaniasis is a treatable and reparable sickness, which requires animmunocom petent framework since prescriptions won't dispose of the parasite from the body, along these lines the danger of backslide if immune suppression happens. All patients determined as to have instinctive leishmaniasis require expeditious and complete treatment. Nitty gritty data on treatment of the different types of the infection by geographic area is accessible in the WHO specialized report arrangement 949, ''Control of leishmaniasis''.

STEPS TAKEN[11]

10 AUGUST 2004 A quick intercession by the World Health Association and its accomplices, the Massoud Foundation and HealthNet Worldwide, in Kabul, Afghanistan, made conceivable by a gift from the Belgian government, ought to significantly lessen the rate of leishmaniasis in under two years. Without prompt activity, the current scourge undermines to grow into a wild circumstance. This crisis activity points not just to treat those right now influenced in the intense period of the pandemic, however to forestall further transmission of the sickness.

Kabul is the biggest focal point of cutaneous leishmaniasis on the planet, with an expected 67,500 cases. The figure represents 33% of the 200,000 cases on the whole of Afghanistan. Cutaneous leishmaniasis is an impairing infection sent by the chomp of the sand fly. The sickness prompts distortion typically on the face and hands, and social shame, especially for ladies and youngsters. As an prompt measure, WHO and accomplices hope to start circulating insect

spray treated bed nets soon to shield in excess of 30,000 individuals from sand flies. While powerful control programs for leishmaniasis once existed in Afghanistan, the previous twenty years of progressing strife has seriously debilitated a significant part of the wellbeing foundation. Natural harm and poor sterile conditions have brought about the multiplication of sand flies; reproducing destinations. At the same time, the convergence of enormous quantities of uprooted individuals threatens to increase the diseases effectively pestilence levels. With little insusceptibility to leishmaniasis, dislodged individuals, or for this situation, individuals getting back from adjoining Pakistan, are regularly more defenseless to the sickness. To deflect a sharp expansion in cases, WHO and its accomplices are today dispatching a crisis activity in Kabul that will incorporate not just medication treatment, yet the conveyance of bug spray treated nets. As previously, the arrangement of first-line drugs has been gotten by WHO as a team with Afghanistan's Ministry of Health. Simultaneously, 16,000 bug spray treated bednets will be circulated all through Kabul. These will assist with ensuring almost 30,000 individuals. Because of an award of €200,000 from the Belgian government, this prompt activity is an ideal intercession that intends to shorten the pinnacle transmission season from September to October. This quick intercession is basically the principal stage in a one-year plan to carry out a public leishmaniasis control program. On the off chance that the underlying activity is fruitful in Kabul, it will at that point be duplicated in different pieces of Afghanistan.

Work of WHO on leishmaniasis control involves

- Supporting public leishmaniasis control programs in fact and monetarily to create refreshed rules and make infectious prevention arrangements, counting economical, successful reconnaissance frameworks, and pandemic readiness and reaction frameworks.
- Monitoring infection drifts and surveying the effect of control exercises which will permit bringing issues to light and support on the worldwide weight of leishmaniasis and elevating fair admittance to wellbeing administrations.
- Developing proof based approach procedures and principles for leishmaniasis avoidance and control and observing their execution.
- Strengthening cooperation and coordination among accomplices and partners.
- Promoting exploration and utilization of successful leishmaniasis control including protected, viable and reasonable prescriptions, just as demonstrative devices and antibodies.
- Supporting public control projects to guarantee admittance to quality- guaranteed medications.

2009 - 2010

U.S. at Center of H1N1 [12]

Another flu infection, named H1N1 and usually alluded to as the pig influenza in view of its connects to flu infections that circle in pigs, starts to spread in mid 2009 in Mexico and the United States. Dissimilar to different strains of flu, H1N1 excessively influences kids and more youthful individuals. The CDC considers it the "first worldwide influenza pandemic in quite a while." The WHO pronounces a PHEIC in April 2009, at that point assigns the spread of H1N1 a pandemic in June, after the infection arrives at in excess of seventy nations. Accordingly, some countries advise against movement to North America, and China forces obligatory isolates for patients and their nearby contacts. The CDC appraises that somewhere in the range of 151,700 and 575,400 individuals bite the dust worldwide around 12,500 in the US in the principal year after the infection is found. Around 80% of the individuals who pass on are more youthful than 65. The WHO reports the pandemic's end in August 2010, however the strain keeps on coursing occasionally.

SYMPTOMS

- ✓ Cough
- ✓ Fever
- ✓ Sore throat
- ✓ Stuffy or runny nose
- ✓ Body aches

- ✓ Headache
- ✓ Chills
- ✓ Fatigue

TREATMENT [13]

Treatment is generally steady and comprises of bedrest, expanded liquid utilization, hack suppressants, and antipyretics and analgesics (eg, acetaminophen, nonsteroidal mitigating drugs) for fever and myalgias. Serious cases may require intravenous hydration and other steady measures. Antiviral specialists may likewise be considered for treatment or prophylaxis (see Drug). Patients ought to be urged to remain at home on the off chance that they become sick, to evade close contact with individuals who are wiped out, to wash their hands frequently, and to maintain a strategic distance from contacting their eyes, nose, and mouth. The CDC suggests the accompanying activities when human contamination with H1N1 flu (pig influenza) is affirmed in a local area.

Antiviral treatments [14, 15]

Standard treatment routine for antiviral medications,

oseltamivir, the standard grown-up treatment course is one 75 mg case double a day for five days. For extreme or delayed ailment, doctors may choose to utilize a higher portion or proceed with the treatment for more. Zanamivir, is taken as a powder by inward breath. The suggested portion for treatment of grown-ups and kids from the age of 5 years is two inward breaths (2 x 5mg) twice every day for five days.

STEPS TAKEN

- CDC carried out a normalized examining methodology for influenza across open wellbeing and clinical research centers that is broadly agent and that guarantees productivity and information certainty. This implies that that another influenza infection with pandemic potential can be recognized all the more effectively and quickly.
- All seasonal infection tests (around 6,000 to 8,000 examples) submitted to CDC presently go through full genetic sequencing as an initial step. This gives a complete image of the various seasonal infections that are circling in individuals, empowers quicker episode reaction, and enormously grows the worldwide influenza hereditary information base[16].
- CDC accomplices with three state labs that currently go about as territorial reference focuses doing hereditary sequencing utilizing CDC's standard trying rehearses. Information from these three National Influenza Reference Centers (NIRCs) are then transferred to a CDC-upheld "cloud" figuring stage, making it in a flash open to approved CDC researchers. The formation of these provincial centers has extended limit, improved coherence of activities, and sped up by and large reaction time.
- CDC-created Reverse Transcription-Polymerase Chain Reaction testing (rRT-PCR) has gotten the best quality level in seasonal infection testing among general wellbeing labs, bringing about information that are more dependable and accessible more quickly. CDC makes these test units accessible to qualified research centers through the online International Reagent Repository, an online assistance that upholds worldwide observation for influenza and which can quickly flood to help interest for testing during a pandemic [17].
- A precise appraisal of the presentation of Rapid Influenza Symptomatic Tests (RIDTs) led to enhancements in the utilization and improvement of quick seasonal infection tests. Working with FDA, CDC upholds yearly testing of all business influenza tests to guarantee that they proceed to fulfill new testing guidelines.
- Testing for potential seasonal infection protection from antiviral medications, which used to happen just at CDC, has extended to 19 different research centers. This development builds limit with respect to testing and speeds up reaction time.

Furthermore, CDC is continually assessing new seasonal infections to decide in the event that they are defenseless to industrially accessible and trial antiviral medications. Flu epidemics can bring about significant wellbeing (clinical ailment, hospitalization, passings) and financial (non-appearance, decline in profitability, decline in movement and exchange) impacts. With globalization, illnesses will in general spread quickly; when they become pandemics, they can rapidly influence huge populaces to extraordinarily duplicate these effects across nations and areas.

For this situation, worldwide travel was huge for the worldwide scattering of the infection. When the novel A(H1N1)2009 infection arose, specialists at first investigated, and depended on, measures to defer or contain the spread, expecting to limit the effect while endeavors were continuous to all the more likely comprehend the epidemiology, clinical course, treatment and its results, just as the expected advancement of an antibody. From the get-go in the flu A(H1N1)2009 episode, the World Health Organization (WHO) gave direction on open wellbeing estimates that could be applied to decrease or postpone the transmission of the flare-up at singular/family and local area levels and in circumstances where people may assemble like schools or mass get-togethers. In managing Part States on pandemic flu readiness and reaction, WHO built up a full scope of direction records to completely address these measures utilizing a consultative methodology. They range from data contained in explicit direction records like the pandemic flu readiness furthermore, reaction direction and the International Health Regulations (IHR 2005) to devices and procedures created from master logical consultative gatherings. As WHO embraces wanting to get ready for the update of the epidemic readiness direction, it is basic to assess exercises learned by Part States and specialists who carried out or explored explicit public wellbeing measures during the flu A(H1N1)2009 epidemic [18, 19].

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Table. 1: Abbrevaitions

SI. NO	ABBERIVATION	MEANING
1	**WHO**	World Health Organization
2	**SARS**	Severe Acute Respiratory Syndrome
3	**CDC**	Centres for disease control and prevention
4	**EOC**	Emergency Operations Centre
5	**GOARN**	Global Outbreak Alert and Response Network
6	**NIRCs**	National Influenza Reference Centres
7	**FDA**	Food Drug Administration
8	**INHR**	International Health Regulations
9	**IHR**	International Health Regulations
10	**rRT-PCR**	Reverse Transcription-Polymerase Chain Reaction testing

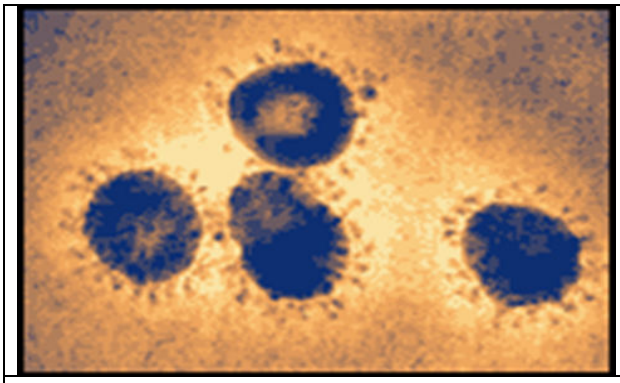

Fig. No. 1: Microscopic view of SARS virus

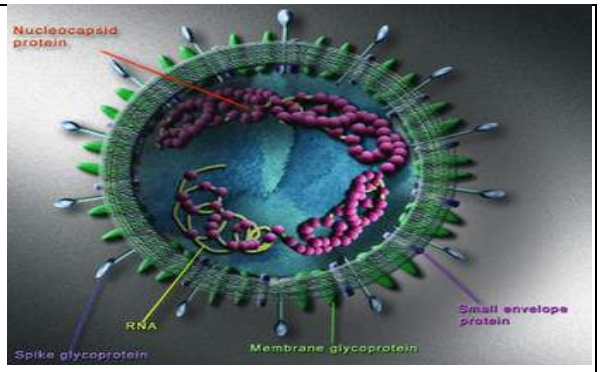

Fig. No. 2: Internal structure of SARS virus with parts

Fig. No. 3: Parasite that cause leishmaniasis

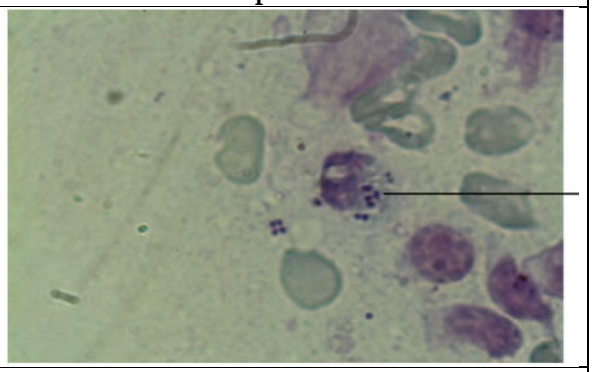

Fig. No. 4: Leishmaniasis inside the macrophages

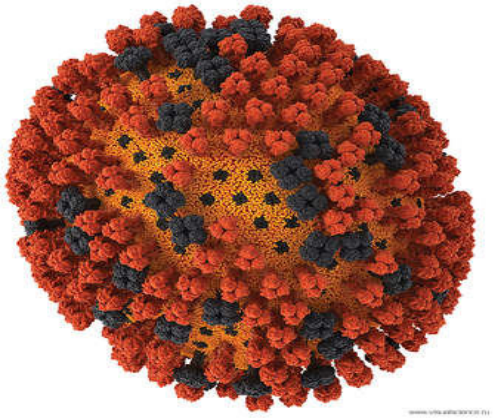

Fig. No. 5: H_1N_1 Virus

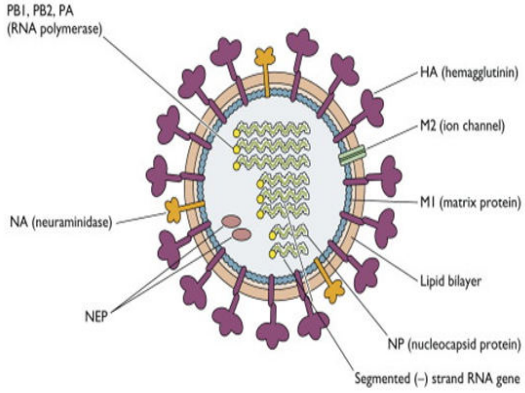

Fig. No. 6: Structure of H_1N_1 virus

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RESEARCH ARTICLE

A New Approaches About Contra $g^*\beta$ −Continuous Functions in Topological Spaces

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ABSTRACT

Initially the concept of $g^*\beta$-closed sets were introduced by Punitha Tharani. A and Sujitha.H [8] in topological spaces in 2020. Now, we introduce a new sets Contra generalized star beta continuous function (briefly,$Contrag^*\beta - continuous\ function$) in topological spaces. Also we present almost contra $g^*\beta$-continuous functions and some of its characteristics and several properties are investigated. **Mathematics Subject Classification (2010):** 54A04, 54C08, 54C10.

Keywords: $contra\ g^*\beta - continuous, almost\ contra\ g^*\beta - continuous, contra\ g^*\beta - irresolute.$

INTRODUCTION

The notion of contra and almost contra was introduced by Dontchev [5] in 1996. Along with him Noiri [6] introduced a new weaker form of functions called contra semi continuous function. Contra pre-continuous functions was introduced by Noiri [7]. In 2004 almost contra pre-continuous function was introduced by Ekici.E [4]. Following this, numerous author presented numerous kinds of new generalizations of contra-continuity, contra semi-continuity,

contra generalized semi- continuity, contra and almost gb-continuity, contra and almost contra g^*p – continuity and so on and they investigated their properties. The authors [8] introduced the concept of generalized star beta closed sets in TS. We define a new notioncontra $g^*\beta$-continuous functions in topological spaces. Also we present almost contra $g^*\beta$-continuous function and contra $g^*\beta$-irresolute and also, a portion of its attributes and few different properties are researched. The straightforward proof of the theorems is omitted. For the concepts of generalized topological spaces we refer [1,3,6,8,10]. Here after in this paper $(\mathcal{U},\tau)$ and $(\mathcal{V},\sigma)$ denotes the non-empty TS on which no separation axiom are assumed unless mentioned for a subset $\mathcal{S}$ of $\mathcal{U}$, $cl(\mathcal{S})$ and $int(\mathcal{S})$ represent the closure of $\mathcal{S}$ and interior $\mathcal{S}$ resp.

Contra $g^*\beta$-Continuous Function

Definition: 2.1 A function $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ is said to be a contra $g^*\beta$-continuous (here after denoted by, $contra\ g^*\beta - cts$) if $h^{-1}(\mathcal{S})$ is $g^*\beta$-closed (briefly, $g^*\beta$-$\mathcal{C}$) in $\mathcal{U}$ for each open set $\mathcal{S}$ in $\mathcal{V}$.

Example: 2.2 Let $\mathcal{U} = \{p,q,r\} = \mathcal{V}$ with $\tau = \{\Phi,\mathcal{U},\{p\}\}$ and $\sigma = \{\Phi,\mathcal{V},\{q\}\}$. Define $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ by $h(p) = p,\ h(q) = q,\ h(r) = q$. Obviously$h$ is $contra\ g^*\beta - cts$function.

Example: 2.3 Let $\mathcal{U} = \{p,q,r,s\},\mathcal{V} = \{p,q,r,s\}$, with $\tau = \{\Phi,\mathcal{U},\{p\},\{q\},\{p,q\},\{p,q,r\}\}$ and $\sigma = \{\Phi,\mathcal{V},\{r\},\{p,r,s\}\}$. Define $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ by $h(p) = p, h(q) = q, h(r) = s$ and $h(s) = r$. Clearly$h$ is $contra\ g^*\beta - cts$function.

Theorem: 2.4 Every $contra - cts$function is $contra\ g^*\beta - cts$ function but not converse.

Proof: We know that every closed set is $g^*\beta - \mathcal{C}$. (Refer ex.2.5).

Example: 2.5 Let $\mathcal{U} = \{p,q,r,s\} = \mathcal{V}$ with $\tau = \{\Phi,\mathcal{U},\{p\},\{q\},\{p,q\},\{p,q,r\}\}$ and $\sigma = \{\Phi,\mathcal{V},\{r\},\{p,r,s\}\}$. Define $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ by $h(p) = s, h(q) = r, h(r) = q$ and $h(s) = p$. Evidently,h is $contra\ g^*\beta - cts$but$h$ is not $contra - cts$. Because$h^{-1}(\{p,r,s\}) = \{p,q,s\}$ is $g^*\beta - \mathcal{C}$set but not closed in $\mathcal{U}$.

Theorem: 2.6 Let $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ be a function, then every $contra\ g^* - cts$is $contra\ g^*\beta - cts$ but not converse.

Proof: Proof follows from the fact that every g-$\mathcal{C}$set is$g^*\beta$-$\mathcal{C}$.

Example: 2.7 Allow$\mathcal{U} = \{p,q,r\},\mathcal{V} = \{p,q,r\}$ with $\tau = \{\Phi,\mathcal{U},\{p\},\{p,q\}\}$ and $\sigma = \{\Phi,\mathcal{V},\{q\}\}$. Define $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ by $h(p) = r, h(q) = r, h(r) = p$. Clearly h is $contra\ g^*\beta - cts$ but not $contra\ g^* - cts$

Theorem: 2.8 Let$h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ be a function. Then

a) Every $contra\ g^* - cts$is $contra\ g^*\beta - cts$.
b) Every $contra\ g^{\#} - cts$is $contra\ g^*\beta - cts$.

Proof: (a) &(b): Proves that every g^*-$\mathcal{C}$and $g^{\#}$-$\mathcal{C}$is $g^*\beta$-$\mathcal{C}$.

But converse not true.(Refer Ex.2.9)

Example: 2.9 Allow $\mathcal{U} = \{p,q,r\},\mathcal{V} = \{p,q,r\}$ with $\tau = \{\Phi,\mathcal{U},\{p\}\}$and $\sigma = \{\Phi,\mathcal{V},\{q,r\}\}$. Define $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ by $h(p) = q, h(q) = p, h(r) = r$. Now h is $contra\ g^*\beta - cts$ but not $contra\ g^{\#} - cts$ and h is $contra\ g^* - cts$.

Theorem: 2.10 Let $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ be a function. Then

a) Every $contra\ g^*\beta - cts$is $contra\ rg - cts$.
b) Every $contra\ g^*\beta - cts$ is $contra\ gpr - cts$.
c) Every $contra\ g^*\beta - cts$is $contra\ gsp - cts$.
d) Every $contra\ g^*\beta - cts$ is $contra\ g^*p - cts$.

Proof: To prove$(\boldsymbol{c})$: Let $\mathcal{S}$ be an open set in $\mathcal{V}$. Since$h$ is a $contra\ g^*\beta - cts$function, $h^{-1}(\mathcal{S})$ is $g^*\beta$-closed in $\mathcal{U}$. Then $h^{-1}(\mathcal{S})$ is gsp-closed in $\mathcal{U}$ for each $\mathcal{S}$ is open in $\mathcal{V}$. Thus h is $contra\ gsp - cts$.

(a) &(b): Proves that every $g^*\beta$-$\mathcal{C}$ set is $rg - \mathcal{C}$, $gpr - \mathcal{C}$ and g^*p- $\mathcal{C}$.

Remark: 2.11 But the converse not true. Refer Ex.2.12

Example: 2.12

(i) Allow $\mathcal{U} = \{p,q,r\}, \mathcal{V} = \{p,q,r\}$ with $\tau = \{\Phi, \mathcal{U}, \{p\}, \{p,q\}, \{p,r\}\}$ and $\sigma = \{\Phi, \mathcal{V}, \{q\}\}$. Define $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ by $h(p) = q, h(q) = r, h(r) = p$. Clearly h is *contra* $rg - cts$ and *contra* $gpr - cts$ but h is not *contra* $g^*\beta - cts$.

(ii) Allow $\mathcal{U} = \{p,q,r\}, \mathcal{V} = \{p,q,r\}$ with $\tau = \{\Phi, \mathcal{U}, \{p\}, \{q\}, \{p,q\}\}$ and $\sigma = \{\Phi, \mathcal{V}, \{p\}, \{p,q\}\}$. Define $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ by $h(p) = p, h(q) = r, h(r) = q$. Clearly h is *contra* $gsp - cts$but h is not *contra* $g^*\beta - cts$.

Remark: 2.13 The notion of $g^*\beta - cts$and *contra* $g^*\beta - cts$are independent. Refer to the below example.

Example: 2.14

(i) Let $\mathcal{U} = \{p,q,r,s\}, \mathcal{V} = \{p,q,r,s\}$ with $\tau = \{\Phi, \mathcal{U}, \{p\}, \{p,s\}, \{p,q,s\}\}$ and $\sigma = \{\Phi, \mathcal{V}, \{q\}, \{r,s\}, \{q,r,s\}\}$. Define $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ by $h(p) = p, h(q) = r, h(r) = s$ and $h(s) = q$. Clearly h is *contra* $g^*\beta - cts$ but $h^{-1}(\{p,q\}) = \{p,s\}$ is not $g^*\beta$-$\mathcal{C}$ in $\mathcal{U}$. So h is not $g^*\beta - cts$.

(ii) Let $\mathcal{U} = \{p,q,r,s\}, \mathcal{V} = \{p,q,r,s\}$ with $\tau = \{\Phi, \mathcal{U}, \{p,r,s\}\}$ and $\sigma = \{\Phi, \mathcal{V}, \{p,s\}\}$. Define an identity mapping$h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$. Clearly h is$g^*\beta - cts$but not *contra* $g^*\beta - cts$because $h^{-1}(\{p,s\}) = \{p,s\}$ is not $g^*\beta$-$\mathcal{C}$in $\mathcal{U}$. So h is not$g^*\beta - cts$.

Remark: 2.15 The composition of two *contra* $g^*\beta - cts$functions need not be *contra* $g^*\beta - cts$. Refer to the below example.

Example: 2.16 Allow $\mathcal{U} = \{p,q,r,s\}, \mathcal{V} = \{p,q,r,s\}$ with $\tau = \{\Phi, \mathcal{U}, \{r\}, \{p,r,s\}\}$ and $\sigma = \{\Phi, \mathcal{V}, \{p\}, \{q\}, \{p,q\}, \{q,r\}, \{p,r,s\}\}$ and $\mu = \{\mathcal{W}, \Phi, \{p,r,s\}\}$. Define a mapping $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ and $k:(\mathcal{V},\sigma) \to (\mathcal{W},\mu)$. Now h and k are *contra* $g^*\beta - cts$, but$k \circ h:\mathcal{U} \to \mathcal{W}$ is not *contra* $g^*\beta - cts$,since $(k \circ h)^{-1}(\{p,r,s\}) = f^{-1}(\{p,r,s\}) = \{p,r,s\}$ which is not $g^*\beta$-$\mathcal{C}$ in $\mathcal{U}$.

Theorem: 2.17 Let$h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ is *contra* $g^*\beta - cts$ and $k:(\mathcal{V},\sigma) \to (\mathcal{W},\mu)$ is *cts* then $k \circ h:\mathcal{U} \to \mathcal{W}$ is *contra* $g^*\beta - cts$.

Proof: Let $\mathcal{S}$ be open in $\mathcal{W}$. Because$k$ is $cts k^{-1}(\mathcal{S})$ is open in $\mathcal{V}$. Then $h^{-1}(k^{-1}(\mathcal{S}))$ is $g^*\beta$-$\mathcal{C}$ in $\mathcal{U}$. Since h is *contra* $g^*\beta - cts$. So$(k \circ h)^{-1}(\mathcal{S})$ is $g^*\beta$-$\mathcal{C}$in $\mathcal{U}$. Therefore$k \circ h$ is *contra* $g^*\beta - cts$.

Corollary: 2.19 If $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ is $g^*\beta$-irresolute and $k:(\mathcal{V},\tau) \to (\mathcal{W},\mu)$ is *contra* $- cts$function then $k \circ h:\mathcal{U} \to \mathcal{W}$ is *contra* $g^*\beta - cts$.

Theorem: 2.20 If a surjective mapping $h:\mathcal{U} \to \mathcal{V}$ is $g^*\beta$-irresolute *cts* and$g^*\beta$-$\mathcal{O}$, let $k:\mathcal{V} \to \mathcal{W}$ be any function then $k \circ h$ is *contra* $g^*\beta - cts$if and only if$k$ is *contra* $g^*\beta - cts$.

Proof: **Necessity:** Assume$k \circ h$is *contra* $g^*\beta - cts$. Let $\mathcal{S}$ be a closed set in $\mathcal{W}$. Now$(k \circ h)^{-1}(\mathcal{S}) = h^{-1}(k^{-1}(\mathcal{S}))$ is $g^*\beta$-$\mathcal{O}$in $\mathcal{U}$. Since h is $g^*\beta$-$\mathcal{O}$and surjective, $g^*\beta$-irresolute $h(h^{-1}(k^{-1}(\mathcal{S})))$ is $g^*\beta$-$\mathcal{O}$in $\mathcal{V}$. That is$k^{-1}(\mathcal{S})$ is $g^*\beta$-$\mathcal{O}$in $\mathcal{V}$. Therefore$k$ is *contra* $g^*\beta - cts$.

Sufficiency: Suppose$k$ is *contra* $g^*\beta - cts$. Let $\mathcal{S}$ be a closed set in $\mathcal{W}$. Then $k^{-1}(\mathcal{S})$ is $g^*\beta$-$\mathcal{O}$in $\mathcal{V}$. Since h is $g^*\beta$-irresolute $h^{-1}(k^{-1}(\mathcal{S}))$ is $g^*\beta$-$\mathcal{O}$. Thus $(k \circ h)^{-1}(\mathcal{S})$ is $g^*\beta$-$\mathcal{O}$in $\mathcal{U}$. Therefore$k \circ h$ is *contra* $g^*\beta - cts$.

Theorem:2.21 If $(\mathcal{U},\tau)$ and $(\mathcal{V},\sigma)$ in TS, then any function $h:\mathcal{U} \to \mathcal{V}$, the following conditions are equivalent.

a) h is *contra* $g^*\beta - cts$.

b) The inverse image of each closed set in $\mathcal{V}$ is $g^*\beta$-$\mathcal{O}$in $\mathcal{U}$.

Proof: Straight forward. So (a) ⇒ (b) & (b) ⇒ (a)

Definition: 2.22 A space $(\mathcal{U},\tau)$ is called a locally $g^*\beta$-indiscrete (here after denoted by, *lc* $g^*\beta - indiscrete$) if every $g^*\beta$-$\mathcal{O}$is closed in $\mathcal{U}$.

Theorem: 2.23 If a function $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$is *contra* $g^*\beta - cts$and $\mathcal{U}$ be a *lc* $g^*\beta - indiscrete$, then h is continuous.

Proof: Consider$\mathcal{S}$ be open in $\mathcal{V}$. Then $h^{-1}(\mathcal{S})$ is $g^*\beta$-$\mathcal{C}$in $\mathcal{U}$. Since $\mathcal{U}$ is *lc* $g^*\beta - indiscrete$space, $h^{-1}(\mathcal{S})$ is open in $\mathcal{U}$. Therefore$h$ is continuous.

Theorem: 2.24 If $h:\mathcal{U} \to \mathcal{V}$ is $g^*\beta - cts$and the space $(\mathcal{U},\tau)$ is $lc\ g^*\beta - indiscrete$then h is contra continuous.
Proof: Consider$\mathcal{S}$ be open in $\mathcal{V}$. Since h is $g^*\beta - cts$, $h^{-1}(\mathcal{S})$ is $g^*\beta$-$\mathcal{O}$in $\mathcal{U}$. Since $\mathcal{U}$ is$lc\ g^*\beta - indiscrete$, $h^{-1}(\mathcal{S})$ is closed set in $\mathcal{U}$. Soh is $contra\ g^*\beta - cts$.

Almost Contra $g^*\beta -$ Continuous

Definition: 3.1 A map$h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ is said to be an almost contra $g^*\beta$-continuous(here after denoted by, $\mathcal{A}\ell m\ contra\ g^*\beta - cts$) if $h^{-1}(\mathcal{S})$ is $g^*\beta$-$\mathcal{O}$set in $\mathcal{U}$ for every regular open(briefly, r-open) set $\mathcal{S}$ of $\mathcal{V}$.
Definition: 3.2 A map$h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ is said to be an$\mathcal{A}\ell m\ contra\ g^*\beta - cts$ if $h^{-1}(\mathcal{S})$ is $g^*\beta$-$\mathcal{C}$set in $\mathcal{U}$ for every r-open set $\mathcal{S}$ of $\mathcal{V}$.

Theorem: 3.3 Let $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ be a function then every $contra\ g^*\beta - cts$ function is $\mathcal{A}\ell m\ contra\ g^*\beta - cts$.
Proof: Proof follows from the fact that every r-open set is open.

Theorem: 3.4 Every$r$- set connected function is $\mathcal{A}\ell m\ contra\ g^*\beta - cts$ but not conversely. (Refer Eg.3.5)
Example: 3.5 $\mathcal{U} = \{p,q,r,s\} = \mathcal{V}$ with $\tau = \{\phi,\mathcal{U},\{p\},\{p,q\},\{p,s\},\{p,q,r\},\{s\},\{p,q,s\}\}$ and $\sigma = \{\phi,\mathcal{V},\{r\},\{s\},\{r,s\},\{q,s\},\{p,r,s\},\{q,r,s\}\}$. Allow a function$h:\mathcal{U} \to \mathcal{V}$. The inverse image of r-open set $\{q,s\}$ is not cl-open in $\mathcal{U}$. Then the inverse image of r-open in $\mathcal{V}$ is $g^*\beta$-$\mathcal{C}$ in $\mathcal{U}$. So,h is $\mathcal{A}\ell m\ contra\ g^*\beta - cts$ but not r- set connected.

Theorem: 3.6 For any two functions$h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$and $k:(\mathcal{V},\sigma) \to (\mathcal{W},\mu)$ also let $k^\circ h:(\mathcal{U},\tau) \to (\mathcal{W},\mu)$ be a composition function. Then

a) If k is $\mathcal{A}\ell m\ contra\ g^*\beta - cts$and k is r-connected, then $k^\circ h:(\mathcal{U},\tau) \to (\mathcal{W},\mu)$ is$\mathcal{A}\ell m\ contra\ g^*\beta - cts$.
b) If h is $\mathcal{A}\ell m\ contra\ g^*\beta - cts$ and k is perfectly continuous, then$k^\circ h$is$g^*\beta - cts$ and $contra\ g^*\beta - cts$.

Proof:

(a) Consider $\mathcal{S}$ be any r-open in $\mathcal{W}$. Because$k$ is r-set connected,$k^{-1}(\mathcal{S})$ is cl-open in $\mathcal{V}$. Because$h$ is $\mathcal{A}\ell m\ contra\ g^*\beta - cts$,then $h^{-1}(k^{-1}(\mathcal{S})) = (k^\circ h)^{-1}(\mathcal{S})$ is $g^*\beta$-$\mathcal{O}$ and $g^*\beta$-$\mathcal{C}$in $\mathcal{U}$. Thus$k^\circ h$is $\mathcal{A}\ell m\ contra\ g^*\beta - cts$ and $\mathcal{A}\ell m\ g^*\beta - cts$.
(b) Let $\mathcal{S}$ be open in $\mathcal{W}$. Because k is $cts, k^{-1}(\mathcal{S})$ is open in $\mathcal{V}$. Since h is $\mathcal{A}\ell m\ contra\ g^*\beta - cts$, then$h^{-1}(k^{-1}(\mathcal{S})) = (k^\circ h)^{-1}(\mathcal{S})$ is $g^*\beta$-$\mathcal{O}$ and $g^*\beta$-$\mathcal{C}$in $\mathcal{U}$. Thus$k^\circ h$ is$g^*\beta - cts$and $contra\ g^*\beta - cts$.

Theorem: 3.7 Let $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ and $k:(\mathcal{V},\sigma) \to (\mathcal{W},\mu)$ be two functions, let $k^\circ h:(\mathcal{U},\tau) \to (\mathcal{W},\mu)$ be a composition function. If h is $contra\ g^*\beta - cts$ and k is $\mathcal{A}\ell m - cts$, then $k^\circ h$is $\mathcal{A}\ell m\ contra\ g^*\beta - cts$.
Proof: Let $\mathcal{S}$ be any r-open in $\mathcal{W}$. Because k is $\mathcal{A}\ell m - cts$, $k^{-1}(\mathcal{S})$ is open in $\mathcal{V}$. Since h is $\mathcal{A}\ell m\ contra\ g^*\beta - cts$, $h^{-1}(k^{-1}(\mathcal{S})) = (k^\circ h)^{-1}(\mathcal{S})$ is $g^*\beta$-$\mathcal{C}$in $\mathcal{U}$. Then $k^\circ h$is $\mathcal{A}\ell m\ contra\ g^*\beta - cts$.
Definition: 3.8A map$h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$ is$contra\ g^*\beta$-irresolute if $h^{-1}(\mathcal{S})$ is $g^*\beta$-$\mathcal{C}$ set in $\mathcal{U}$ for every $g^*\beta$-$\mathcal{O}$ set $\mathcal{S}$in $\mathcal{V}$.
Definition: 3.9A map$h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$is perfectly contra $g^*\beta$-irresolute if $h^{-1}(\mathcal{S})$ is$g^*\beta$-$\mathcal{C}$and $g^*\beta$-$\mathcal{O}$ set in $\mathcal{U}$ for every $g^*\beta$-$\mathcal{O}$set $\mathcal{S}$in $\mathcal{V}$.

Theorem: 3.10 If $h:(\mathcal{U},\tau) \to (\mathcal{V},\sigma)$perfectly contra $g^*\beta$-irresolute if and only if h is $contra\ g^*\beta$-irresolute and $g^*\beta$-irresolute.
Proof: Straightforward.
Remark: 3.11 If $g^*\beta$-irresolute and contra $g^*\beta$-irresolute are independent of each other and we have provided the proof in below example.
Example:3.12$\mathcal{U} = \{p,q,r\} = \mathcal{V}$with$\tau = \{\phi,\mathcal{U},\{p\},\{q\},\{p,q\}\}and\sigma = \{\phi,\mathcal{V},\{p,q\}\}$.
Define $h:\mathcal{U} \to \mathcal{V}$ by$h(p) = q, h(q) = p\ and\ h(r) = r$. Clearly h is $g^*\beta$-irresolute but$h$ is not contra $g^*\beta$-irresolute. Since $h^{-1}(\{p\}) = \{q\}$ is not $g^*\beta$-$\mathcal{C}$in $\mathcal{U}$.
Remark: 3.13 Every contra $g^*\beta$-irresolute function is $contra\ g^*\beta - cts$. But the converse need not be true (Refer Eg.3.14).

Example:3.14 $\mathcal{U} = \{p,q,r,s\}, \mathcal{V} = \{p,q,r,s\}$ with $\tau = \{\phi, \mathcal{U}, \{p\}, \{p,q\}, \{p,s\}, \{p,q,r\}, \{s\}, \{p,q,s\}\}$ and $\sigma = \{\phi, \mathcal{V}, \{r\}, \{p,r,s\}\}$.
Define an identity mapping $h: \mathcal{U} \to \mathcal{V}$. Hence h is $contra\ g^*\beta - cts$, but h not contra $g^*\beta$-irresolute.

Theorem: 3.15 Let $h: (\mathcal{U}, \tau) \to (\mathcal{V}, \sigma)$ and $k: (\mathcal{V}, \sigma) \to (\mathcal{W}, \mu)$ be two functions, if k is $g^*\beta$- irresolute and h is $contra\ g^*\beta$- irresolute then $k^\circ h$ is $contra\ g^*\beta$- irresolute.
Proof: Let T be $g^*\beta$-$\mathcal{O}$in $\mathcal{W}$. Because k is $g^*\beta$-irresolute, $k^{-1}(T)$ is $g^*\beta$-$\mathcal{O}$in $\mathcal{V}$. Thus $h^{-1}(k^{-1}(T))$ is $g^*\beta$-$\mathcal{C}$ in $\mathcal{U}$. Since h is $contra\ g^*\beta$-irresolute. That is $(k^\circ h)^{-1}(T)$ is $g^*\beta$-$\mathcal{C}$ in $\mathcal{U}$. Hence $k^\circ h$ is $contra\ g^*\beta$-irresolute.

Theorem: 3.16 Let $h: (\mathcal{U}, \tau) \to (\mathcal{V}, \sigma)$ and $k: (\mathcal{V}, \sigma) \to (\mathcal{W}, \mu)$ be two functions, if h is $g^*\beta$- irresolute and k is $contra\ g^*\beta$- irresolute then $k^\circ h$ is $contra\ g^*\beta$- irresolute.
Proof: Let T be $g^*\beta$-$\mathcal{O}$in $\mathcal{W}$. Because k is $contra\ g^*\beta$-irresolute, $k^{-1}(T)$ is $g^*\beta$-$\mathcal{C}$in $\mathcal{V}$. Thus $h^{-1}(k^{-1}(T))$ is $g^*\beta$-$\mathcal{C}$in $\mathcal{U}$. Since h is $g^*\beta$-irresolute. That is $(k^\circ h)^{-1}(T)$ is $g^*\beta$-$\mathcal{C}$in $\mathcal{U}$. Henceforth $k^\circ h$ is contra $g^*\beta$-irresolute.

Theorem: 3.17 If $h: (\mathcal{U}, \tau) \to (\mathcal{V}, \sigma)$ is contra $g^*\beta$-irresolute and $k: (\mathcal{V}, \sigma) \to (\mathcal{W}, \mu)$ is $g^*\beta - cts$ then $k^\circ h$ is $contra\ g^*\beta - cts$.
Proof: Let T be $g^*\beta$-$\mathcal{O}$in $\mathcal{W}$. Since k is $g^*\beta - cts$, $k^{-1}(T)$ is $g^*\beta$-$\mathcal{O}$in $\mathcal{V}$. Thus $h^{-1}(k^{-1}(T))$ is $g^*\beta$-$\mathcal{C}$in $\mathcal{U}$. Since h is contra $g^*\beta$-irresolute. That is $(k^\circ h)^{-1}(T)$ is $g^*\beta$-$\mathcal{C}$in $\mathcal{U}$. Thus $k^\circ h$ is $contra\ g^*\beta - cts$.
Remark: 3.18 Every perfectly contra $g^*\beta$-irresolute function is $contra\ g^*\beta$-irresolute and $g^*\beta$-irresolute.
Remark: 3.19 The below illustration proves that a $contra\ g^*\beta$ -irresolute function should not be perfectly contra $g^*\beta$-irresolute.
Example:3.19 Allow $\mathcal{U} = \{p,q,r\}, \mathcal{V} = \{p,q,r\}$ with $\tau = \{\phi, \mathcal{V}, \{p\}\}$ and $\sigma = \{\phi, \mathcal{U}, \{q\}, \{q,r\}\}$. Define an identity mapping $h: \mathcal{U} \to \mathcal{V}$. Thus h is $contra\ g^*\beta$- irresolute but h is contra not perfectly contra $g^*\beta$-irresolute.
Example: 3.20 $\mathcal{U} = \{p,q,r,s\} = \mathcal{V}$ with $\tau = \{\phi, \mathcal{U}, \{r\}, \{p,q\}, \{p,q,r\}\}$ and $\sigma = \{\phi, \mathcal{V}, \{p\}, \{q,r\}, \{p,q,r\}\}$. Define an identity mapping $h: \mathcal{U} \to \mathcal{V}$. Then h is $g^*\beta$- irresolute but not perfectly contra $g^*\beta$-irresolute.
Theorem: 3.21 A function is perfectly contra $g^*\beta$-irresolute if and only if h is contra $g^*\beta$-irresolute and $g^*\beta$-irresolute.
Proof: Straightforward.

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RESEARCH ARTICLE

Practice as a Major Tool in the Process of Learning a Second Language

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ABSTRACT

The student of a second language will think in their native language and express their thoughts in the second. Getting comfortable with this procedure takes a long time. The guy becomes flawless with practice. As a result, with consistent practice, one can become proficient in both their primary and second languages. Our ideas and feelings are expressed via language, both verbally and nonverbally. The impact of one's mother tongue on one's foreign language acquisition will be felt. This is inescapable. The sound patterns of the mother tongue language impact Indian people's Indianism phrases. When learners try to express their thoughts and feelings, they run against language barriers. Teaching English as a second language and studying English as a second language are not easy tasks. There are several strategies that may be used to improve communication skills in a second language. Students and learners who are attempting to transcend the impacts of their original language will find that practicing communication skills and comprehensive skills is quite beneficial. This paper seeks to discuss the obstacles that students and learners of English as a second language encounter, as well as strategies to overcome such obstacles.

Keywords: Mother tongue influences – Skills of English language –comprehensive skills Practice more-Pronunciation skill – Avoid Indianism

INTRODUCTION

"The limits of my language are the limits of my world".
- Ludwig Wittgenstein

The learner's ability to acquire the second language will be significantly hampered by the effect of the native language. It's known as Mother-Tongue Interference, and it affects learners' ability to speak and write in the second language, English. In the process of acquiring a second language, one cannot resist the effect of their mother tongue. It will have an impact on the academic progress of the students. In India, English is regarded as a sophisticated language to learn and teach. Learning English as a second language needs more work and time. The majority of Indian courses focus on the fundamental principles and conventions of English grammar. The pupils' soft skills and understanding levels should also be taught and practiced adequately. As a result, Indian pupils are less confident in their ability to communicate in English.

The importance of pronunciation in communication cannot be overstated, since it is as important as grammar and vocabulary. The impact of the mother tongue on the second language, on the other hand, is undeniable. It's easy to spot in the structure of incorrect pronunciation. In most classes, pronunciation instruction and the benefits of a native-like accent are not given much weight. Because of the different Indian dialects located throughout the country, it is almost impossible to teach all the accents to the pupils. This is a major point of contention in Indian schools. In order to overcome the barriers to learning English effectively, the topics of soft skills, pronunciation, phonetics, and spoken English must be intentionally handled from an Indian viewpoint.

As the world becomes more globalized, the benefits of studying foreign languages are multiplying, and bilingualism is now perhaps the most valuable real-world ability to have ever existed, rather than just a cool party trick. You are a special breed indeed if you are considering making the effort to learn a foreign language rather than wanting the world to tolerate your unilingualism. With the right approach and attitude, you will blossom into the amazing polyglot you've always wanted to be. Learning a foreign language is all about learning how to truly communicate and connect with others—a crucial life skill that can only be developed through interaction with others. You will use your new superhuman ability to understand what someone is saying, remember the proper vocabulary and grammar, bring the vocabulary and grammar into the proper sense, and respond back—all on the spot and in a timely manner—when you learn a foreign language. You've made contact. And that is the crux of the matter. Hearing someone speak a foreign language is like hearing gold come to greet you, with its warmth and voluptuous sounds. Speaking a foreign language is extremely enticing, as it can make you seem more beautiful, interesting, and intelligent.

MATERIALS AND METHODS

The instructor will serve as the pupils' initial role model in terms of communication. Students should be able to grasp the second language at first. If the instructor encourages students to speak in class frequently, they will gain confidence in their ability to communicate effectively in English as a second language. Students will benefit from learning a foreign language from the beginning of their schooling since it will help them connect the second language to their mother tongue. They will compare and contrast the two languages, and they will have a better understanding of both, which will help them enhance their speech skills. Learners should be able to rehearse these sound samples with a replica voice over and over again in order to keep up with the successful English language lab. The use of a student's mother tongue when teaching English helps them develop their literacy and critical thinking skills. If students are studying a second language in their mother tongue, they will be able to grasp it quickly. They can interrupt the course and gain a better understanding of the curriculum.

The most significant benefit of using one's mother tongue in a language classroom is that it is compatible with the majority of students' preferred learning styles. After comprehending the statements in their native language, the beginner and intermediate students will most likely translate the sentences into English. Knowing exactly what a new grammatical structure or lexical item signifies in the native tongue gives learners a sense of security. It's difficult to ignore the pupils' requirements. However, as second-language instructors, we must know when and how to employ our mother tongue as an effective teaching tool. Because pupils learn and utilize the mother language from childhood, it is extremely difficult to escape its imprint. They are less confident in their ability to communicate in a foreign language. Native speakers who can communicate well will feel inferior to nonnative speakers. Only when second language learners can comprehend the notion in their mother tongue can they translate the information. When students/learners are in schools, they will usually speak with one another in their first language. They have trouble communicating because of their lack of English language practice.

English language learners should apply their evolving language skills to rich academic content in all subjects rather than learning the fundamentals of English in isolation. Learning a second language is a significant achievement that one should be proud of! It will not only aid our intellectual and emotional growth, but it will also improve our communication skills, inspire us to achieve the goals, and boost the self-esteem. Languages are an excellent skill to have on the students' profile. College admissions officers admire students who have dedicated themselves to learning a second language for many years or more. Whether or not want to attend college, language skills will offer the students a significant competitive advantage in the job market. Languages are one of the top eight skills needed by all professions, regardless of sector or skill level, and are in high demand in the public and private sectors. Bilinguals have enhanced problem-solving abilities, as well as greater memory, focus, and mental flexibility. Students who study languages appear to do well on standardized exams and make academic gains in other subjects as well. The most direct path to another culture is learning another language. It helps you to gain a deeper understanding of other cultures and perspectives on the world. Having that kind of insight is a huge plus. The sooner the learners start, the more likely they are to be able to complete a long, uninterrupted series of instruction, which is the best way to learn a new language. So go ahead and do it! Languages will help you learn and lead.

As an instructor, I believe it is important to consider the emotional challenges that come with learning a language. Putting yourself in the shoes of a language learner is a fantastic way to do this. When you're in a language class as a learner, you get a sense of how it feels to make mistakes, how difficult it is to express yourself clearly, how difficult it is to understand grammar rules, how difficult it is to pronounce words correctly, how embarrassing it is to talk. This knowledge can then be used to help you develop your communication skills with your own students as a teacher and give you ideas about how to react to their difficulties. Most significantly, you'll have a clearer idea of how to assist them in overcoming their difficulties. Although I don't believe that learning a second language is required to have empathy as a language teacher, I do believe that being on the other side of the desk offers a humbling experience that can be useful in the classroom. Try to keep track of and activities the instructor did with that the learners found to be helpful, useful, interesting, engaging, or effective, as well as which ones you found to be counterproductive, dull, or too difficult. Then they can adapt and refine these exercises for their own lessons by adding the own twist and/or improving them.

Learning a second language is a time-consuming process that necessitates commitment, hard work, and perseverance. Many students assume that learning a second language will give them a competitive edge when applying for internships and jobs. Another advantage of learning a second language is the opportunity to form connections with a wide range of people and gain new perspectives. There are a variety of successful learning and research methods available to students. There are three main elements to learning a foreign language: comprehensible input, comprehensible output, and examination. Hearing or reading a new language and then comprehending it are referred to as comprehensible input. Producing anything from the new language, such as speaking or writing, is referred to as comprehensible production. The term review refers to the process of finding and correcting errors. In order to successfully learn a foreign language, all of these components must be present

during the learning process. When learning a second language, it's important to remember that study plans are essential. Students may use study plans to remain on track and learn more. It's critical to devise a strategy that maximizes the three main elements. Immersion in the language is another critical part of learning a second language. This involves listening to music, watching television shows and movies, and, most importantly, conversing with native speakers of the language.

Students learning a foreign language often experience feelings of defeat when they believe they are not absorbing the language well enough or at the rate they desire. This is a significant obstacle to overcome, but in order to learn a language, it is important to keep moving beyond it. In order to learn from their mistakes, students must make them. It is important to be comfortable with making mistakes while learning a foreign language in order to break out of your comfort zone. It is not necessary to complete full immersion; instead, they can begin by finding a study partner who is on the same level as them and working together to improve. There are several successful research styles while studying with someone else but figuring out which one works best is what makes the learning process more productive. Distributed practice is a common study technique for learning a new language. This technique teaches the importance of breaking down ideas into smaller chunks so that the material is easier to grasp. Those sessions must be spaced out over time in order for progress to be made. Although learning a new language requires a lot of practice and can quickly exhaust a student, it's important to remember why they started learning in the first place. Learning a new language will open doors to a plethora of possibilities and it also aids in the creation of new ways of expressing oneself, emotions, or ideas. Communication is an important aspect of life and learning another language will help everyone improve their communication skills in a variety of ways.

No matter how old the learners are, studies have shown that learning another language has cognitive benefits. Bilinguals have larger brains, better memory, are more imaginative, and are better problem solvers, and so on, according to these findings. These benefits not only make it easier to learn new languages, but they also make it easier to learn something. In today's hectic multitasking environment, the ability to move between tasks quickly is critical. Bilinguals can move between tasks much faster than monolinguals, and they can perform a lot more tasks at the same time. Meeting new and interesting people and forming lifelong friendships are definitely goals worth pursuing, and learning another language is a surefire way to speed up the process. Language allows us to communicate our emotions and desires, as well as interact with other people and form meaningful relationships. When you meet native speakers, speaking a foreign language not only opens up a huge pool of potential mates, but it also serves as an instant common denominator. Foreign language learning is merely a requirement of a fundamental liberal education. Educating means leading people out of their confinement, narrowness, and darkness. Learning a foreign language and immersing oneself in a new culture and worldview is the most surefire way to become a more open-minded, compassionate, and accepting individual, and that is priceless. It's a wonderful, eye-opening experience to see the world from a different viewpoint and to realize where you and others come from. Learning a foreign language may have the opposite effect, allowing you to gain a greater understanding of your own native tongue and culture. One of the most surprising benefits of learning a foreign language is this. Not only will you become more aware of cultural norms, but also of your first language's grammar, vocabulary, and pronunciation patterns. Former monolinguals' listening, reading, and writing skills are likely to develop as a result of learning a foreign language. The value of learning a foreign language is undeniable, and there are many reasons to do so. Learning a foreign language and eventually speaking it fluently helps to break down barriers and bind people on a deeper level of mutual understanding. Furthermore, achieving this shared understanding would eventually open a set of doors that will lead to a more interesting and fulfilling individual and proficient life!

RESULTS AND DISCUSSION

With mother tongue experience, a second language student will comprehend the meaning of terms in a target language. The teacher can explain difficult topics in the first language, but this should not impede the student's

ability to communicate effectively in the second language, English. There is more time for observation and practise, and no need for non-natural conditions as a result. As a result, the extra time may be used by the teachers to practise sentence patterns, vocabulary, and structures. It can be beneficial in terms of enhancing one's English language skills. Students can comprehend material in a second language when the teacher explains the meaning of the information in the original language. Learners gain greater practice speaking and communicating in English. However, there are significant drawbacks to having your mother tongue impact your study of English as a second language. Students will be perplexed by the similarities and discrepancies between the first and target languages. The goal of getting pupils to enhance their communication skills will be futile if the instructor uses his or her mother tongue instead of English. The pupils' pronunciation and fluency will only improve with additional practise in the second language.

When a learner begins to understand or use a second language, they are usually very young. They converse in both their first and second languages at home and at school. In both languages, they process the world around them. There isn't any distinction. The learner uses their native language in one environment like at home and the second language in another environment like at school, so both languages are segregated depending on the environment. When a learner learns a second language, they usually do so by filtering it into their first language in translating, memorizing grammar rules, and then using these ideas in a real-world perspective. If there an adult student, there's a good chance that some of them are in the second group, filtering English into their native tongue. This essentially means that when they speak English, they are filtering or translating their thoughts from their native tongue, and when they listen to someone speak English, they are translating it back to their native tongue. This is how a lateral bilingual's interaction and comprehension usually works.

If the teachers have students who fall into this group, studying and mastering their native language will help to communicate with them more effectively and clearly. If understand their language's grammatical and phonetic structure, the instructor be able to figure out why they're making mistakes and what they're trying to say when they speak. Explaining how to use these idiomatic expressions can take far longer than simply translating them into your students' native language. It's always more efficient to simply translate them and then look up meanings and examples of these terms in English. It's also worth mentioning that don't have to and probably should not use the students' native language in the entire class. However, the instructor will discover how useful and beneficial it is to be able to communicate with them in their native language on occasion. The nucleus of a society is also said to be its language.

When learn a foreign language, we will almost certainly learn a lot about the culture and citizens of the country or countries where that language is spoken. The learners gain a better understanding of what customs, sports, activities, films, public figures, holidays, and a variety of other topics the students know a lot about, want to learn about, and have a strong emotional connection to when do this. Students are more inspired to speak their minds about learning material when they have an emotional link to it. And the more speaking in the lesson, the more chances the teachers have to correct their expression and assist them in expressing themselves. When learning a second language, many of these unique cultural topics will emerge and become part of the curriculum. As a result, we have a lot of great material to turn around and use in our own classes. Though it can seem counterintuitive, learning a foreign language will also teach us a lot about English. This is because the learners will be comparing and relating everything they hear in a foreign language to their native tongue, which will help them understand the fundamentals of English.

CONCLUSION

Nowadays, learning English is required to graduate from high school and acquire a college diploma. Both professors and students aim for a high passing percentage. As a result, pupils acquire the second language for test purposes rather than as a means of communication. They are unable to learn English as a communication language due to their apathy. A second language instructor should pay specific attention and care to each and every student in the

class. Students and learners who are terrified of public speaking should practice communicating and expanding their vocabulary in the target language. Learners of a second language will gradually be able to successfully talk and write in English without any difficulties. Instead of rushing through the curriculum, teachers should work with pupils to help them enjoy learning the new language one step at a time. It will benefit both students and teachers in terms of fluency. Some psychological disorders might also obstruct successful English learning. The learners' and students' financial backgrounds, as well as a lack of understanding, prevent them from receiving a decent education. The inferiority mindset that plagued the disadvantaged pupils slowed their progress in learning the second language.

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RESEARCH ARTICLE

Mathematical Modeling of Time Delayed Reactants

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ABSTRACT

The concept of delayed reactants and its consequences is discussed in this paper. In particular, by considering an example, I had discussed two delayed models one for discrete and other for continuous and arriving solutions to each case. The solutions provide expected results

Keywords: Linear Differential Equation, Taylor's series expansion, Mean time delay, Discrete delay equation, Homeostatic differential equations.

INTRODUCTION

The mechanism of delayed equations is discussed in detail in this paper by considering a delayed reactant equation. First, I have modeled a discrete delay equation, next I extended to discuss system of delayed ordinary differential equations related to continuous time delay between the entrance of a virus in to a T-cell and the exit of a newly produced various from the stricken cell. The solutions of these equations provide a better understanding and need for having delayed systems.

Discrete Delay Model

The ordinary differential equation description by necessity chooses a few cellular and molecular types to focus on. The effect of neglected reactants is typically to buffer and delay the reaction taking place. As a trivial example, let us consider the sequence $\rightarrow A \xrightarrow{k} B \xrightarrow{\ell} C \quad (2.1)$ Now imagine that B is ignored by design or due to some other factor. From (2.1), we see that $\dot{C} = \ell B \ (2.2)$ and $\dot{B} = kA - \ell B \ (2.3)$. Now equation (2.3) is a first linear

differential equation in B. Hence solving (2.3) using the Integrating factor term we get Integrating Factor I.F. $= e^{\ell t}$.

Thus the solution to (2.3) is given by $B(t)e^{\ell t} = \int_0^t kA(t-u)\,e^{\ell u}\,du + K$ from which we get

$$B(t) = Ke^{-\ell t} + k\int_{u=0}^{t} A(t-u)\,e^{-\ell u}\,du \quad (2.4)$$

Hence from (2.2), we see that $\dot{C}(t) = K\ell e^{-\ell t} + k\ell\int_{u=0}^{t} A(t-u)\,e^{-\ell u}\,du \quad (2.5)$

We note that as $t \to \infty, K \to 0$.

Hence, from (2.5) we get $\dot{C}(t) = k\ell\int_{u=0}^{\infty} A(t-u)\,e^{-\ell u}\,du = k\,\bar{A}(t) \quad (2.6)$

From (2.6) we see that the intermediate *B* does not change the rate $A \xrightarrow{k} C$ but all $A(u)$ for $u < t$ contribute to $\bar{A}(t)$, although in decreasing weight as one goes back in time. Now using Taylor's series expansion we can simplify the term $A(t-u)$ in (2.6).

Doing this, we get $A(t-u) = A(t-\tau) + (\tau-u)A'(t-\tau) + \cdots \quad (2.7)$. Using this in (2.6), we have

$$\bar{A}(t) = \ell\int_{u=0}^{\infty} A(t-u)\,e^{-\ell u}\,du = \ell\int_{u=0}^{\infty}\left[A(t-\tau) + (\tau-u)A'(t-\tau) + \cdots\right]e^{-\ell u}\,du$$

$$= A(t-\tau) + \ell A'(t-\tau)\int_{u=0}^{\infty}(\tau-u)e^{-\ell u}\,du + \cdots = A(t-\tau) + \left(\tau - \frac{1}{\ell}\right)A'(t-\tau) + \cdots \quad (2.8)$$

Now the mean time delay τ is given by $\tau = \dfrac{\int_{u=0}^{\infty} ue^{-\ell u}\,du}{\int_{u=0}^{\infty} e^{-\ell u}\,du} = \dfrac{1}{\ell} \quad (2.9)$

We now notice that for this value of mean time delay the right hand side of (2.8) vanishes except the first term. Hence substituting (2.9) in (2.8) we get $\bar{A}(t) = A(t-\tau) \quad (2.10)$. Hence (2.6) becomes $\dot{C}(t) = k\,A(t-\tau) \quad (2.11)$.

Equation (2.11) represents a discrete delay equation.

Continuous Delay Model

We now take into account of the fact that there is certainly a time delay between the entrance of a virus into a T-cell and the exit of newly produced virions from the stricken cell. Then the basic equations at Homeostatic controlled T_0 become

$$\frac{dT^*(t)}{dt} = -\delta T^*(t) + kT_0 V(t) \qquad (3.1)$$

$$\frac{dV(t)}{dt} = N\delta T^*(t-\tau) - cV(t) \qquad (3.2)$$

These are still linear homogeneous, and so we still have elementary solutions of the form $\begin{pmatrix} C_{T^*} \\ C_V \end{pmatrix} e^{\lambda t}$. With these from (3.1), (3.2)

$\lambda C_{T^*} = -\delta C_{T^*} + kT_0 C_V$ (3.3), $\lambda C_V = N\delta e^{-\lambda\tau} C_{T^*} - c C_V$ (3.4)

In view of (3.3) and (3.4), we can determine λ through the following quadratic equation

$q\lambda^2 + (q+1)\lambda + 1 - Ne^{-\lambda\tau} = 0$ (3.5)

CONCLUSION

In this paper, by considering a delayed reactant sequence as in (2.1), I formed the linear differential equation (2.3). Solving it and using it in (2.2), we obtained (2.6). From this equation, we saw that the intermediate reactant B does not change the rate of $A \xrightarrow{k} C$. Using Taylor's series expansion and the mean time delay value we can reduce the complexity of (2.6) down to a nice equation as in (2.11) which represents a discrete delay equation.

In section 3, considering Homeostatic controlled variable T_0 we could produce systems of linear differential equations in $T^*(t)$ and $V(t)$. Equations (3.3) and (3.4) form the solution of the system of differential equations. Finally, from (3.5), we notice that when $\lambda < 0$, the effect of drug therapy which is used to decrease N is compensated by the delay. Hence, overall, the effect of delay will not affect the effectiveness of the system thereby providing the same optimal results.

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REVIEW ARTICLE

A Overview: Endemic Diseases

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ABSTRACT

The world has built up an expansion worldwide wellbeing framework as a defense against known and obscure irresistible sickness dangers. The framework comprises of different formal and casual organizations of associations that serve various partners; have changing objectives, modalities, assets, and responsibility; work at various provincial levels and cut across people in general, private-for-benefit, and private-not-revenue driven areas. The advancing worldwide wellbeing framework has done a lot to ensure and advance human wellbeing. Nonetheless, the world keeps on being stood up to by longstanding, arising, and reappearing irresistible infection dangers. These dangers contrast generally regarding seriousness and likelihood. They likewise have differing ramifications for dreariness and mortality, just as for an unpredictable arrangement of social and financial results. To different degrees, they are additionally manageable to elective reactions, going from clean water arrangement to guideline to biomedical counter measures. Regardless of whether the worldwide wellbeing framework as right now established can give powerful assurance against a unique exhibit of irresistible illness dangers has been raised doubt about by late flare-ups of Ebola, Middle East respiratory disorder, SARS, and flu and by the approaching danger of rising antimicrobial obstruction. The worry is amplified by quick populace development in regions with powerless wellbeing frameworks, urbanization, globalization, environmental change, common clash, and the changing idea of microbe transmission among human and creature populaces. This Council would fortify the worldwide wellbeing framework by improving cooperation and coordination across associations filling in information holes concerning (for instance) irresistible sickness reconnaissance, innovative work needs, financing models, production network co-ordinations, and the social and monetary effects of possible dangers; and making significant level, proof based proposals for overseeing worldwide dangers related with irresistible illness.

Keywords: worldwide wellbeing, worldwide wellbeing frameworks, irresistible sickness, symptoms, measure, WHO advices and reaction.

INTRODUCTION

An epidemic is the quick spread of irresistible disease to countless individuals in a given populace inside a brief timeframe. As per current ideas, an epidemic is characterized as the event locally or district of instances of an ailment or other wellbeing related occasions plainly in abundance of ordinary hope. The people group or locale, and the time span in which the cases happen are determined definitely. An epidemic disease isn't needed to be contagious, and the term has been applied to West Nile fever and the obesity epidemic (e.g. by the World Health Organization), among others [1]. Consequently, epidemics allude to the "unordinary" event locally or area of disease, explicit wellbeing related conduct (e.g., smoking) or other wellbeing related occasions (e.g., car crashes) plainly in overabundance of "anticipated event". The quantity of cases differs as indicated by the disease-causing specialist, what's more, the size and sort of past and existing openness to the specialist [2].

Epidemics of infectious disease are generally caused by several factors including
Change in the biology of the host populace (for example expanded pressure or expansion in the thickness of a vector animal group)

1. Genetic change in the microorganism supply or the presentation of an arising microorganism to a host populace (by the development of microbe or have).
2. Generally, an epidemic happens when have insusceptibility to one or the other an set up microorganism or recently arising novel microbe is abruptly diminished beneath that found in the endemic balance and the transmission edge is surpassed.
3. The conditions which administer the episode of epidemics additionally incorporate tainted food supplies, for example, sullied drinking water and the movement of populaces of specific creatures, like rodents or mosquitoes, which can go about as disease vectors.
4. Certain epidemics happen at specific seasons. For instance, challenging hack happens in spring, while measles produces two epidemics, one in winter and one in March. Flu, the regular cold, and other diseases of the upper respiratory plot, like sore throat, happen transcendently in the colder time of year [3].
5. Disease flare-ups are generally brought about by a contamination, sent through individual to-individual contact, creature to-individual contact, or from the climate or other media.
6. Outbreaks may likewise happen following openness to synthetics or to radioactive materials. For instance, Minamata disease is brought about by openness to mercury.
7. Epidemics might be the outcome of debacles of another sort, for example, typhoons, floods, seismic tremors, dry spells, and so forth
8. Occasionally the reason for an episode is obscure, even after intensive examination [4].

TYPES OF EPIDEMIC DISEASES [3]
COMMON-SOURCE EPIDEMICS
Normal source epidemics are habitually, yet not generally, due to openness to an irresistible agent. They can result from tainting of the climate (air, water, food, soil) by modern synthetics or pollutant. E.g., Bhopal gas misfortune in India and Minamata disease in Japan coming about because of utilization of fish containing a high centralization of methyl mercury.

Single Exposure Or "Point-Source" Epidemics

These are otherwise called "point-source" epidemics. The openness to the disease specialist is brief and basically synchronous, the resultant cases all create inside one brooding time of the disease. E.g., an epidemic of food harming. The principle highlights of a "point-source" epidemic are:

1. The epidemic bend rises and falls quickly, with no optional waves
2. The epidemic will in general be hazardous, there is a grouping of cases inside a restricted time period, and
3. More critically, every one of the cases creates inside one brooding time of the disease.

Continuous or Multiple Exposure Epidemics

On the off chance that the epidemic proceeds over more than one hatching period, there are either a constant or numerous openings to a typical source or a proliferated spread. Sometimes the openness from a similar source might be delayed – consistent, rehashed or irregular – not really simultaneously or place. For model, a whore might be a typical source in a gonorrhea flare-up, however since she will taint her customers throughout some undefined time frame there might be no unstable ascent in the quantity of cases. A well of tainted water, or a broadly disseminated brand of antibody (for example polio immunization), or food, could result in comparative outbreaks. In these occurrences, the subsequent epidemics will in general be more broadened or irregular. The flare-up of respiratory ailment, the Legionnaire's disease, in the mid year of 1976 in Philadelphia (USA) was a typical source, ceaseless or rehashed openness outbreak. This flare-up, as in other outbreaks of this sort, proceeded past the scope of one hatching period. There was no proof of who had contact with sick people. auxiliary cases among people.

Propagated Epidemics [5]

An engendered epidemic is regularly of irresistible cause and results from individual to-individual transmission of an irresistible specialist (e.g., epidemics of hepatitis An and polio). The epidemic as a rule shows a progressive ascent and tails off over an any longer time of time. Transmission proceeds until the quantity of susceptibles is exhausted or defenseless people are not, at this point presented to tainted people or delegate vectors. The speed of spread relies on group resistance, openings for contact and optional assault rate. Propagated epidemics are bound to happen where countless powerless are totaled, or where there is an ordinary inventory of new helpless people (e.g., birth, migrants) bringing down crowd invulnerability.

Mixed Epidemics [6]

A few epidemics have highlights of both basic source epidemics and proliferated epidemics. The example of a typical source flare-up followed by auxiliary individual to-individual spread isn't uncommon. These are called mixed epidemics.

2012

MERS UNCOVERED IN THE MIDDLE EAST [7]

Another Covid, named Middle East Respiratory Syndrome (MERS), is communicated to people from camels in 2012 in Saudi Arabia. The biggest episode happens on the Arabian Peninsula in the primary portion of 2014, with the Saudi city of Jeddah as its focal point. In 2015, South Korea is home to the second-biggest flare-up. In excess of two dozen nations report instances of viral respiratory illness before very long, however most of cases are in Saudi Arabia. The infection usually causes pneumonia in those contaminated and has a generally high casualty rate: of the around 2,500 individuals determined to have MERS since its disclosure, more than 850 have kicked the bucket from the infection. A gathering of 24 patients that got steady consideration and corticosteroids was viewed as the benchmark group. At 14 days after the affirmed analysis of MERS, endurance was expanded in the treated gathering (70%) contrasted with the control bunch (29%). By 28 days post-determination, 30% of treated subjects endure versus 17% of the benchmark group. In an extra contextual analysis, a 69- year-old Greek patient who contracted MERS in Jeddah was treated with oral lopinavir/ritonavir (400/100 mg twice every day), pegylated IFN (180 μg SC once each week for 12 weeks), and ribavirin (2000 mg starting portion; 1200 mg each 8 h for 8 days, started on day 13 post-finding).

Two days after treatment inception, viremia couldn't be recognized; in any case, viral RNA was recognized in a few patient examples (dung, respiratory discharges, and serum) up to 14weeks post-analysis. Regardless of delayed endurance, the patient capitulated to septic stun 2months post-determination. An progressing randomized clinical preliminary in Saudi Arabia is assessing the treatment of Antiviral treatments.

SYMPTOMS [8]

Most people confirmed to have MERS-Co V infection have had a severe respiratory illness with symptoms of:

- Fever
- Cough
- Shortness of breath

Some people also had diarrhea and nausea/vomiting. For many people with MERS, more severe complications followed, such as pneumonia and kidney failure. About 3 or 4 out of every 10 people reported with MERS have died. Most of the people who died had a pre-existing medical condition that weakened their immune system or an underlying medical condition that hadn't yet been discovered. Medical conditions sometimes weaken people's immune systems and make them more likely to get sick or have severe illness.

MERS-CoV viral vector vaccine [9]

Several adenovirus-based MERS-CoV vaccines have been developed. Human adenovirus type 5 (Ad5) and type 41 (Ad41) expressing MERS-CoV S or S1 protein have been shown to induce neutralizing antibodies in mice.

TREATMENT [10]

The assessment of medicines in MERS patients has been hampered as great clinical information from randomized clinical preliminaries are restricted. Ribavirin (with or without IFN, or corticosteroids) was the essential treatment during the MERS episode. In a review examination, an associate of 20 patients was dealt with oral ribavirin and SC PEGylated IFN-α2a at a portion of 180 μg/week for 2 weeks. The underlying portion of ribavirin was 2000 mg, trailed by a 200–1200 mg portion contingent upon creatinine leeway. A gathering of 24 patients that got steady consideration and corticosteroids was viewed as the benchmark group. At 14 days after the affirmed determination of MERS, endurance was expanded in the treated gathering (70%) contrasted with the control bunch (29%). By 28 days post-finding, 30% of treated subjects endure versus 17% of the benchmark group. In an extra contextual investigation, a 69- year-old Greek patient who contracted MERS in Jeddah was treated with oral lopinavir/ritonavir (400/100 mg twice every day), pegylated IFN (180 μg SC once each week for 12 weeks), and ribavirin (2000 mg beginning portion; 1200 mg each 8 h for 8 days, started on day 13 post-finding).

Two days after treatment inception, viremia couldn't be distinguished; in any case, viral RNA was distinguished in a few patient examples (defecation, respiratory discharges, and serum) up to 14weeks post-conclusion. In spite of delayed endurance, the patient capitulated to septic stun 2months post-conclusion. An continuous randomized clinical preliminary in Saudi Arabia is assessing the treatment of MERS patients with IFN (interferon)- β1b in blend with lopinavir/ritonavir.

- Host-coordinated/ - inferred treatments
- MERS Co V-antibody
- Monoclonal antibodies

3B11-N or E410-N, a monoclonal counter acting agent are utilized during this MERS flare-up in 2012, (these antibodies are explicitly used to treat HIV.

TREATMENT ACCORDING TO WHO [11]

No immunization or explicit treatment is at present accessible; anyway a few MERS-CoV explicit antibodies and medicines are being developed. Treatment is steady and dependent on the patient's clinical condition.

As an overall safety measure, anybody visiting ranches, markets, horse shelters, or other places where dromedary camels and different creatures are available should rehearse general cleanliness measures, including standard hand washing previously, then after the fact contacting creatures, and ought to keep away from contact with wiped out creatures. The utilization of crude or half-cooked creature items, including milk furthermore, meat, conveys a high danger of disease from an assortment of life forms that may cause illness in people. Creature items that are prepared properly through cooking or purification are ok for utilization, yet ought to likewise be maneuvered carefully to dodge cross tainting with uncooked food sources. Camel meat and camel milk are nutritious items that can keep on being devoured after sanitization, cooking, or other warmth medicines. Until more is perceived about MERS-CoV, individuals with diabetes, renal disappointment, persistent lungs illness, and immune-compromised people are thought of to be at high danger of serious illness from MERS-CoV contamination. These people should stay away from contact with camels, drinking crude camel milk or camel pee, or eating meat that has not been as expected cooked.

STEPS TAKEN

Since its recognizable proof in the Kingdom of Saudi Arabia (KSA) and Jordan in 2012, Middle East Respiratory Syndrome (MERS) has gotten a worldwide general wellbeing danger. Regular of an emerging zoonosis, Middle East respiratory disorder coronavirus (MERS-CoV) has a creature supply, i.e. dromedary camels in which the infection makes minimal no sickness. Numerous insights concerning the degree of course and the systems of transmission inside dromedary camel crowds, or factors identified with zoonotic transmission and contrasts in circulating MERS-CoV strains, stay obscure. The infection has more than once gushed out over from dromedary camels to people, essentially in nations on the Arabian Peninsula, causing significant morbidity and mortality. Bunches of cases locally and among relatives are uncommon.

Nonetheless, delays in determination in emergency clinics have once in a while prompted auxiliary cases among medical care laborers, patients sharing rooms, or family individuals because of unprotected direct contact with a patient before separation. This human-to-human transmission in health care facilities can now and then be enhanced, causing extremely enormous episodes, as has been found in the Middle East and the Republic of Korea, with critical general wellbeing and monetary effects. As of August 2018, in excess of 2249 human cases from 27 nations have been answered to the World Health Organization (WHO) [12].

The FAO, OIE, and WHO Tripartite have routinely united influenced part states, general wellbeing and creature authorities, and scholastics to examine what is known and obscure about the zoonotic inception of MERS-CoV. The reasons for these gatherings and workshops have been to advocate for additional reconnaissance and examination on MERS-Co V in creatures and people, to share information about how MERS-Co V is communicated between creatures, from creatures to people and between people, to depict the sicknesses it causes, and to create strategies and rules for discovery, announcing of creature and human contaminations, and avoidance of human cases and bunches.

In the a long time since the keep going worldwide specialized interview on MERS-Co V in 2016, there have been remarkable enhancements in reconnaissance and detailing of human cases, multidisciplinary research, cross-sectoral cooperation at the nation level, public mindfulness about the illness, and research center and reconnaissance limit in influenced nations. Likewise, a few nations in the Arabian Peninsula and Africa have occupied with research exercises and observation of camel populaces to reveal insight into the more extensive conveyance of this infection or explore transmission examples and courses for viral shedding. As a development to past gatherings, FAO, OIE, and WHO Tripartite held a Global Technical Meeting on MERS-CoV with delegates from Services of Health and Ministries of Agriculture, topic specialists, analysts, funders, and modern accomplices from 25 to 27 September 2017 in Geneva, Switzerland. The targets were to survey the most recent logical proof on MERS-CoV, further improve cross-sectoral cooperation and correspondence during readiness and reaction exercises, and recognize research needs given the progressions in our insight.

With 130 members, this was the biggest MERS-CoV Technical Meeting to date and the primary gathering went to by agents from both influenced and in danger nations. That is, nations that have detailed human contamination, nations with proof of MERS-CoV in dromedary camels yet no detailed human cases, and nations in danger for importation [13].

STEPS TAKEN BY WHO[14]

WHO is working with general wellbeing subject matter experts, creature wellbeing trained professionals, clinicians and researchers in influenced and in danger nations and globally to assemble and share logical proof to all the more likely comprehend the infection and the infection it causes, and to decide episode reaction needs, treatment systems, and clinical administration draws near. WHO is likewise working with the Food and Agriculture Organization of the United Nations (FAO) and the World Association for Animal Health (OIE) and public governments to create general wellbeing anticipation procedures to battle the infection.

Along with influenced nations and global specialized accomplices and networks, WHO is organizing the worldwide wellbeing reaction to MERS, including: the arrangement of refreshed data on the circumstance; leading danger appraisals and joint examinations with public specialists; gathering logical gatherings; and creating direction and preparing for wellbeing specialists also, specialized wellbeing organizations on break reconnaissance suggestions, research facility testing of cases, disease counteraction and control, and clinical the board. The Director-General assembled an Emergency Committee under the Worldwide Health Regulations (2005) to exhort concerning whether this occasion comprises a Public Health Emergency of International Concern (PHEIC) and on the general wellbeing estimates that ought to be taken. The Committee has met a number of times since the illness was first recognized. WHO supports all Part States to improve their reconnaissance for serious intense respiratory contaminations (SARI) and to deliberately audit any bizarre examples of SARI or pneumonia cases. Nations, regardless of whether MERS diseases have been accounted for in them, ought to keep an undeniable degree of cautiousness, particularly those with enormous numbers of voyagers or transient specialists getting back from the Middle East. Observation should keep on being improved in these nations as indicated by WHO rules, alongside disease counteraction and control methods in wellbeing care offices. WHO keeps on mentioning that Member States report to WHO all affirmed and plausible instances of disease with MERS-CoV along with data about their openness, testing, and clinical course to educate the most successful global readiness and reaction.

2013-2014

EBOLA SWEEPS WEST AFRICA

In 2014, instances of the Ebola infection, an uncommon and serious irresistible infection that prompts demise in generally 50% of the individuals who contract it, are recognized in Guinea and not long after in Liberia and Sierra Leone. It is the first run through the sickness moves into thickly populated metropolitan regions, considering fast transmission. The flare-up in the end spreads to seven different nations, counting a few European states and the United States, causing more than eleven thousand passings in all. Question of wellbeing laborers and tales is once more present difficulties to control. The WHO, which announces the episode a PHEIC in August 2014, is censured for what many call a lethargic reaction. In September 2014, the UN Security Council receives a goal calling on part states to pool worldwide assets to battle the emergency, and nations counting the United States and the United Kingdom convey wellbeing laborers and other guide. The hardest-hit nations pronounce themselves without ebola in June 2016[7] .

Transmission of Ebola between people can happen through:

- Direct contact through broken skin and mucous layers with the blood, emissions, organs, or other body liquids of contaminated individuals.
- Indirect contact with conditions tainted with such liquids.
- Exposure to tainted items, like needles.
- Burial services in which grievers have direct contact with the body of the perished.

- Exposure to the semen of individuals with Ebola or who have recuperated from the sickness the infection can in any case be sent through semen for up to 7 weeks after recuperation from disease.
- Contact with patients with suspected or affirmed EVD – medical services laborers have habitually been contaminated while treating patients [13].

SYMPTOMS [15]

The time interval from infection with Ebola to the onset of symptoms is 2-21 days, although 8-10 days is most common. Signs and symptoms include:

- Fever
- Headache
- Joint and muscle aches
- Weakness
- Diarrhoea
- Vomiting
- Stomach pain
- Lack of appetite
- Some patients may experience:
- Rash
- Red eyes
- Hiccups
- Cough
- Sore throat
- Chest pain
- Difficulty breathing
- Difficulty swallowing
- Bleeding inside and outside of the body

Laboratory tests may show low white blood cell and platelet counts and elevated liver enzymes. As long as the patient's blood and secretions contain the virus, they are infectious. Ebola virus was isolated from the semen of an infected man 61 days after the onset of illness.

TEST AND DIAGNOSIS [16]

According to the WHO, samples from patients with Ebola are an extreme biohazard risk. Testing should be conducted under maximum biological containment conditions.Before Ebola can be diagnosed, other diseases should be ruled out, and, if Ebola is suspected, the patient should be isolated. Public health professionals should be notified immediately. Ebola virus infections can be diagnosed definitively in a laboratory through several types of tests, including:

- Antigen-capture enzyme-linked immunosorbent assay (ELISA) testing.
- IgM ELISA.
- Polymerase chain reaction (PCR).
- Virus isolation.

In the more advanced stages of the disease or after recovery, diagnosis is made using IgM and IgG antibodies. Ebola can be diagnosed retrospectively in deceased patients by other forms of testing.

TREATMENTS

There is no demonstrated treatment for Ebola except for basic mediations right off the bat can fundamentally improve odds of endurance. This incorporates rehydration with liquids and body salts (given orally or intravenously), and treatment of explicit indications, for example, low pulse, regurgitating, the runs, and diseases.

A scope of potential medicines including blood items, resistant treatments, and medication treatments are at present being assessed. Hand cleanliness is the best method to forestall the spread of the Ebola infection. A trial Ebola antibody known as rVSV-ZEBOV demonstrated exceptionally defensive against the destructive infection in a significant preliminary in Guinea in 2015. It is being utilized in light of the current flare-up in the Democratic Republic of the Congo utilizing a ring inoculation convention [17].

During a flare-up, wellbeing accomplices apply a bundle of mediations counting case the board, observation, contact following, research center testing, safe internments, and local area commitment.

Working with networks to decrease hazard factors for Ebola transmission is basic to controlling episodes [18].

TREATMENT ACCORDING TO WHO [19]

Steady consideration - rehydration with oral or intravenous liquids - and treatment of explicit manifestations improves endurance. A scope of potential medicines including blood items, insusceptible treatments and medication treatments are at present being assessed. In the 2018-2020 Ebola episode in DRC, the first-ever multi-drug randomized control trial was directed to assess the adequacy and wellbeing of medications utilized in the treatment of Ebola patients under a moral system created in conference with specialists in the field and the DRC. Two monoclonal antibodies (Inmazeb and Ebanga) were affirmed for the treatment of Zaire (Ebolavirus) disease in grown-ups and kids by the US Food and Drug Administration in late 2020.

Ebola antibodies [20]

In October 2014, the World Health Organization (WHO) coordinated an master conference to evaluate, test, and in the long run permit two promising Ebola antibodies:

- **cAd3-ZEBOV** –GlaxoSmithKline has built up this antibody in cooperation with the United States National Institute of Allergy and Irresistible Diseases (NIH). It utilizes a chimpanzee-inferred adenovirus vector with an Ebola infection quality embedded.
- **rVSV-ZEBOV** –this was created by the Public Health Agency of Canada in Winnipeg with New Link Genetics, an organization, situated in Ames, IA. The immunization utilizes a debilitated infection found in domesticated animals; one of its qualities has been supplanted by an Ebola infection quality.

On July 31, 2015, Lancet published starter consequences of an antibody preliminary supported and coordinated by the WHO; the Ebola caSuffit antibody had 100% viability in the preliminary, which occurred in Guinea and included 4,000 individuals. The full consequences of this preliminary were distributed in Lancet in February 2017.

The following stage is to make these antibodies accessible quickly – furthermore, in adequate amounts – to secure basic bleeding edge laborers and to make a contrast in the epidemic's future development.

STEPS TAKEN

CDC (Centers for infectious prevention and counteraction) initiated its Crisis Operations Center in July 2014 to help organize specialized help and infectious prevention exercises with accomplices. CDC staff sent to West Africa to help with reaction endeavors, including observation, contact following, information the executives, lab testing, and wellbeing instruction. CDC staff also offered help with co-ordinations, staffing, correspondence, examination, and the executives.

To forestall cross-line transmission, explorers leaving West Africa were screened at air terminals. Leave screening distinguished those in danger for EVD and forestall the spread of the infection to different nations. The United States too carried out improved section evaluating for voyagers coming from Guinea, Liberia, Sierra Leone, and Mali by directing them to assigned air terminals better ready to survey voyagers for hazard. During the tallness of the

reaction, CDC prepared 24,655 medical services laborers in West Africa on disease anticipation and control practices. In the United States, in excess of 6,500 individuals were prepared during live preparing occasions all through the reaction. Likewise, research facility limit was extended in Guinea, Liberia, and Sierra Leone with 24 research centers ready to test for the Ebola infection before the finish of 2015 [21] . Albeit through natural specialty demonstrating the expected spread of EVD in West Africa was estimated, the flare-up of EVD in Guinea got all nearby also, global well being local area ill-equipped. The main issue was infection acknowledgment; in fact different endemic illnesses, like intestinal sickness and Lassa fever, present numerous similitudes in symptomatology with EVD.

Ebola infection dispersion, in the principal long stretches of the flare-up in Guinea, went unseen till the presence of the main genuine symptomatology and passings. Whenever was distinguished the danger, the Ministry of Health, teaming up with WHO what's more, different accomplices, put forth attempts to carry out measures to control the episode also, in particular, forestall a further spread of the contamination. To assess the topographical spread of the EVD epidemic, reports gave at similar dates previously considered to decide the quantity of cases what's more, passings by WHO and by the Centers for Disease Control and Prevention (CDC) were utilized. The influenced countries from the blasting until the center of August 2014 (Guinea, Liberia, and Sierra Leone) were partitioned into the particular managerial territories. Guinea incorporates 33 prefectures, notwithstanding the capital Conakry. Liberia is partitioned into 15 nations, while Sierra Leone is partitioned into 12 regions in addition to the metropolitan and the provincial west territories that separated the capital Freetown into two extra areas [22].

STEPS TAKEN BY WHO [23]

WHO means to forestall Ebola flare-ups by keeping up observation for Ebola infection sickness and supporting in danger nations to create readiness plans. This record gives in general direction to control of Ebola and Marburg infection flare-ups:

- Ebola and Marburg infection sickness epidemics: readiness, alert, control, also, assessment.

At the point when an episode is identified WHO reacts by supporting local area commitment, illness discovery, contact following, inoculation, case the executives, research center administrations, disease control, co-ordinations, and preparing and help with protected and noble entombment rehearses.

WHO has created point by point counsel on Ebola disease avoidance and control:

- Infection counteraction and control direction for care of patients with suspected or affirmed Filovirus haemorrhagic fever in medical services settings, with center around Ebola.

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REVIEW ARTICLE

An Overview of (SARS – COV- 2) –The Rise and Impact of COVID -19 in India

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ABSTRACT

An outbreak of 2019 novel corona virus diseases (COVID-19) began in Wuhan, China, and quickly spread throughout the country. The findings of a descriptive, exploratory study of all patients diagnosed as of February 11, 2020 are presented here. Methodologies The Chinese Infectious Disease Information System was used to extract all COVID-19 cases recorded through February 11, 2020. The following is some of the analyses: 1) History of SARS-COV-2 2) Age ranges and sex ratios analysis 3) Event fatality and death rates calculation 4) Analysis of virus spread 5) Epidemiological construction 6) Mutant COVID 19 and Conclusions. There were 72 314 medical records in all, with 44 672 (61.8%) positive cases, 16 186 (22.4%) suspicious cases, 10567 (14.6%) clinical diagnosed cases (Hubei only), and 889 asymptomatic cases (1.2%)-contributed data for the analysis. The majority of confirmed cases were between the ages of 30 and 79 (86.6%), were diagnosed in Hubei (74.7%), and were classified as mild/mild pneumonia (80.9%). There were a total of 1 023 deaths among confirmed cases, resulting in a case-fatality rate of 2.3 percent. COVID-19 spread outward from Hubei after December 2019, and by February 11, 2020, it had infected 1 386 counties in all 31 provinces were affected. The majority of confirmed cases (86.6%) were in people aged 30 to 79, were diagnosed in Hubei (74.7%), and were graded as mild/mild pneumonia (80.9 percent). A total of 1 023 deaths were recorded within confirmed cases, for a case-fatality rate of 2.3 percent. Since spreading outward from Hubei in December 2019, COVID-19 had affected 1 386 counties in all 31 provinces by February 11, 2020.

Keywords: COVID 19, SARS-COV-2, Mutant COVID 19, Cases, Medical Records.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) may be an infectious infection caused by serious acute respiratory disorder crown infection 2 (SARS-CoV-2). The primary case was distinguished in Wuhan, China, in December 2019. It has since spread around the world, driving to a progressing widespread [1]. Side effects of COVID-19 are variable, but frequently incorporate fever, hack, weariness, breathing challenges, and misfortune of scent and taste. Symptoms start one to fourteen days after the introduction to the infection. Around one in five contaminated people does not create any side effects. Whereas most individuals have mellow indications, a few individuals create Acute Respiratory Distress Syndrome (ARDS). ARDS can be accelerated by cytokine storms, multi-organ disappointment, septic stun, and blood clots. Longer-term harm to organs (specific, the lungs and heart) has been watched [2]. There's concern around a noteworthy number of patients who have recouped from the intense stage of the infection but proceed to encounter a extend of impacts known as long COVID-19 for months a while later. These impacts incorporate extreme weakness, memory misfortune and other cognitive issues, low-grade fever, muscle shortcoming, and breathlessness. The infection that causes COVID-19 spreads basically when a contaminated individual is in near contact with another individual. Little beads and pressurized canned products containing the infection can spread from a contaminated person's nose and mouth as they breathe, hack, sniffle, sing, or talk. Other individuals are tainted on the off chance that the infection gets into their mouth, nose, or eyes. The infection may moreover spread by means of contaminated surfaces, in spite of the fact that usually not thought to be the most course of transmission. It can spread as early as two days sometimes recently contaminated people appear indications, and from people who never encounter side effects. Individuals stay irresistible for up to ten days in direct cases and two weeks in severe cases. Different testing strategies have been created to analyze the infection. The standard determination strategy is by real-time turn around translation polymerase chain response (RT-PCR) from a nasopharyngeal swab [3].

History

The infection is thought to be characteristic and has a creature beginning, through spillover contamination [4]. The primary known human contaminations were in Wuhan, Hubei, China. A consideration of the primary 41 cases of confirmed COVID- 19, distributed in January 2020 within The Lancet, detailed the most punctual date of onset of indications as 1 December 2019. Official distributions from the WHO detailed the most punctual onset of indications as 8 December 2019. The human-to-human transmission was affirmed by the WHO and Chinese specialists by 20 January 2020. Agreeing to official Chinese sources, these were generally connected to the Huanan Fish Discount Advertise, which too sold live creatures. In May 2020, George Gao, the chief of the Chinese Center for Illness Control and Anticipation, said creature tests collected from the fish advertise had tried negative for the infection, showing that the advertising was the location of an early super-spreading occasion, but it was not the location of the starting episode. Follows of the infection have been found in wastewater that was collected from Milan and Turin, Italy, on 18 December 2019.

The Wuhan Municipal Health Commission made the primary open declaration of a pneumonia flare-up of obscure cause on 31 December, affirming 27 cases sufficient to trigger an investigation. During the early stages of the flare-up, the number of cases multiplied roughly each seven and a half days. In early and mid-January 2020, the infection spread to other Chinese territories, made a difference by the Chinese Unused Year movement and Wuhan being a transport center and major rail interchange. On 20 January, China detailed about 140 modern cases in one day, counting two individuals in Beijing and one in Shenzhen. Afterward, official information appears 6,174 individuals had as of now created side effects at that point, and more may have been infected. A report within The Lancet on 24 January demonstrated human transmission, emphatically prescribed individual defensive hardware for wellbeing specialists, and said testing for the infection was basic due to its "widespread potential". On 30 January, the WHO pronounced the corona-virus an Open Wellbeing Crisis of International Concern. By this time, the outbreak wide a severity of 100 to 200 times.

On 31 January 2020, Italy had its to begin with affirmed cases, two visitors from China. As of 13 March 2020, the World Health Organization (WHO) considered Europe the dynamic middle of the widespread. On 19 Walk 2020, Italy surpassed China as the nation with the foremost passings. By 26 March, the Joined together States had overtaken China and Italy with the most noteworthy number of confirmed cases within the world. Investigate corona infection genomes shows the larger part of COVID-19 cases in New York came from European voyagers, instead of straightforwardly from China or any other Asian nation. Retesting of earlier tests found an individual in France who had the virus on 27 December 2019 and an individual within the Joined together States who passed on from the disease on 6 February 2020. On 11 June 2020, after 55 days without a locally transmitted case, Beijing detailed the primary COVID-19 case, taken after by two more cases on 12 June. By 15 June 79 cases were formally confirmed. Most of these patients went to Xinfadi Wholesale Market [5].

Possible Earlier Cases

Research in Italy on tests from 959 volunteers in a test lung cancer treatment attempted from September 2019 has appeared COVID-19 anti-bodies in 14% of the tests. National Cancer Institute in Milan executive Giovanni Apolone recommends that the major flare-up in Italy seem to have been caused since COVID-19 was widespread in Italy from summer 2019.

Epidemiology [6].

A few measures are commonly utilized to measure mortality. These numbers shift by region and over time and are impacted by the volume of testing, healthcare system quality, treatment choices, time since the introductory episode, and population characteristics such as age, sex, and by and large wellbeing. The death-to-case proportion reflects the number of passings isolated by the number of analyzed cases inside a given time interval. Based on Johns Hopkins College measurements, the worldwide death-to-case proportion is 2.2% as of 18 December 2020. The number shifts by region. Other measures incorporate the case fatality rate (CFR), which reflects the rate of analyzed people who pass on from a disease, and the infection fatality rate (IFR), which reflects the rate of contaminated people (analyzed and undiscovered) who pass on from an infection. These measurements are not time-bound and take after a particular population from contamination through case determination. Numerous scholastics have endeavored to calculate these numbers for specific populations. Outbreaks have happened in jails due to swarming and a failure to implement satisfactory social removing. Within the Joined together States, the prisoner population is maturing and numerous of them are at a tall chance of poor results from COVID-19 due to tall rates of coexisting heart and lung infections, and poor get to high-quality healthcare.

Infection Fatality Rate

The infection fatality rate (IFR), too called infection casualty ratio, is different from the case fatality rate (CFR). The CFR of infection is calculated by isolating the full number of passings from the infection by the whole number of individuals analyzed with the disease (inside a certain period of time) [7]. Firm lower limits of IFRS have been built up in a number of areas such as New York City and Bergamo in Italy since the IFR cannot be less than the population casualty rate. As of 10 July, in New York City, with a populace of 8.4 million, 23,377 people (18,758 affirmed and 4,619 likely) have passed on with COVID- 19 (0.3% of the population). Antibody testing in New York City proposed an IFR of ~0.9%, and ~1.4%. In Bergamo territory, 0.6% of the population has died [8].

Gender Differences [9]

Early audits of epidemiologic information appeared more prominent effect of the pandemic and the next mortality rate in men in China and Italy. The Chinese Center for Disease Control and Prevention detailed the passing rate was 2.8% for men and 1.7% for ladies. Afterward, surveys in June 2020 demonstrated that there's no noteworthy distinction in helplessness or in CFR between sexes. One survey recognizes the distinctive mortality rates in Chinese men, proposing that it may be inferable to lifestyle choices such as smoking and drinking liquor instead of hereditary components. Gender-based immunological contrasts, the lesser predominance of smoking in ladies and men creating

co-morbid conditions such as hypertension at a more youthful age than ladies might have contributed to the higher mortality in men. In Europe, 57% of the contaminated individuals were men and 72% of those passed on with COVID-19 were men. As of April 2020, the US government isn't following sex-related information of COVID-19 contaminations. Inquire about has appeared that viral ailments like Ebola, HIV, flu, and SARS influence men and ladies differently.

Transmission and Prevention Research

Modeling research has been conducted with a few destinations, counting expectations of the dynamics of transmission, conclusion, and guess of contamination, estimation of the effect of mediations, or allotment of assets. Displaying thinks about are generally based on epidemiological models, assessing the number of infected individuals over time beneath given conditions [10]. Assist, conceptual systems from emergency administration research have been connected to way better get it the impacts of COVID-19 on organizations worldwide [11].

Treatment-Related Research

Repurposed antiviral drugs make up most of the investigation into COVID-19 medications. Other candidates in trials incorporate vasodilators, corticosteroids, resistant treatments, lipoic corrosive, bevacizumab, and recombinant angiotensin-converting enzyme 2 [12]. In March 2020, the World Health Organization started the Solidarity Trial to survey the treatment impacts of a few promising drugs: a test sedate called remdesivir; anti-malarial drugs chloroquine and hydroxychloroquine; two anti-HIV drugs, lopinavir/ritonavir; and interferon-beta. More than 300 dynamic clinical trials were underway as of April 2020 [13].

Signs and Symptoms [14]

Symptoms of COVID-19 are variable, extending from mild symptoms to serious illness. Common indications incorporate fever, hack, weakness, breathing troubles, and misfortune of scent and taste. Individuals with the same disease may have diverse side effects, and their indications may alter over time. For example, one individual may have a tall fever, a hack, and weariness, and another individual may have a low fever at the beginning of the illness and create trouble breathing a week afterward. However, in individuals without earlier ears, nose, and throat (ENT) disorders, the misfortune of taste combined with the misfortune of smell is related with COVID-19 with a specificity of 95%. As is common with contaminations, there's a delay, known as the incubation period, between the minute an individual to begin with gets to be contaminated and the appearance of the primary side effects. The middle incubation period for COVID-19 is four to five days. Most symptomatic individuals encounter side effects two to seven days after introduction, and nearly all symptomatic individuals will involve one or more indications sometime recently day twelve. Other contaminated individuals will create indications afterward (called pre-symptomatic) or have exceptionally mild symptoms, and can too spread the virus.

Cause

COVID-19 is caused by infection with the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) virus strains.

Transmission

COVID-19 spreads from individual to individual basically through the respiratory course after an infected individual hacks, sniffles, sings, talks, or breathes. A new infection occurs when virus-containing molecules breathed out by an infected person, either respiratory droplets or aerosols, get into the mouth, nose, or eyes of other individuals who are in near contact with the contaminated individual. During human to human transmission, a normal 1000 irresistible SARS-CoV-2 infection is thought to start unused contamination. Social distancing and the wearing of cloth confront masks, surgical covers, respirators, or other face covers are controls for droplet transmission. Transmission may be diminished inside with well-kept up warming and ventilation frameworks to preserve great discuss circulation and increment the utilize of outdoor air.

Virology

Acute respiratory syndrome corona-virus 2 (SARS-CoV-2) may be a novel extreme intense respiratory disorder corona-virus. It was, to begin with, confined from three individuals with pneumonia associated with the cluster of intense respiratory sickness cases in Wuhan. All features of the novel SARS-CoV-2 infection take place in related corona-viruses in nature. Exterior the human body, the infection is destroyed by a household cleanser, which bursts its protective bubble. SARS-CoV-2 is closely related to the initial SARS-CoV. It is an idea to have an animal (zoonotic) beginning. The hereditary investigation has uncovered that the crown virus genetically clusters with the class Betacoronavirus, in subgenus Sarbecovirus (lineage B) along with two bat-derived strains. It is 96% indistinguishable at the entire genome level from other bat crown infection tests (BatCov RaTG13) [16]. The basic proteins of SARS-CoV-2 incorporate layer glycoprotein (M), an envelope protein (E), nucleocapsid protein (N), and the spike protein (S). The M protein of SARS-CoV-2 is 98.6% alike to the M protein of bat SARS-CoV, keeps up 98.2% homology with pangolin SARS-CoV, and has 90% homology with the M protein of SARS-CoV; while, the similarity is only 38% with the M protein of MERS-CoV. In silico inquiry conveyed that the M protein of SARS-CoV-2 characteristics a triple helix bundle that moulds a single 3-transmembrane space, and is homologous to the prokaryotic sugar transport protein semi-sweet. [17].

Pathophysiology

Coronavirus can influence the upper respiratory tract (antrum, nose, and gullet) and the under respiratory tract (airpipe and lungs). The lungs are the organs most influenced by COVID-19 since the infection gets to have cells by means of the protein angiotensin-converting protein 2 (ACE2), which is almost inexhaustible in sort II alveolar cells of the lungs. The infection employments an extraordinary surface glycoprotein called a "spike" (peplomer) to associate with ACE2 and enter the host cell. The thickness of ACE2 in each tissue connects with the seriousness of the infection in that tissue and some have recommended diminishing ACE2 action can be protective, in spite of the fact that another see is that expanding ACE2 utilizing angiotensin II receptor blocker medications might be defensive. As the alveolar infection advances, respiratory disappointment might create and pass may take after [18]. Whether SARS-CoV-2 is able to attack the nervous system remains obscure. The infection isn't recognized within the CNS of the majority of COVID-19 patients with neurological issues. The infection may moreover enter the circulation system from the lungs and cross the blood-brain boundary to pick up get to the CNS, conceivably inside a contaminated white blood cell by a "Trojan horse" mechanism. [19].

Immunopathology

Although SARS-CoV-2 encompasses a tropism for ACE2-expressing epithelial cells of the respiratory tract, patients with extreme COVID-19 have indications of systemic hyper-inflammation. Clinical research facility discoveries of raised IL-2, IL-7, IL-6, granulocyte-macrophage colony-stimulating calculate (GM-CSF), interferon-γ inducible protein 10 (IP-10), monocyte chemo attractant protein 1 (MCP-1), Macrophage provocative protein 1-α (MIP-1α), and tumor corruption factor-α (TNF-α) demonstrative of cytokine discharge disorder (CRS) recommend a fundamental immunopathology [20]. Systemic inflammation comes about in vasodilation, permitting provocative lymphocytic and monocytic penetration of the lung and the heart. In particular, pathogenic GM-CSF-secreting T-cells were revealed to connect with the recruitment of provocative IL-6-secreting monocytes and serious lung pathology in COVID-19 victims. Lymphocytic invades have too been detailed at autopsy [21].

Diagnosis [22]

COVID-19 can temporarily be analyzed on the premise of side effects and affirmed utilizing turn around translation polymerase chain response (RT-PCR) testing of contaminated emissions. In conjunction with research facility testing, chest CT looks may be accommodating to analyze COVID-19 in people with a high clinical doubt of contamination. Discovery of earlier contamination is conceivable with serological tests, which distinguish antibodies delivered by the body in reaction to infection.

Pathology [23]

The most obsessive discoveries at post-mortem examination are Macroscopy: pericarditis, lung combination, and aspiratory edema. Lung discoveries: minor serous exudation, minor fibrin exudation aspiratory edema, pneumocyte hyperplasia, expansive atypical pneumocytes, interstitial irritation with lymphocytic penetration, and multinucleated monster cell arrangement diffuse alveolar harm (Dad) with diffuse alveolar exudates. Organization of exudates in alveolar cavities and pneumonic interstitial fibrosis plasmacytosis in BAL Blood: dispersed intravascular coagulation (DIC); leukoerythroblastic reaction. Liver: microvesicularsteatosis.

Corona Test [24]

There are non-identical types of coronavirus tests that can be done:

• Swab Test – In this case, a special swab is used to take a specimen from your nose or throat

• Nasal aspirate – In this case, a saline solution will be vaccinated into your nose and, then a specimen is taken with a light suction

• Tracheal aspirate – In this case, a thin tube with a flashlight, also known as a bronchoscope, is put into your mouth to stick out your lungs from where a sample is collected.

• Sputum Test – Sputum is thick mucus that gets collected in the lungs and comes out with a cough. During this test, your essential cough-up sputum in a special cup or a scrub is used to take a sample from your nose.

• Blood test – In this case, a blood sample is drawn from a vein in the arm.

RT-PCR-Based Test [25]

RT-PCR is the foremost exact symptomatic test. It regularly has high sensitivity and specificity in a research facility setting: however, in one consider affectability dropped to 66–88% clinically. In one study affectability was most noteworthy at week one (100%), taken after by 89.3%, 66.1%, 32.1%, 5.4%, and zero by week six. A Dutch CDC-led research facility examination compared 7 PCR kits. Test units made by BGI, R-Biopharm AG, BGI, KH Medical, and See gene appeared high sensitivity. High sensitivity kits are prescribed to evaluate individuals without indications, whereas lower affectability tests are satisfactory when diagnosing symptomatic patients. On 7 September, the UK government issued "direction for strategies to be actualized in research facilities to supply confirmation of positive SARS-CoV-2 RNA comes about during periods of low predominance when there's a decrease within the prescient esteem of positive test results".

Process [26]

The causative agent for Covid19 is the SARS-CoV-2 infection. It is an RNA infection meaning it invades a healthy cell to duplicate and survive. Hence the RT-PCR test is for the distinguishing proof of SARS-CoV-2 RNA. In this, the RNA is changed over to DNA through a process called 'reverse transcription' for recognizing viruses. The SARS-CoV-2 RNA is generally recognizable in respiratory examples amid the intense stage of the disease. For that upper and lower respiratory examples (such as nasal, nasopharyngeal or oropharyngeal swabs, sputum, lower respiratory tract suctions, bronchoalveolar lavage, and nasopharyngeal wash/aspirate or nasal suction) are collected. This test is treated with a few chemical arrangements that expel substances, such as proteins and fats, and extricates only the RNA display within the sample.

Isothermal Nucleic Amplification Test

One thing about reported that the ID Presently COVID-19 test appeared affectability of 85.2%. Abbott reacted that the issue seems to have been caused by analysis delays. Another study rejected the test in their clinical setting since of this low sensitivity.

Prevention [27]

Preventive measures to diminish the chances of contamination include remaining at home, wearing a mask in open, avoiding swarmed places, keeping a distance from others, ventilating indoor spaces, washing hands with cleanser

and water frequently and for at least 20 seconds, practicing great respiratory cleanliness, and maintaining a strategic distance from touching the eyes, nose, or mouth with unwashed hands. Those analyzed with COVID-19 or who accept they may be contaminated are advised by the CDC to remain domestic but to induce medical care, call ahead before going by a healthcare supplier, wear a confront mask sometime recently entering the healthcare provider's office and when in any room or vehicle with another individual, cover hacks and wheezes with a tissue, frequently wash hands with cleanser and water and maintain a strategic distance from sharing individual family items. The first corona virus antibody was permitted administrative approval on 2 December by the UK drug controller MHRA. It was assessed for crisis utilizes authorization (EUA) status by the US FDA and in a few other nations. Usually done by abating the contamination rate to diminish the chance of wellbeing administrations being overpowered, permitting for superior treatment of current cases, and postponing extra cases until effective medicines or an immunization become available.

Social Distancing [28]

Social distancing (too known as physical distancing) incorporates disease control activities aiming to moderate the spread of the illness by limiting near the contact between people. Strategies incorporate quarantines; travel limitations; and the closing of schools, work environments, stadiums, theaters, or shopping centers. Individuals may follow social distancing strategies by remaining at home, constraining travel, avoiding crowded ranges, utilizing no-contact welcome, and physically isolating themselves from others. Starting suggestions included keeping up a six-foot/two-meter separate from others exterior the family unit. Be that as it may, a case happening in South Korea proposed that's lacking, citing transmission in spite of a brief introduction (5 minutes) at 20 feet from the carrier in a restaurant. In a study investigating the spread of Corona-virus at a restaurant on January 24, Chinese New Year, analysts found among 21 burger joints at three adjoining tables, 10 had contracted the disease from the list quiet, the furthest situated 4.6 meters/15 feet, absent from the spreader. In late March 2020, the WHO and other health bodies started to replace the utilize of the term "social distancing" with "physical distancing", to clarify that the point is to reduce physical contact whereas keeping up social associations, either essentially or at a separate.

Self-Isolation [29]

Self-isolation at home has been prescribed for those analyzed with COVID-19 and those who suspect they have been infected. Health offices have provided point-by-point illuminating for appropriate self-isolation. Many governments have ordered or prescribed self-quarantine for whole populations. The most grounded self isolate enlightening has been issued to those in high-risk bunches. Those who may have been exposed to somebody with COVID-19 and those who have as of late voyage to a nation or region with the far-reaching transmission have been exhorted to self-quarantine for 14 days from the time of final conceivable exposure.

Face Masks and Respiratory Hygiene [30].

The WHO and US CDC suggest people wear non-medical confront covers in open settings where there's an expanded chance of transmission and where social distancing measures are troublesome to maintain. This suggestion is implied to diminish the spread of the disease by asymptomatic and pre-symptomatic people and is complementary to established preventive measures such as social distancing. Masks are too strongly suggested for those who may have been infected and those taking care of somebody who may have the illness. Proper hand cleanliness after any cough or wheeze is energized. Healthcare experts interacting specifically with COVID-19 patients are prompted to utilize respirators at the slightest as defensive as NIOSH certified N95 or equivalent, in expansion to other individual defensive equipment.

Hand-washing and Hygiene [31]

When not wearing a mask, the CDC, WHO, and NHS prescribes covering the mouth and nose with a tissue when coughing or sniffling and prescribes utilizing the interior of the elbow in case no tissue is accessible. Legitimate hand cleanliness after any cough or sneeze is energized. The WHO moreover suggests that people wash hands frequently

with cleanser and water for at slightest 20 seconds, particularly after attending to the toilet or when hands are visibly messy, sometimes recently eating, and after blowing one's nose. The CDC prescribes utilizing alcohol-based hand sanitizers with at slightest 60% liquor, but only when cleanser and water are not promptly accessible. For zones where commercial hand sanitizers are not promptly accessible, the WHO gives two definitions for local generation. In these definitions, the antimicrobial movement arises from ethanol or isopropanol. Hydrogen peroxide is utilized to assist dispose of bacterial spores within the alcohol; it isn't "an active substance for hand antisepsis". Glycerol is included as humectants.

Surface Cleaning [32]

Surfaces may be cleaned with a number of solutions (inside one minute of presentation to the disinfectant for a stainless steel surface), counting 62–71 percent ethanol, 50–100 percent isopropanol, 0.1 % sodium hypochlorite, 0.5% hydrogen peroxide, and 0.2–7.5% povidone-iodine. Bright germicidal illumination may too be utilized. The CDC prescribes that in case a COVID-19 case is suspected or confirmed at an office such as an office or daycare, all ranges such as workplaces, washrooms, common ranges, shared electronic gear like tablets, touch screens, keyboards, remote controls, and ATM machines utilized by the sick people should be disinfected.

Ventilation and Air Filtration

The WHO advises ventilation and air filtration in common spaces to help clear out infectious aerosols.

Healthy Diet and Lifestyle [33]

The Harvard T.H. Chan School of Open Health prescribes that COVID-19 has made the support of one's safe framework more vital than ever. In this manner, eating a solid count of calories, being physically dynamic, overseeing mental stress, and getting sufficient rest are basic. Dark-skinned individuals are at a specific hazard of vitamin D insufficiency which can impair the immune system.

Vaccine [34]

A COVID-19 vaccine could be a vaccine expecting to supply acquired resistance against COVID-19. Earlier to the COVID-19 widespread, work to create an antibody against the corona-virus illnesses SARS and MERS had set up information around the structure and work of corona-viruses, which quickened development during early 2020 of changed innovation stages for a COVID-19 vaccine. As of mid-December 2020, 57 antibody candidates were in clinical inquire about: to be specific, 40 in Stage I–II trials and 17 in Stage II–III trials. Moreover, Bahrain gave crisis marketing authorization for the vaccine made by Sinopharm, taken after by the United Arab Emirates. By 16 December, within the United Kingdom, 138,000 individuals had gotten the Pfizer-BioNTech COVID-19 vaccine during the first week of their vaccination program. By December, more than 10 billion antibody measurements had been preordered by nations, with around half of the dosages obtained by high-income nations comprising as were 14% of the world's population. The producers of three vaccines closest to worldwide dispersion – Pfizer, Moderna, and AstraZeneca – anticipated a fabricating capacity of 5.3 billion measurements in 2021, which may be utilized to immunize around 3 billion individuals (as the immunizations require two measurements for a defensive impact against COVID-19). Due to the tall request of preorders in 2020–21, people in low-income creating nations may not get vaccinations from these producers until 2023 or 2024, expanding the requirement for the worldwide COVAX initiative to supply vaccines equitably.

Treatment

The administration of COVID-19 incorporates supportive care, which may incorporate liquid treatment, oxygen support, and supporting other affected vital organs. The WHO is within the process of including dexamethasone in the rules for treatment for hospitalized patients, and it is prescribed for thought in Australian rules for patients requiring oxygen. CDC prescribes those who suspect they carry the infection wear a basic confront mask. Extracorporeal membrane oxygenation (ECMO) has been utilized to address the issue of respiratory disappointment,

but its benefits are still under consideration. Individual cleanliness and a solid lifestyle and eat less have been suggested to progress resistance. Steady medicines may be valuable in those with gentle indications at the early organize of contamination. Nasal breathing is recommended as such a strategy based on several peer-surveyed studies. [35]. The WHO, the Chinese National Health Commission, and the United States' National Organizing of Health have published suggestions for taking care of individuals who are hospitalized with COVID 19. Intensivists and pulmonologists in the U.S. have compiled treatment proposals from different offices into a free resource, the IBCC [36].

Medications

Remdesivir [37]

As of late October 2020, Remdesivir was the only drug endorsed by the FDA with a particular sign to treat COVID-19. In Australia and the European Union, remdesivir (Veklury) is demonstrated for the treatment of COVID-19 in grown-ups and young people matured twelve a long time and more seasoned with bodyweight at slightest 40 kilograms (88 lb) with pneumonia requiring supplemental oxygen. Late November 2020, the World Health Organization (WHO) made a conditional recommendation against treatment with remdesivir for hospitalized patients, regardless of seriousness (based on information from the Solidarity Trial). Remdesivir was approved for therapeutic utilize within the Joined together States in October 2020. It is the primary treatment for COVID-19 to be affirmed by the U.S. Food and Drug organization (FDA). It is demonstrated for utilizing in adults and young people matured twelve years and older with body weight at the slightest 40 kilograms (88 lb) for the treatment of COVID-19 requiring hospitalization.

Mechanism of Action [38]

As an adenosine nucleoside triphosphate cognate (GS-443902), the active metabolite of remdesivir obstructs the activity of viral RNA-dependent RNA polymerase and eludes proofreading by viral exoribonuclease (ExoN), causing a diminish in viral RNA production. In a few infections such as the respiratory syncytial virus, it causes the RNA-dependent RNA polymerases to delay, but its overwhelming impact (as in Ebola) is to initiate an irreversible chain end. Unlike with numerous other chain eliminators, typically not interceded by anticipating the expansion of the instantly consequent nucleotide, but is instead postponed, happening after five extra bases have been included in the developing RNA chain. For the RNA-Depending on RNA Polymerase of MERS-CoV, SARS-CoV-1, and SARS-CoV-2 arrest of RNA synthesis happens after joining of three added nucleotides. Hence, remdesivir is classified as a direct-acting antiviral specialist that works as a delayed chain terminator.

Dosage Form and Strength

Injection, lyophilized powder for reconstitution - 100mg/vial
Injection, concentrated solution - 100mg/20mL (5mg/mL)

Baricitinib [39]

In November 2020 the FDA allowed Emergency Utilize Authorization (EUA) for the drug baricitinib to be given to certain patients hospitalized with suspected or confirmed COVID-19, but as it were in conjunction with remdesivir. In a single clinical trial, this combination treatment was appeared to have a little, but the factually critical impact on quiet results compared to organization of remdesivir alone. Utilization of baricitinib was limited to adults and children two a long time of age or more seasoned requiring supplemental oxygen, mechanical ventilation, or ECMO.

Mechanism of Action

Baricitinib may be a Janus kinase (JAK) inhibitor that reversibly inhibits Janus kinase 1 with a half-maximal inhibitory concentration (IC50) of 5.9 nm and Janus kinase 2 with an IC50 of 5.7 nm. Tyrosine kinase 2, which has a place in the same protein family, is influenced less (IC50 = 53 nm), and Janus kinase 3 far less (IC50 > 400 nm).

Dosage Form and Strengths
Tablet
•2mg

Dexamethasone [40]
In September 2020, the European Medications Agency (EMA) embraced the utilize of dexamethasone in grown-ups and teenagers (from twelve a long time of age and weighing at slightest 40 kg) who require supplemental oxygen treatment.

Mechanism of Action
The short-term impacts of corticosteroids are diminished vasodilation and penetrability of capillaries, as well as decreased leukocyte relocation to sites of inflammation. Corticosteroids authoritative to the glucocorticoid receptor intercedes changes in gene expression that lead to different downstream impacts over hours to days. Glucocorticoids inhibit neutrophil apoptosis and emargination; they inhibit phospholipase A2, which diminishes the arrangement of arachidonic corrosive subsidiaries; they repress NF-Kappa B and other incendiary translation components; they advance anti-inflammatory qualities like interleukin-10.

COVAXINTM - India's First Indigenous COVID-19 Vaccine [41]
COVAXINTM, India's innate COVID-19 vaccine by Bharat Biotech is created in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV). The indigenous inactivated immunization is created and made in Bharat Biotech's BSL-3 (Bio-Safety Level 3) high control facility. The immunization is created using Whole-Viron Inactivated Vero Cell-derived platform technology. Inactivated immunizations don't imitate and are hence impossible to return and cause neurotic impacts. They contain dead viruses, unable of infecting individuals but still able to taught the resistant framework to mount a cautious response against a disease.

COVISHIELD [42]
The Oxford-AstraZeneca vaccine is being made locally by the Serum Established of India, the world's biggest vaccine producer. It says it is creating more than 50 million doses a month. The antibody, which is known as Covishield, is made from a debilitating form of a common cold infection (known as an adenovirus) from chimpanzees. It has been altered to see more like a crown infection - in spite of the fact that it can't cause illness. It can be securely put away at temperatures of 20C to 80 C, around the same as a household fridge, and can be conveyed in existing health care settings such as doctors' surgeries. The jab created by Pfizer-biotech, which is right now being managed in a few nations, must be put away at -70C and can as it was being moved a limited number of times - a specific challenge in India, where summer temperatures can reach 500C.

Effectiveness of COVISHIELD
International clinical trials of the Oxford-AstraZeneca vaccine appeared that when individuals were given a half dosage and after that a full dosage, viability hit 90%. However, unpublished information recommends that leaving a longer gap between the primary and moment dosages increments the general viability of the hit - in a sub-group given the antibody this way it was found to be 70% viable after the first dose. A few of the first dosages have been already dispatched to Bhutan, Maldives, Bangladesh, Nepal, Myanmar, and Seychelles. In June last year, AstraZeneca had come to a licensing agreement with Serum to supply one billion doses for low-and-middle-income nations, with a commitment to supply 400 million sometime recently the conclusion of 2020. India is additionally arranging to send doses to Sri Lanka, Afghanistan, and Mauritius after regulatory clearances from these nations. It has moreover cleared commercial sends out of the Covishield vaccine to Brazil. The Foreign Service says India will proceed to supply antibodies all over the world after taking into consideration residential requirements and universal requests and obligations.

Complications of COVID-19 [43]

Complications may include pneumonia, acute respiratory distress syndrome (ARDS), multi-organ disappointment, septic stun, and passing. Cardiovascular complications may incorporate heart failure, arrhythmias, heart inflammation, and blood clots. Approximately 20–30% of individuals who display COVID-19 have raised liver enzymes reflecting liver damage. Neurologic appearances incorporate seizure, stroke, encephalitis, and Guillain–Barre disorder (which incorporates misfortune of engine capacities). In extraordinarily uncommon cases, severe encephalopathy can occur, and it can be reviewed in those who have been examined with COVID-19 and have a altered mental status.

Immunity [44]

The immune feedback by people to CoV-2 contamination happens as a mixture of cell-mediated resistance and antigen production, fair as with most other diseases. In a few of these cases, the RNA from the primary and moment diseases demonstrates a distinctive strain of the virus. Some reinfection cases are accepted to be waiting for contamination instead of reinfection, or false positives due to remaining non-infectious RNA parts. A few other coronaviruses circulating in individuals are competent of reinfection after generally a year.

Lockdown in India

Phase 1 (25 march – 14 april) [45]: On 25 Walk, the first day of the lockdown, about all administrations and industrial facilities were suspended. People were rushing to stock basics in a few parts. Arrests over the states were made for abusing standards of lockdown such as wandering out for no crisis, opening businesses, and home quarantine violations. On 27 March, the Reserve Bank of India announced a slew of measures to help relieve the financial impacts of the lockdown. Earlier to the declaration of the across the country lockdown, on 22 March, the government had declared that the Indian Railroads would suspend traveler operations through 31 March. The national rail network has kept up its cargo operations during the lockdown, to transport essential goods. On 29 March, the Indian Railways reported that it would begin administrations for uncommon allocate trains to transport fundamental merchandise, in expansion to the normal cargo service. As the conclusion of the beginning lockdown period came close, numerous state governments communicated their choice to extend it till the conclusion of April. Among them were Odisha, Punjab, Maharashtra, and Karnataka with a few relaxations, West Bengal and Telangana. Towards the conclusion of the starting period, the rate of development of COVID contaminations in India had essentially moderated, from a rate of multiplying each three days earlier to the lockdown to one of multiplying every eight days on 18 April.

Phase 2 (15 April – 3 May): On 14 April, Modi extended the across the nation lockdown till 3 May, with a conditional relaxation guaranteed after 20 April for the regions where the spread had been contained by then. He said that each town, each police station region, and each state would be carefully assessed to see in case it had contained the spread. The regions that we're able to do so would be discharged from the lockdown on 20 April. On the off chance that any unused cases emerged in those regions, lockdown may be reimposed. On 16 April, lockdown ranges were classified as "red zone", indicating the nearness of disease hotspots, "orange zone" indicating a few diseases, and "green zone" with no infections. On 25 April, small retail shops were permitted to open with half the staff. Once more social distancing standards were to be followed. On 29 April, The Service of Domestic Affairs issued rules for the states to permit inter-state development of the stranded people.

Phase 3 (4–17 May): On 1 May, the Ministry of Home Affairs (MHA) and the Government of India (GoI) encourage extended the lockdown period to two weeks past 4 May, with a few relaxations. The nation has been split into 3 zones: red zones (130 areas), orange zones (284 locales), and green zones (319 locales). Red zones are those with high coronavirus cases and a high multiplying rate, orange zones are those with comparatively fewer cases than red zone and green zones are those without any cases within the past 21 days. Typical development is allowed in green zones with buses restricted to 50 percent capacity. Orange zones would permit as it were private and

contracted vehicles but no open transportation. The red zones would stay beneath lockdown. The zone classification would be reexamined once a week.

Phase 4 (18–31 May): On 17 May, the National Disaster Management Authority (NDMA) and the Ministry of Home Affairs (MHA) expanded the lockdown for a period for two weeks past 18 May, with extra relaxations. Not at all like the past expansions, states were given a larger say within the boundary of Green, Orange, and Red zones, and the execution

Unlock [46]

Unlock 1.0 (1–30 June): The MHA issued new rules for the month of June, expressing that the stages of reviving would "have a financial focus". Lockdown restrictions were as it were to be forced in control zones, whereas activities were allowed in other zones in a staged way. This to begin with the stage of reviving was named "Unlock 1.0" and allowed shopping centers, religious places, hotels, and eateries to revive from 8 June. In future stages of reopening, advance activities are to be allowed. In Stage II, all educational institutions are planned to reopen in July, pending discussions with state governments. In Stage III, facilitating of confinements on worldwide discuss travel, operation of metros and recreational exercises (swimming pools, exercise rooms, theaters, excitement parks, bars, auditoriums and get together halls) would be chosen upon in August.

Unlock 2.0 (1–31 July): Phase II of Open started on 1 July beneath the rules and enlightening of the MHA and the NDMA. Lockdown measures were as it was forced in control zones. In all other ranges, most activities were allowed. Night curfews were in impact from 10 p.m. to 5 a.m. in all zones. Educational institutions, mass transit, recreational projects remained closed till 31 July. Advance rules with respect to utilization of AarogyaSetu and covers were repeated.

Unlock 3.0 (1–31 August): Unlock 3.0 for August 2020 evacuated night curfews and allowed gymnasiums and yoga centers to revive from 5 August. Educational institutions will stay closed till 31 August. Maharashtra and Tamil Nadu forced a lockdown for the complete month, whereas West Bengal forced lockdowns twice a week. On 30 August the Delhi Metro began its operations with two metro lines.

Unlock 4.0 (1–30 September): On 29 August 2020, the Ministry of Home Affairs issued rules for activities allowed in Unlock 4.0. It said that "Lockdown should stay in steer within the Control Zones till 30th September 2020". Marriage capacities with get-togethers of up to 50 individuals and funereal/last customs ceremonies with up to 20 individuals were allowed. Religious, entertainment, political, sports, scholarly functions, and social occasions of up to 100 individuals were permitted.

Unlock 5.0 (1–31 October): On 30 September 2020, the Ministry of Home Affairs issued rules for activities allowed in Unlock 5.0. For schools, it features an inclination for online learning in case possible, but States and Union Regions will be able to form those choices from 15 October, in an evaluated way. On 3 November the Government of Kerala opened its tourism division by reopening slope stations, beaches, national stop and inter-state open transport movement.

Unlock 6.0 (1–30 November): On 27 October 2020, the Ministry of Home Affairs issued rules for activities permitted in Unlock 6.0. The Ministry of Home Affairs did not make any modern changes to the existing Open 5.0 rules in its most later enlightening for another set of opening and said that they would continue to be executed inside the month of November as well. As well, an unassuming bunch of states has allowed the opening up of more activities outside control zones and detailed partial reviving of schools.

Impact [47]

Food delivery services were prohibited by a few state governments in spite of the central government's approval. Thousands of individuals emigrated out of major Indian cities, as they got to be jobless after the lockdown. The lockdown broke the provide chain of narcotics drugs in Punjab. Numerous states were sharp on opening up alcohol shops during the lockdown which was at long last allowed within the 3rd stage starting on 4 May. Due to the lockdown, more than 350 deaths were detailed as of 10 May, with reasons extending from starvation, suicides, depletion, street and rail accidents, police brutality, and refusal of convenient medical care. Among the detailed deaths, most were among the marginalized migrants and laborers.

Economic Impact [45]

India had already been encountering a drawn-out financial lull. The GDP development rate had fallen from 8.2% in January–March 2018 to 3.1% in January–March 2020. In the first quarter of the monetary year 2020-2021, this number went into negative. The GDP development rate for April–June 2020 was -23.9%, which happened to be the most exceedingly bad ever in history. Vital parameters like fabricating, development, exchange, hotel industry saw a decrease and slid into negative. Fabricating development at -39.3%, Mining development at -23.3%, Development at -50%, Trade & hotel industry development at -47%.

Migrant Workers

With factories and working environments closed down, millions of migrant workers had to deal with the misfortune of pay, nourishment shortages, and instability approximately their future. Taking after this, numerous of them and their families went famished. Whereas government plans guaranteed that the destitute would get extra proportions due to the lockdown, the dispersion system failed to be effective. With no work and no cash, thousands of migrant workers were seen walking or bicycling hundreds of kilometers to go back to their local towns. Despite the casting of particular trains and buses by the government, the emigrant workers chose to either travel together in large batches. Also, they felt that going back to their hometowns; they may return to farming and take up little occupations beneath the MNREGA. On 26 May, the Supreme Court admitted that the issues of the transients had still not been solved which there had been "inadequacies and certain slips" on the portion of the governments. It hence requested the Centre and States to supply free food, shelter, and transport to stranded migrant workers.

Relief

On 26 March 2020, the Indian government declared a help collection of $22.6 billion to help the poor population hit economically by the COVID-19 widespread. In any case, on 9 April 2020, financial analysts and activists argued that a critical extent of the influenced population was incapable to profit from the offices. According to a Government of India report recorded with the Supreme Court of India, as of 7 April, state governments worked 22,567 alleviation camps for stranded migrant workers, of which 15,541 camps (summing to 68% of all) were worked by Kerala, 1,135 camps by Maharashtra, 178 camps by Tamil Nadu and smaller numbers by other states. Non-governmental associations were working 3,909 camps. On 12 May, Narendra Modi announced that the government would give a 20 trillion rupees ($266 billion) support collection in tax and financial measures to support the economy.

Impact on Environment

Rivers have become cleaner as factories are closed due to the lockdown. The quality of air has altogether progressed during the lockdown.

Clinical Trial Phase [48]

Clinical trial programs include three, multiple-year stages toward item approval, and a fourth, post-approval organize for continuous security observing of the vaccine or drug treatment:

- Phase I trials, usually in healthy participants, determine safety and dosing.

- Phase II trials are used to initiate an initial reading of efficacy and further explore safety in small numbers of people having the illness targeted by the US.
- Phase III trials are large, urgent trials to decide security and viability inadequately huge numbers of individuals with the COVID19 contamination. In the event that security and viability are enough proved, clinical testing may stop at this step and the NCE progresses to the new drug application (NDA) organize to start promoting.

Phase IV trials are post-approval trials which will be a condition joined by the FDA, also called post-market surveillance studies. Until a vaccine is given to the common population, all potential adverse events remain unidentified, requiring that vaccines experience Stage IV considers with standard reports by the producer to the Vaccine Adverse Event Reporting System (VAERS) to identify issues after utilize within the populace starts.

Mutant COVID-19 [49]

A variant of Concern 202012/01, abbreviated VOC 202012/01 (also known as lineage B.1.1.7, 20I/501Y.V1 and popularly as UK crown infection variation; see § Names), is a variant of SARS-CoV-2, the infection that causes COVID-19, one of several causing concern. Assessed to be 36%–75% more transmissible than wild-type SARS-CoV-2, it was identified in November 2020 from a test taken in September, during the COVID-19 widespread within the United Kingdom; it started to spread rapidly by mid-December, and it is related with a critical increase in SARS-CoV-2 contaminations within the United Kingdom. This increment is thought to be at least partly because of one or more changes within the virus's spike protein. The variation is additionally eminent for having more transformations than ordinarily seen.

Detection

VOC 202012/01 was, to begin with, recognized in early December 2020 by combining genome information with knowledge that the rates of disease in Kent were not falling in spite of national confinements. The two most dependable genomes that have a place in the B.1.1.7 lineage were composed on 20 September 2020 in Kent and another on 21 September 2020 in greater London. These arrangements were submitted to the GISAID sequence database (grouping promotions EPI ISL 601443 and EPI ISL 581117 individually). As of 15 December, there were 1623 genomes within the B.1.1.7 lineage. Of these 519 were tested in Greater London, 555 in Kent, 545 in other locales of the UK counting both Scotland and Ribs and 4 in other nations. Backward tracing using genetic evidence recommends this modern variation that emerged in September 2020 and after that circulated at exceptionally low levels within the population until mid-November. The increment in cases connected to the modern variant, to begin with, got to be clear in late November when Public Health England (PHE) was exploring why disease rates in Kent were not falling in spite of national limitations.

Rapid-Antigen-Test Effectiveness

Several rapid antigen tests for SARS-CoV-2 are in broad use all-inclusive for COVID-19 diagnostics. They are accepted to be valuable in stopping the chain of transmission of SARS-CoV-2 by giving the implies to quickly recognize an expansive number of cases as a portion of a mass testing program. Taking after the growth of VOC-202012/01, there was at the first job that quick tests might not differentiate it, but Public Health England decided that quick tests evaluated and utilized within the United Kingdom detect the variation.

Vaccine Effectiveness

As of late 2020, several COVID-19 vaccines were being sent or beneath development. However, as further changes happen, concerns were raised as to whether antibody advancement would have to be changed. As of the conclusion of 2020, German, British, and American health authorities and specialists accept that existing vaccines will be as viable against the modern VOC-202012/01 variation as against past variations. On 18 December, NERVTAG decided "that there is right now insufficient information to draw any conclusion on antigenic escape".

Spread

Cases of VOC-202012/01 are likely to be undetected in most nations as most tests don't recognize between this variation and other SARS-CoV-2 variations, and as numerous SARS-CoV-2 contaminations are not recognized at all. The first victim was probably in mid-September 2020 in London or Kent, UK. As of 13 December 2020, 1,108 cases with this variation had been recognized within the UK in about 60 distinctive nearby authorities. These cases were predominantly in the southeast of Britain. The variation has to been distinguished in Ridges and Scotland. By November, around one-fourth of cases in the COVID-19 pandemic in London were being caused by the new variant, and by December, that was a third. In mid-December, it was evaluated that nearly 60 percent of cases in London included VOC-202012/01. On 16 January, the Los Angeles County Department of Open Health affirmed the variation was identified in L.A. Province, with open health authorities accepting that it is spreading in the community.

Government Rules For COVID 19 [50].

1. These rules may be called The Delhi Epidemic illness, COVID-19 Regulations, 2020
2. "Epidemic illness" in these rules means COVID-19 (Corona Virus Disease 2019)
3. Authorized Persons under this act are Secretary (Health & FW), Director General Health Services (DGHS), at State Level and District Magistrate, Chief District Medical Officer (COMO), Sub Divisional Magistrate (SOM), and District Surveillance Officer (DSO) in the districts and officers as permitted by Department of Health & Family Welfare Department, Govt. of NCT of Delhi
4. All Hospitals (Government & Private) should have infection comers for shielding, of suspected victims COVID-19 (Corona Virus Disease 2019).
5. All Hospitals (Government & Private) during the screening of such cases might record to discover the history of travel of the individual in the event that he/she has traveled to any nation or zone where COVID-19 has been detailed. In the expansion the history of coming in contact with a suspected or confirmed case of COVID-19 might be recorded.
6. No individual/ institution/ organization will utilize any print or electronic media for data with respect to COVID-19 without earlier consent of the Department of Health & Family Welfare, Govt. of NCT of Delhi. No Particular Laboratory has been permitted to take or test samples for COVID-19 within the NCT of Delhi.
7. In the event that any individual with a history of travel in the last 14days to a nation or zone from where COVID-19 has been detailed, he must contact the State/District control rooms (as per Annexure-1) so that fundamental measures in case required may be started by the Department of Health & Family Welfare, Govt. of NCT of Delhi.
8. All people with a history of travel to a nation or zone from where COVID19 has been detailed in the final 14days, but who don't have any indications as fever, trouble in breathing, should isolate themselves at home. Such people must take safety measures to avoid contact with any individual including family individuals for 14 days from the date of entry from such range.
9. Authorized people as per section 3 of these regulations are authorized beneath this act to confess an individual and confine the individual in the event that required in case he/ she incorporates a history of the visit to a zone where COVID-19 is endemic and the concerned individual is symptomatic.
10. There are adequate reasons, cause, or data to suspect or accept that any people may well be infected with COVID-19 and his proceeded presence in premises is hazardous to the open security, it might be legal for an Observation Faculty to enter such premises, after giving reasonable opportunity to the proprietor, for the reason of observation of occasions of fever or hack or respiratory trouble, enquire into or attempt the physical examination, as he/she fits, and such people might be bound to coordinate and render all conceivable help to encourage such reconnaissance, assessment, inquiry, and examination.

CONCLUSION

The COVID-19 outbreak has spread rapidly. The extension from Hubei to the rest of China took just 30 days. With many people coming home after a long vacation, China must brace for a potential disease resurgence. In India, the

covid-19 is now expanding. The COVID -19 wave was also primarily growing. Vaccines are inserted into individuals, and they yield 81 percent of the outcomes. Preventive measures for COVID 19 includes regularly wash your hand for 20 seconds with soaps, wear a mask in public places, avoid high risk areas and social distancing for two meters.

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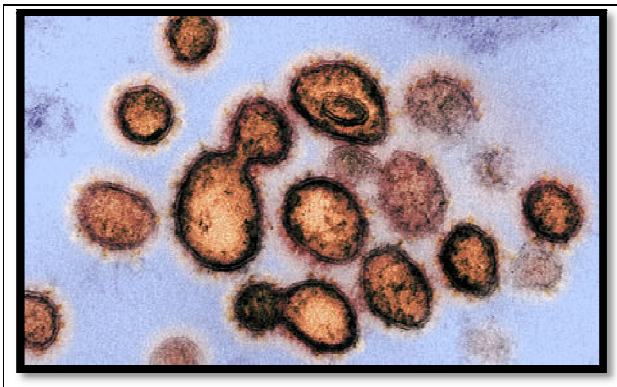

Fig.1 : COVID – 19

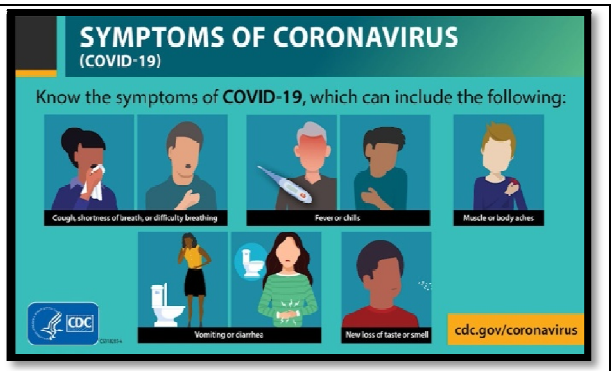

Fig.2: Symptoms of Coronavirus (COVID-19)

Viral RNA load[a]	Direct RT-PCR (3 µL swab diluent)[b]	
	95°C[c]	No heat
High (CT < 20)	30/30 (100%)	30/30 (100%)
Intermediate (CT 20 – 30)	102/103 (99%)	94/103 (91%)
Low (CT > 30)	6/17 (35%)	2/17 (12%)
Total	138/150 (92%)	126/150 (84%)

Fig. 3 : RT-PCR-BASED TEST

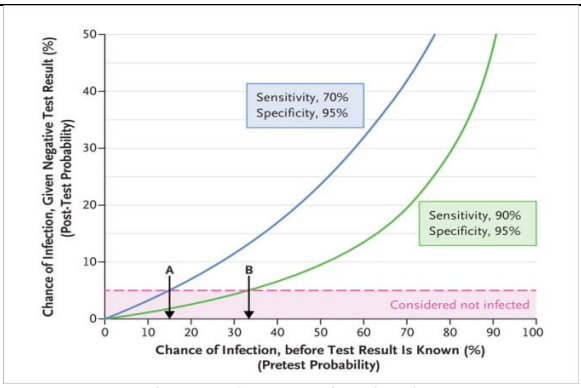

Fig.4 : Chance of Infection

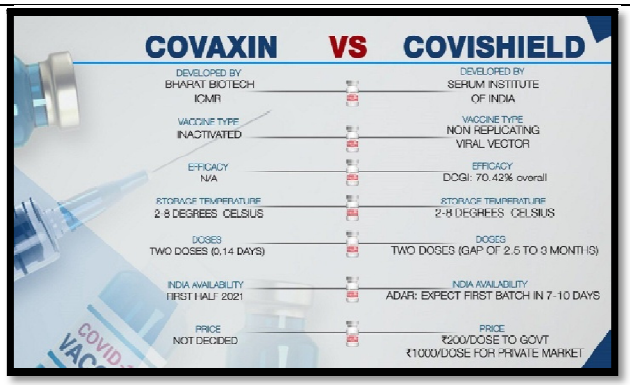

Fig.5 : Effectiveness of Covishield

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RESEARCH ARTICLE

In vitro Antifungal Activity of Salicylic Acid against *Fusarium oxysporum f. sp. Lycopersici*

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ABSTRACT

The present study is aimed to evaluate the *in vitro* antimicrobial activity of salicylic acid (SA) against *Fusarium oxysporum* f. sp. *Lycopersici* (*FOL*), a causal agent of vascular wilt disease of tomato (*Lycopersicon esculentum).* SA was made into different concentrations (0.01, 0.05, 0.1, 0.15, 0.2 %, w/v) and they were tested against the growth of *FOL* on PDA plates. The maximum *in vitro* growth inhibition of *FOL* by SA was noticed as 66.6% in both 0.05 and 0.2 % SA concentrations, suggests that SA is one of the growth inhibitors of *FOL*.

Keywords: Salicylic acid, *Fusarium oxysporum* f. sp. *Lycopersici,* Antimicrobial activity, tomato.

INTRODUCTION

Tomato (*Solanum lycopersicum* L.) is one of the widely cultivating horticulture crops in the world and second most consumed vegetable after potato and about 7500 tomato varieties are grown for various purposes with an estimated production of 180 million tonnes (FAOSTAT, 2019; Khurshid et al., 2016). India is the second largest tomato producing country in the world (19007000 tonnes in 781000 ha; FAOSTAT, 2019). It is fact that tomato is an everyday consumable food item in every house in India. Further, India is one major country in terms of export of tomatoes to various countries across the world. However, the crop is susceptible to many pests and pathogens and account for significant yield loss. Of the many plant diseases of tomato, Fusarium vascular wilt is ever devastating problem in tomato growing regions caused by soil born fungus *Fusarium oxysporum* f. sp. *Lycopersici*. The characteristic symptoms of *FOL* on tomato include leaf wilting, stunting of plant, leaf death, browning of vascular system, lack of fruit production (Snyder and Hansen, 2003). There are effective fungicides to control the disease; however their wide and uncontrolled usage associated with increased fungal resistance and environment as well as human health issues. SA, a phenolic eco-friendly component which promotes the plant growth, induce plant disease resistance against plant pathogens and act as an antifungal agent (Amborabé et al., 2002; Joyce, et al., 2001; Cao et al., 2006). It was reported that SA exhibits a significant growth inhibition against *R. solani* and *Eutypa lata* (Husien and Yousif, 2018;

Amborabé et al., 2002). da Rocha Neto et al., 2016 reported that SA solution inhibited the germination of *P. expansum* and the blue mold incidence in apples. Alamir et al., 2020, reported *in vitro* antifungal activity of Miconazole and salicylic acid with 2.8 cm and 1.5 cm inhibition zones respectively against *Trichophyton mentagrophytes.* The present study is under taken to evaluate *in vitro* antifungal effect of SA against the *FOL*.

MATERIALS AND METHODS

Culture and Chemicals

The pure culture of *FOL* strain (MTCC No. 10270) procured from MTCC, Chandigarh, India. The required chemicals for experiments were of analytical grade purchased from Himedia and SRL, India.

Subculture and microscopic observation of *FOL*

The obtained *FOL* was further sub cultured on PDA plates and newly grown culture was examined initially under simple microscope by following Lactophenol cotton blue (LPCB) staining procedure and later under a SEM (JEOL JSM-IT500). The obtained characteristics of culture like morphological features, type of spores and nature of growth were documented.

In vitro antifungal activity of SA

In vitro antifungal activity was evaluated by food poisoning technique using different concentrations of SA (0.01, 0.05, 0.1, 0.15 and 0.2 % in sterile distilled water, w/v) against control. Initially, the molten sterile potato dextrose agar (PDA) medium was poured into sterile petriplates and allowed for solidification. 100 µl of each concentration of SA solution was spread on PDA plates separately by using a sterile glass spreader. A small portion of 7 day old culture of the *FOL* was aseptically inoculated to the centre of the each petriplates and incubated at 25^0C for four days. The plate with PDA medium without SA served as control. After incubation the colony diameter was measured in centimetre (cm). Duplicates were maintained for each SA concentration and percent inhibition of mycelia growth was calculated by using the formula (Vincent, 1947).

$$\% \text{ Inhibition} = \frac{\text{mycelial growth in control} - \text{mycelial growth in treatment}}{\text{mycelial growth in control}} \times 100$$

RESULTS AND DISCUSSION

The productivity of agricultural crops are severely affected by several plant pathogens, among them, fungal pathogens occupied first place. *Fusarium oxysporum* is a fungal plant pathogen infects wide range of hosts includes tomato (Snyder and Hansen, 1940), tobacco (Rodríguez-Molina et al., 2007), sweet potato (Mousa, et al., 2018), cucurbits (Egel et al., 2007), potato (Manici, et al., 1994), banana (Pegg, et al., 2019) and legumes (Kraft et al., 1988) and account for significant yield loss upto 45 % (McGovern, 2015). In order to control plant fungal diseases, unusual application of chemical fungicides associated with several consequences including environmental pollution, degradation of agro-ecosystem and enhancement of microbial resistance (Kashyap, Xiang & Heiden, 2015). Hence, eco-friendly approaches for diseases management is highly advisable. In several studies, natural compounds including oligosaccharides, glycosides, amides, vitamins, carboxylic acids, and aromatic compounds have been claimed to be strong plant resistance inducers (Aranega-Bou et al., 2014). Priming of these compounds on plants has induced systemic resistance which subsequently gives protection from multiple plant pathogens.

Salicylic acid, a well known phytohormone identified to be a potential systemic plant resistance inducer and also has fungicidal attributes. For example, SA significantly inhibited the growth of *R. stolonifer* in peach fruits (Panahirad et al., 2012), *Botrytis cinerea* in pears (Zhang et al., 2008), *Fusarium oxysporum* in tomatoes (Mandal et al., 2009), and *P. expansum* in apples (da Rocha Neto et al., 2016). Blue mold (*Penicillium expansum*) is one of the postharvest diseases of

apples, its germination was inhibited 100% *in vitro* with SA (2.5 mM) and also controlled *in situ* when applied eradicatively (da Rocha Neto et al., 2016). The inhibitory effect of SA treatment on the growth of *Rhizopus stolonifer* was evaluated *in vitro* and *in vivo* (Panahirad *et al.,* 2012). The biological efficacy of *C. laurentii* in combination with SA against *Penicillium expansum* on apple fruit could be significantly enhanced (Yu and Zheng, 2006). However the actual fungicidal action of SA has not yet been found. In view of the above studies SA seems to be a best alternative to hazardous chemical fungicides in part of management of fungal diseases in agriculture. The present study is intended to evaluate the effect of SA on *in vitro* growth of *FOL*. Initially *FOL* culture was procured from MTCC, Chandigarh and it was sub-cultured on PDA plates and the grown white cottony mycelium was examined under light and scanning electron microscope.

The observed morphological features of *FOL* including non septate macroconidia, 3-septate macroconidia formed from monophialides on branched conidiophores and chlamydospores with a smooth or rough wall appearance formed singly or in pairs (Fig1a & 1b). Kee et al., 2020 also reported similar characteristic features for *FOL*. In order to study the antifungal activity of SA against *FOL*, five different concentrations (0.01, 0.05, 0.1, 0.15, 0.2 %, w/v) of SA were tested against *FOL* on PDA plate method. Among the SA treatments, the maximum growth inhibition of 66.6 % was observed in both 0.05 % and 0.2 % concentrations and the minimum growth inhibition of 48% was noticed in 0.01% concentration. The remaining 0.1 and 0.15 % concentrations showed 51.3 and 53.3 % of growth inhibition, respectively (Fig.2& table 1). In a similar *in vitro* study, 20 mM SA has shown maximum growth inhibition of 77.2 % against *Fusarium oxysporum* f. *sp*. *Melongenae* followed by 40 mM (61.2 %) and 80 mM (47.4 %), the minimum growth inhibition was noticed in 10 mM (29.6%) (Naziya et al., 2017). In a field study, application of SA significantly controlled stem cancker disease and stemphylium blight disease on tomato and onion respectively (Esmailzadeh et al., 2008; Bhasker et al., 2020). Pre-treatment of SA and BTH showed significant control in rice against sheath blight disease (Neerja et al., 2013).

CONCLUSION

In this *in vitro* study, it was found that SA has antifungal activity against *FOL*. The maximum growth inhibition of *FOL* was found in 0.05 and 0.2 % of SA concentrations.

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Table 1. Effect of different concentrations of SA on mycelial growth of *Fusarium oxysporum* f. sp. *Lycopersici*

SA concentrations	Zone of inhibition (cm)	% inhibition rate of mycelial growth
Control	7.5	-
0.01 %	3.9	48%
0.05 %	2.5	66.6%
0.1 %	3.65	51.3%
0.15 %	3.5	53.3%
0.2 %	2.5	66.6%

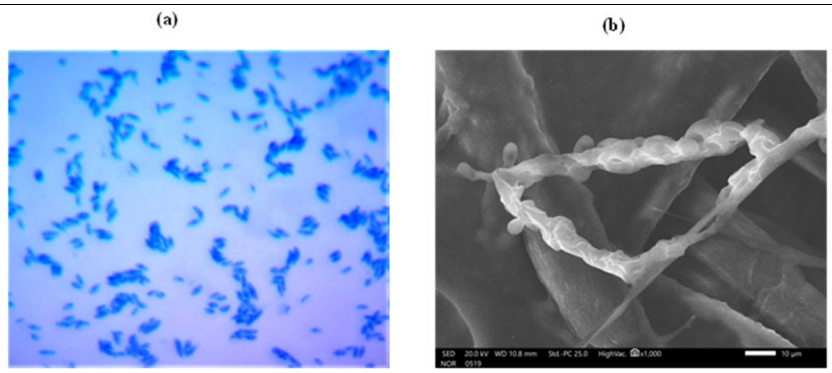

Fig1. *Fusarium oxysporum .sp.* L image under a) Light microscopy b) SEM

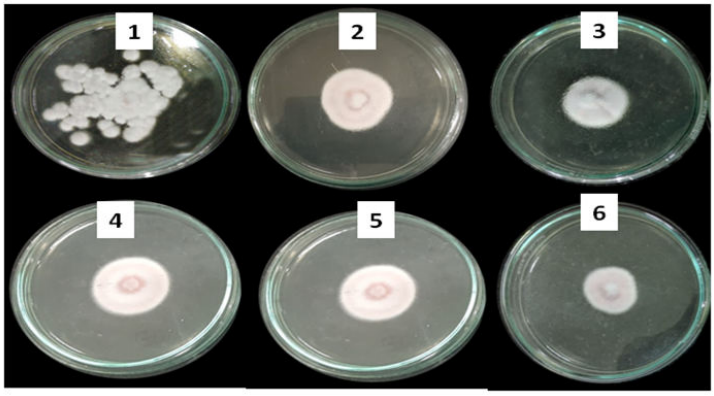

Fig 2. Effect of different concentrations of SA on mycelial growth of *Fusarium oxysporum* f. sp. *Lycopersici*, Control (1), SA 0.01 % (2), SA 0.05 % (3), SA 0.1 % (4), SA 0.15 % (5), and SA 0.2 % (6)

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RESEARCH ARTICLE

Fake Profile Identificationusing Machine Learning

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ABSTRACT

In the current age, the public activity of everybody has gotten related with the online informal communities. These locales have rolled out an extraordinary improvement in the manner we seek after our public activity. Making companions and staying in touch with them and their updates has gotten simpler. Be that as it may, with their quick development, numerous issues like phony profiles, online pantomime have additionally developed. There are no possible arrangement exist to control these issues. In this task, we concocted a system with which programmed recognition of phony profiles is conceivable and is efficient. This structure utilizes classification methods like SVM, Choice trees and arbitrary backwoods to order the profiles into phony or authentic classes. As, this is a programmed identification technique, it tends to be applied effectively by online informal organizations which has a large number of profile whose profiles can't be inspected physically. SVMs are among the awesome (many accept are without a doubt the best) "off-the- rack" administered learning calculations. Arbitrary timberland or irregular choice woodland are a gathering preparing strategy for grouping, worsen and other assignments which process by building a large number of choices plate preparing time and processing the class that is the greater amount of classes or mean expectation of the individual trees. The way that a record had a copy profile appears to have had an effect in the exactness of theexpectations. In view of the prescient outcomes from the AI models, it appears to be that current highlights and AI models used to recognize counterfeit records are not fit to distinguish authentic human records. As indicated by the 'Local area Norms Requirement Report' distributed by Facebook on Walk 2018, around 583 million phony records were brought down in quarter 1 of 2018 and upwards of 3- 4% of its dynamic records during this time were as yet phony. In this task, we propose a model that could be utilized to arrange a record as phony or certified. This model uses Backing Vector Machine as an arrangement procedure and can deal

with a huge dataset of records on the double, disposing of the need to assess each record physically. The people group of worry to us here is Phony Records and our concern can be supposed to be an arrangement or a bunching issue.

Keywords: Machine Learning, Support Vector Machine, Classification.

INTRODUCTION

States of AI is a utilization of artificial intelligence that gives the capacity to naturally take in and improves in the absence of unequivocally customized. The entire interaction of AI is clarified. If there should arise an occurrence of a typical interaction the information is offered as information and the yield would the responses or results in a summed up way. Yet, in AI the client makes the model to break down so it offers information alongside responses as info and the yield will be the enhanced arrangements. Character duplicity on large information stages (like web-based media) is an expanding issue, because of the proceeded with development and dramatic evolvement of these stages. In the particular age, the public activity of everyone has been related by online interpersonal organizations. Summing up other companions and staying in touch with everyone and their upgrades has got peaceful. The virtual informal communities affect the science, training, work, business, and so forth. Specialists has been contemplating the online interpersonal organizations to see effect it makes on persons. Web-based media is one of the prioritized way for correspondence and have become impartial for spammers and tricksters the same. Digital dangers inclusive of spamming, the posting of spontaneous information, are basic in email applications. These threats presently arise via online based media stages (SMPs), albeit in various indications. Records can be either human- created, PC produced or cyborgs. Interpersonal organization is huge band of correspondence which continues improving in the field they are given with alongside the public help. The digital dangers making people consistently figures out how to interfere through the public frameworks than to private. Since once they got in contact or drawn in with the public level framework they might actually meddle to a few records or frameworks through the public worker as an escape clause. These people are named as "interlopers". In the present online informal organizations, there have been a perfect deal of issues like phony profile, virtual pantomime, and till era, nobody even thought of an answer for these. In this undertaking, we meant to provide a system by which the processed discovery of phony profiles are possible so the public activity of persons become gotten and by making use of the programmed recognition technique we can make it eaiser for the stations to deal with the gigantic unit of profiles, which is impossible one by one.

Goal of the Topic

The personality of an online media account is depicted through different credits that are accessible in SMPs. For instance, the name, area, and profile picture, companions, adherents check, likes, shares and so on Certifiable records and phony records have Comparative ascribes and they share comparative qualities. For instance, real records have a name thus do the phony records. Highlights can be designed from SMP credits like what has been designed in past research, regardless of whether the record is a copy of another. Designing highlights that have been made to distinguish counterfeit personalities can be put in to the current corpus of certified people records.

The prescient outcomes from the prepared AI models just capitulate F1 score of 49.7%. Offered that anticipating the right response by instance wouldbe addressed as half which isn't ideal. Despite the fact that solitary three AI models were utilized in the examinations, these AI models have effectively utilized in the past to spam and phony recognition. These AI models can't identify counterfeit human records. Entropy presents a sign of which designing highlights perform well and which are most certainly not. For instance, the way that a record had a copy profile appears to have had an effect in the precision of the forecasts. Inview of the prescient outcomes from the AI models, it appears to be that current highlights and AI models used to distinguish counterfeit records are not fit to identify certifiable human records. A corpus of veritable human records is advanced with designing highlights that had recently been utilized to distinguish counterfeit records made by counterfeit clients somewhat. These highlights were

applied to different directed AI models. The AI models were prepared to utilize designed highlights without depending on social information. This made it workable for these AI models to be prepared on next to no information, contrasted with when conduct information is incorporated (SVM). The discoveries show that designed highlights that were recently used to identify counterfeit records, best case scenario, anticipated authentic records with a F1 score of 49.75%. This can be credited to the way that real clients have various attributes and practices than counterfeit clients which can't be demonstrated correspondingly. The people group of worry to us here is Phony Records and our concern can be supposed to be a characterization or a bunching issue. As, this is a programmed discovery strategy, it tends to be applied effectively by online informal communities which has a great many profiles, whose profiles can't be analyzed physically.

Proposed System

The proposed system consists of the designing highlights made during the examination were investigated to comprehend the corpus and it was noticed that most records had not many companions and devotees. Then, the information investigation took a gander at the side view depictions of the records. The investigation manifesed that all records were not real and had a profile portrayal and that some side view depictions were divided between other descriptions. A couple of side view portrayals likewise included Uniform Resource Locators. These exploratory outcomes that despite the fact that we are managing human records just, they actually show attributes familiar to bots, for example, having a Uniform Resource Locator in their side view portrayal. It farther confirmed that exploration recently directed to identify counterfeit botprofiles on SMPs could be relevant to distinguish counterfeit person characters apparatuses.

Existing System

The method used to detect fake person profiles on SMPs is pretty less to reach its accuracy. Same harmful intent with false profiles circulating false rumors with Spam behavior that are found in emails and SMS. Other than spam, counterfeit personalities are likewise there on SMP as bots. Past research towards comprehension and distinguishing spam conduct introduced strategies like sifting, rules, and AI to identify counterfeit characters. Only when the other threat is found then Filtering is mostly reactive and verified and the sender will be added to a blacklist. Comparable techniques for managing junk have been put forward on Twitter to boycott realized noxious Uniform Resource Locator information and to isolate known bots. When spammers implement the proposed methods using dynamically adaptive and automated techniques, It becomes very hard. This is even more particular for SMPs. People effectively adjust to evade location and, on account of boycotting, they essentially make another record and phony way of life when the current distinguished record is boycotted. Some of the disadvantages of our existing system is that the use of machine learning algorithm is limited. Along these lines it requires some comprehension of the current issue to apply the correct calculation.

Literature Survey

Personality trickiness on huge information stage is a huge topic, owing to the fact of the proceedings with expansion and increased progress of these platforms. In the current age, the public activity of everyone has gotten related with the online interpersonal organizations. Staying in touch with new people and adding new companions, their updates has gotten simpler. The online interpersonal organizations affect the science, schooling, things getting sorted out, work, business, and so forth .Scientists have been contemplating these virtual informal communities to see the effects they made on individuals. Most relevant to our paper, however, is the facebook immune system in which the Immune System performs real-time checks and classifications on each peruse and compose activity. As of March 2011, this is 25B checks per day, arriving at 650K each second at top. The framework additionally produces signals for use as input in classifiers and different parts. This paper diagrams the plan of the Facebook Immune System, the difficulties we have confronted and survived, and the difficulties we keep on confronting. There is more work to be finished improving components to stretch guard control and abbreviate aggressor control. An engaging future bearing lies progressively preparing of AI models that better influence both client input and peculiarity identification. Another

paper relevant to our work was detection of spam bots in which the study of suspicious activities of bots was studied. To differentiate spam bots from normal one was their goal to apply machine learning methods. A few well known classification calculations are contemplated and assessed. The outcomes show that the Bayesian classifier has a superior in general presentation.

System Architecture

Social media platform: In the architecture of our model we have used social media platform to collect data set from different social accounts. The data set includes those features or attributes which common to both bots as well as human.

Cleaning data: Cleaning data or data cleansing is the process where data is altered or modified in a given storage resource to make sure that it is accurate and correct.

Feature extraction: Attribute extraction or feature engineering starts from fundamental permutations of estimated records or details and gives controlled highlights expected to be enlightening and non-repeating, and at times urging good human translations promising the assure learning and contemplating steps or ideas.

Training data: It is used to train the algorithm which is used in the project. The better the training data the better the algorithm or classifier works.

Testing data: Some test data is used to affirm the normal outcome, for example, some test information is utilized to check the product conduct to invalid information, At the point when test information is entered the normal outcome should come.

Machine learning model: ML is a class of calculations that permits programming application to turn out to be more correct in giving results without doing any kind of changes or modifications. The primary reason of AI is to collect calculations that can get data details and utilize truthful examination to foresee a yield refreshing other yields as new thing opens up.

System implementation

Modules

Pre-processing: It refers to the modification applied to the data before feeding it to the algorithm. Information Preprocessing is a strategy that is utilized to change over the crude information into a spotless informational index. All in all, at whatever point the information is assembled from various sources it is gathered in crude arrangement which is not attainable for the exam. For giving better results from the processed model in Machine Learning projects the organization of the information must be in an appropriate way. Some predetermined Machine Learning model necessities data in a predefined design, for instance, Random Forest calculation doesn't uphold invalid qualities, hence to execute arbitrary timberland calculation invalid qualities mustbe overseen from the first crude dataset. More than one Machine Learning and Deep Learning calculations are executed in one informational index is the another perspective informational index to be arranged and best out of them is picked.

Feature extraction: Feature decision is furthermore called as factor decision or property adoption. It is customized variety of characteristics in our input (like segments in plain input) that, for all the part material to the farsighted showing issue you are doing work on. Feature assurance is the route toward picking a subset of critical points for use in model turn of events. Attribute decision isn't exactly equivalent to dimensionality decline. The two process attempt to finish the amount of attributes in the data, anyway a proportions decline methodology do as such by making new blends of characteristics, however feature decision techniques consolidate and bar credits are in the data

without developing them. Occasions of proportion decline strategies join.

Classification: In classification technique LOGISTIC REGRESSION approach is used as it is an amazing factual method of displaying a binomial result with at least one logical factors. It estimates the connection between the downright needy variable and at least one free factors by assessing probabilities utilizing a calculated capacity. Also, SUPPORT VECTOR MACHINE (SVM) is used in implementing the project. SVM is a binary classification algorithm. We can undoubtedly put the aim of the SVM calculation is to make the best line or option limit that can isolate n-dimensional information points in the right classification later on. space into classes. This best choice limit is referred as a hyper plane.

Ordinary least squares regression

Regression: In the business that you know insights, you have known about direct recurrence previously. Least squares are a technique for performing direct relapse. There are numerous potential techniques to do this, and normal less squares procedure goes like this. We can draw line, and for every one of the information focuses, and the vertical distance between the point and the line to be measured, and add them together and the properly fitted line would be the one where this amount of spaces is just about as little as could be expected. Linear the sort of example we are utilizing to suit the information, whilst fewer squares are known to the sort of blunder metric we are limiting beyond.

Logistic Regression: LR is an incredible accurate method of describing at least one logical factors which has a binomial result. It estimates the connection within the clear cut ward variable by assessing probabilities utilizing a strategic capacity, and at least one free factors which is the total calculated logistic distribution.

As a rule, relapses can be utilized in true applications, for example,

- Credit Scoring
- Measuring the achievement paces of showcasing efforts

Support vector machine

Support Vector Machine is dual (binary) classification algorithm. There is a group of set of two kind of dots (points) in N dimensional place, Support Vector Machine generates a (N—1) structural hyper plane to split those dots into two divisions. Let us assume that we have two kinds of points or dots in a paper which are linearly removable. So Support Vector Machine will locate a straight line which splits those points into two types and locates them as far as possible from all the other dots.

The screenshots of graphical representation is provided in fig 2

Generating confusion matrix and accuracy finding: The accuracy is provided in fig 3

RESULT

The prototype introduced in the undertaking exhibits that SVM is a rich as well as strong strategy for twofold grouping in an enormous record. Notwithstanding the straightness of the choice limit, Support Vector Machine can group among phony and certified accounts with a healthylevel of precision of less than ninety percent. This strategy can be stretched out on any stage that requires parallel orders which are sent on open accounts for different requirements. This task utilizes just freely accessible data which makes it helpful for associations that need to maintain a strategic distance from any penetrate of protection, yet associations can likewise utilize private information accessible to them to additionally expand the capacities of the intended prototype.

Future Work: Though we have restricted information to prepare the allocation, our methodology is confronting a high change issue which can be seen in the expectation to learn and adapt as follows High fluctuation issues can generally be relieved by expanding dataset's height which ought not be of much worry to Social Network Organizations which as of now have genuinely huge dataset.

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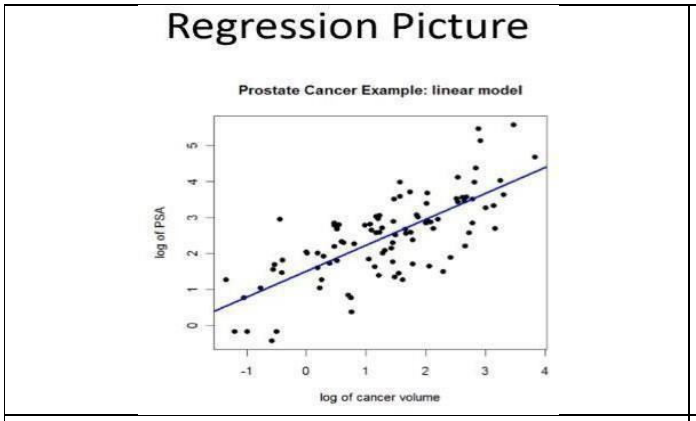


Fig 1

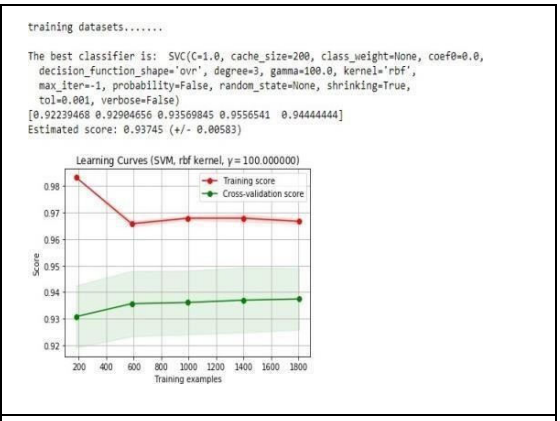
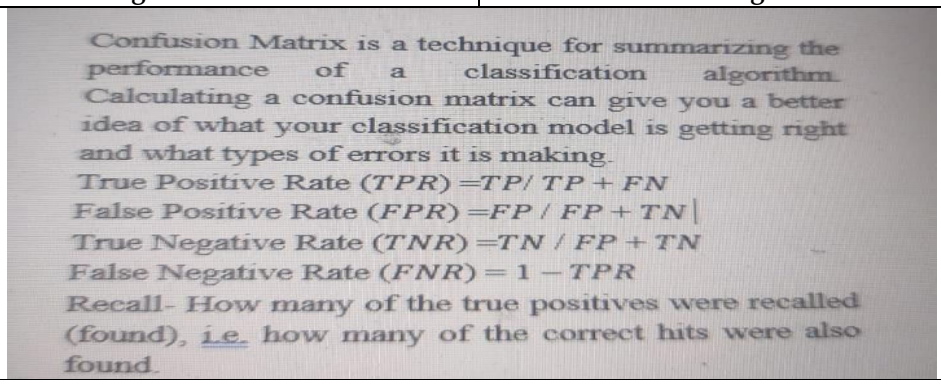


Fig 2



The accuracy is provided in fig 3

```
In [66]: print ('Classification Accuracy on Test dataset: ' ,accuracy_score(y_test, y_pred))

Classification Accuracy on Test dataset:  0.900709219858156
```

```
Confusion matrix, without normalization
[[265   3]
 [ 53 243]]
```

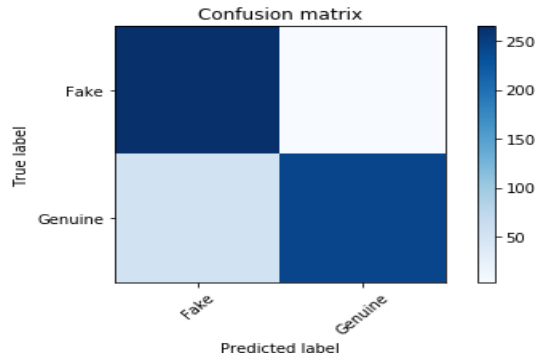


Fig 4

```
Normalized confusion matrix
[[0.98880597 0.01119403]
 [0.17905405 0.82094595]]
```

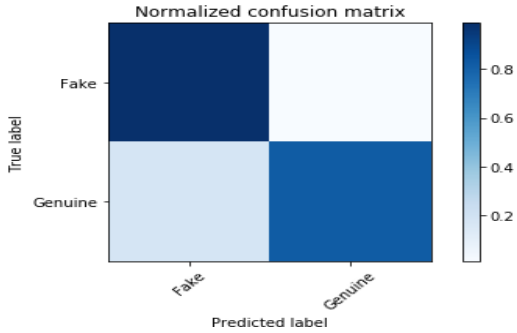


Fig 5

The confusion matrix for the above graph is fig

	precision	recall	f1-score	support
Fake	0.83	0.99	0.90	268
Genuine	0.99	0.82	0.90	296
avg / total	0.91	0.90	0.90	564

Fig 6

```
False Positive rate:  [0.         0.01119403 1.        ]
True Positive rate:  [0.         0.82094595 1.        ]
```

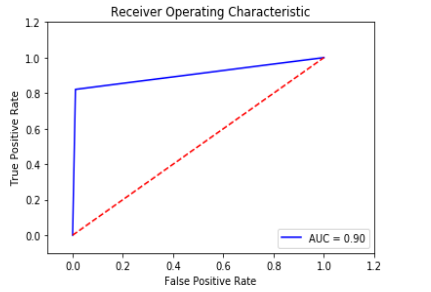
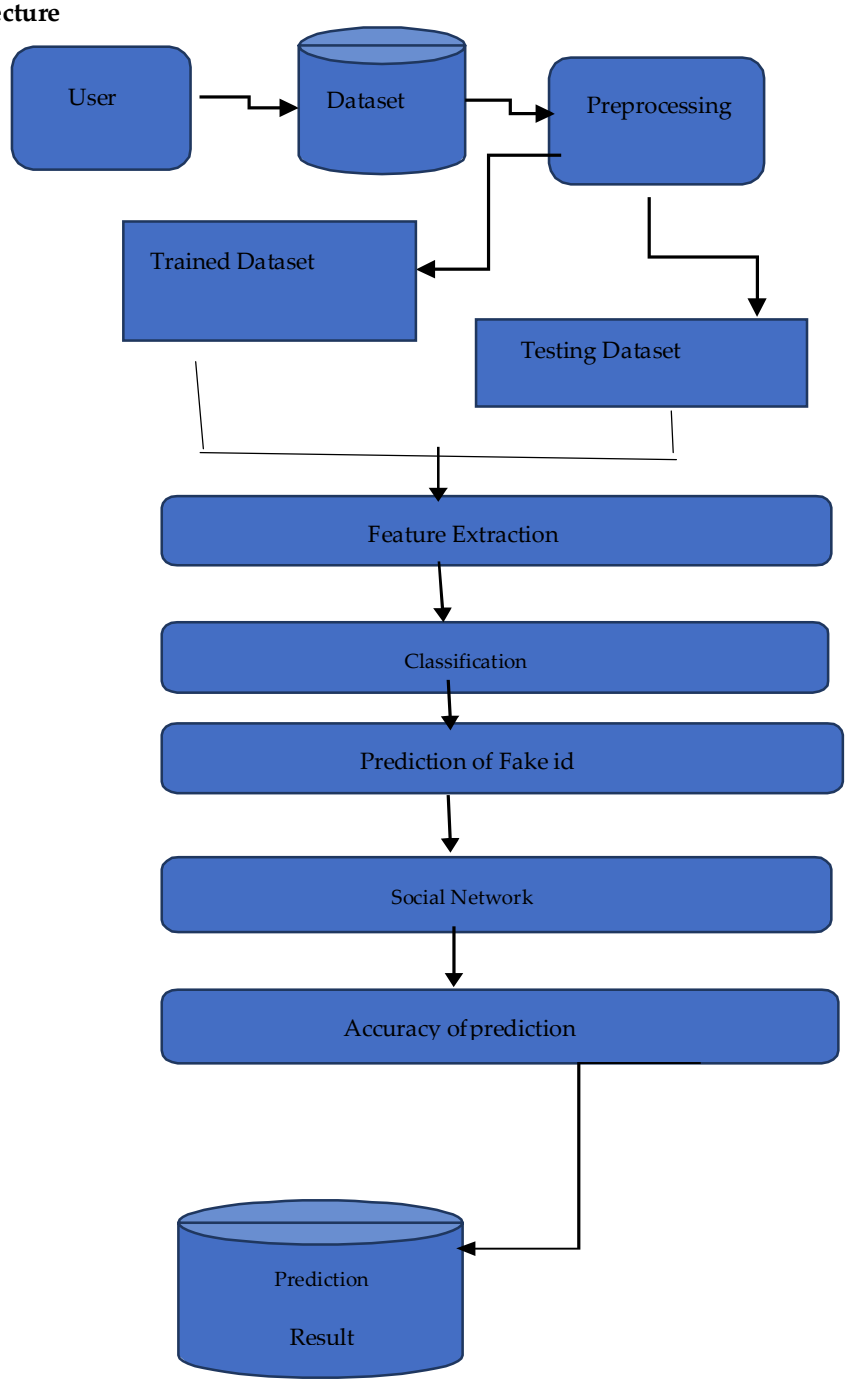


Fig 7

System Architecture



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RESEARCH ARTICLE

A Recent Trends in : Communicable Diseases

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ABSTRACT

An epidemic is the quick spread of transmittable disease of huge number of people in given inhabitans within short time period. According to current concepts, an epidemic is defined as the incident in community or area of cases of an illness or other health-related events clearly in excess of normal expectancy. The community or area, and the time period in which he cases takes place are specified recisely. This condition which administers the outbreak of epidemics also include infected food supplies such as infected drinking water and the movement of inhabitants of certain animals, such as rats or mosquitoes, which can be disease vectors. Certain epidemics occur at certain seasons. For example, whooping-cough occurs in spring, wherever measles produces two epidemics, one in winter & one in March. Influenza, the cold, and other infections of the respiratory tract(upper), such as sore throat, occur mainly in the winter.Eg.an outbreak of food poison. The outbreak curve rise and falls quickly, with no secondary waves. If the outbreak continues over more than one incubation of period, there are moreover a continuous or multiple exposures to a common source or a propagated spread. Sometimes the exposure from the same source may be long-lasting – nonstop, frequent or alternating – not necessarily at the same time or place. ZIKV be first secluded from a febrile sentinel monkey in Uganda in 1947.Serological data propose that ZIKV was spread widely throughout Africa as well as consequently within Asia in spite of the lack of describing morbidity.

Keywords: epidemics, zika virus, infection, outbreaks, vaccine.

INTRODUCTION[1, 2]

- An epidemic is the quick spread of transmittable disease of huge number of people in given inhabitans within short time period
- According to current concepts, an epidemic is defined as the incident in community or area of cases of an illness or other health-related events clearly in excess of normal expectancy.
- The community or area, and the time period in which he cases takes place are specified recisely.
- An epidemic disease is not necessary to be transmittable, and he term as been applied to Nile fever and the obesity epidemic(e.g. by he World Health organization), among others.
- Thus, epidemics refer to the remarkable" occurrence in community or area of disease, specific health-related behavior (e.g., smoking), or other health connected actions clearly in excess of "estimated occurrence".
- The total amount of cases differs according to the disease causing agent, and the range and type of earlier and present exposure to the agent.

EPIDEMICS OF TRANSMITTABLE DISEASE ARE COMMONLY CAUSED BY SEVERAL FACTORS INCLUDING[3-4]

Change in the ecology of the multitude population (e.g: increased stress or increase in the density of a vector species)

- Gene change in the pathogen reservoir or the introduction of an emergence pathogen to a host population.
- Usually, an epidemic may occur when host immunity to either an established pathogen or newly emerging novel pathogen is unexpectedly reduced below that found in the widespread equilibrium and the transmission threshold is exceeded.
- This condition which administers the outbreak of epidemics also include infected food supplies such as infected drinking water and the movement of inhabitants of certain animals, such as rats or mosquitoes, which can be disease vectors.
- Certain epidemics occur at certain seasons. For example, whooping-cough occurs in spring, wherever measles produces two epidemics, one in winter & one in March. Influenza, the cold, and other infections of the respiratory tract(upper), such as sore throat, occur mainly in the winter.
- Disease epidemics may usually be caused by an infection, pass-through person-to-person contact, animal-to-person contact, or from the environment or other media.
- Epidemics may also occur following experiments with chemicals or to a radioactive substance. Epidemics may be the consequence of disasters of other kinds, such as tropical storms, floods, earthquakes, droughts, etc.
- Occasionally the cause of an epidemic is unknown, even after thorough investigation.

Types of epidemic diseases

Common-Source Epidemics[5]

- Common-source epidemics are regular, but not always, due to exposure to an transmittable agent.
- They can outcome from defect of the surroundings by industrial chemicals or pollutant.
- E.g. Bhopal gas tragedy in India and Minamata virus in Japan resultant from utilization of fish containing a high concentration of methyl mercury.

Single exposure or "point-source" epidemics [5]

- These are identified as "point-source" epidemics.
- The contact to the disease mediator is brief and basically instantaneous, the resultant cases all develop within one incubation period of the disease. Eg. an outbreak of food poison
- The main quality of a "point-source" outbreak are:
- The outbreak curve rise and falls quickly, with no secondary waves
- The outbreak tend to be explosive, there is a cluster of cases within a fine period of time, and
- More significantly, all the cases increase within one incubation period of the illness.

Continuous or multiple exposure epidemics[5]

- If the outbreak continues over more than one incubation of period, there are moreover continuous or multiple exposures to a common source or a propagated spread.
- Sometimes the exposure from the same source may be long-lasting – nonstop, frequent or alternating – not necessarily at the same time or place.
- For example, a prostitute may be a regular source in a gonorrhea outbreak, but since she will communicate a disease to her clients over a time period there may be no volatile rise in the number of cases. A well of stained water, or a nationwide circulated brand of vaccine (eg: polio vaccine), or food, could result in related outbreaks.
- In these instances, the resulting outbreak tends to be more extensive or irregular.
- The outbreak of respiratory illness, the Legionnaire's disease, in the summer of 1976 in Philadelphia (USA) was a regular-source, continuous or repeated exposure epidemics.
- This outbreak, as in other outbreaks of this type, continuous afar the array of one incubation period. There was no evidence of who had contact with ill persons. secondary cases among persons

Propagated Epidemics [6]

- A propagated outbreak is most frequently infectious source and results from person-to-person transmission of an infectious agent.
- The outbreak usually shows a regular rise and tails off over a much longer time period.
- Transmission continues until the number of susceptibles is minimal or susceptible individuals are no longer exposed to stained persons or intermediary vectors.
- The speed of spread depends upon herd immune, opportunity for contact and inferior attack rate.
- Propagated epidemics are more likely to occur where a large number of susceptible are aggregated, or where there is a regular supply of new susceptible individuals lowering herd immunity.

Mixed Epidemics[7]

- Some epidemics have character of both general-source epidemics and propagated epidemics.
- The pattern of a general-source epidemic followed by secondary person-to-person spread is not exceptional.
- These are mixed epidemics.

MAJOR EPIDEMIC DISEASES (2015-2016)

2015-2016

HISTORY OF ZIKA VIRUS[8-12]

ZIKV be first secluded from a febrile sentinel monkey in Uganda in 1947.Serological data propose that ZIKV was spread widely throughout Africa as well as consequently within Asia in spite of the lack of describing morbidity. The first ZIKV epidemic to gather global attention occurs on Yap Island within the Western Pacific Ocean in 2007. Forty-nine confirmed human cases were reported. More than half of the population of Yap were thought to have been infected, with many experiencing rash, fever, and arthralgia. ZIKV activity was after that notice in the islands of French Polynesia in 2013, with an improved amount of infections. Some of the exclusive proven features of ZIKV (for example, Guillain–Barre condition, hereditary malformations and the existence of the virus in semen) were recognized during this outbreak or later on in performance studies.

ZIKV was introduced in Brazil in late 2013 or early 2014, extend quickly within the northeast part of the country, and was frequently introduced into regions of the Americas. A large number of infections and associations to congenital neuro developmental defects identified this epidemic as a global public health emergency. ZIKV movement in the Americas pointed to the early mechanism of2016, followed by a noticeable decrease in reported cases in 2017, which is probably attributable to the effect of herd immunity. Sero-

prevalence studies suggest that 63% of the population of Salvador, Brazil were infected during this epidemic. By 2017, more than 220,000 established and 580,000 assumed cases report in 52 countries or territories in America (PAO Zika Cumulative Cases; 4 January 2018).

VIROLOGY[13-16]

Zika virus is a mosquito-borne flavivirus, positive(S); Flaviviridae (Family) single-strand element (group IV) have 10794 bases with two non-coding regions (5′NCR-3′NCR-ORF-5′-C-PRM-E-NS1-NS2A-NS2B-NS3-NS4A NS4B-NS5-3′). The 3' NCR forms a disk arrangement and the 5' NCR allow translation via a methylated nucleotide cap or a genome-linked protein. The complete genome is translated in a polyprotein, which is process co-and position translationally by host and viral proteases, the replication process is less similar to another known flavi virus. The virion attaches to the host cell membrane receptors via the wrap protein which bring virion endocytosis, then virus wrapper fuse with the endosomal casing and the ssRNA genome of the virus is at large into the cytoplasm of the host cell, they interpret into polyproteins, non-structural proteins. Replication occurs in cytoplasmic viral factories in the dsRNA genome. New virions are transported to the Golgi apparatus and then excreted into the intracellular liberty where the new virions can transmit a disease to new host cells

BLOOD TRANSFUSION [18-19]

As of April 2016, two cases of Zika diffusion during blood transfusions have been reported worldwide, equally since Brazil, after which the Food and Drug Administration (FDA) recommended screening blood donors and deferring high-risk donors for 4 weeks. A probable possibility had been assumed based on a blood-donor program studyduring the French Polynesian Zika outbreak, in which 2.8% of donors fromNov 2013 and Feb 2014 experienced positive for Zika RNA and were all asymptomatic at the time of blood donation. Eleven of the positive donors report symptoms of Zika fever gone the donation, but only three of 34 samples grew in culture

PATHOGENESIS [20]

Zika virus replicates in the mosquito's standard burn up epithelial cells after that its salivary gland cells. Later than 5–10days, the virus can be established in the mosquito's spit. If the mosquito's spit is inoculated into human skin, the virus can transmit a disease to epidermal keratinocytes, skin fibroblasts in the skin, and the Langerhans cells.

SYMPTOMS AND CARE

- Passing away is occasional, major symptom typically fever, Headache, joint pain, Rash, conjunctivitis, rarely nervous system disarray occur which can cause temporary paralysis, calcium deposit in the brain.
- In the case of microcephaly, symptoms are the small head, abnormalities in the brain
- The function can cause death in the foetus [29,39-41].
- For prevention avoid mosquito bite off by using suitable insect repellents, if men frequent home from unnatural countries use condoms if their colleague is pregnant or might become pregnant.
- CDC advised pregnant women to travel in infected territories or countries, who traveling in infected areas should consult with physicians [28,34,42].

DIAGNOSIS[21-29]

- Zika virus diagnosis by Zika Virus real-time Polymer Chain Reaction(PCR) and MAC-ELISA (which detect viral Zika virus)[21].
- Zika virus antibody (IgM) in serum, antibodies find out after 3-4 days after infection but symptoms and tests are closely related to dengue and chikungunya, yellow fever, West Nile viruses [22].
- ZIKV infection was detected using the anti4G2 MAb by flow cytometry [15].

- There are some cross-react with tests for dengue viruses. NS-5 gene (3'coding region) is used for speedy discovery of flaviviruses which show less amino acid identity. cDNA from mosquito used in dot-blot membrane digoxigenin diagnosis method. Available primers and probes have been designed on the basis of ZIKV genome sequences [23-26].
- No single detection test is present for a confirmed diagnosis, sometimes a neurological exam finds out loss of sensation. Electro-diagnostic checking of the nerves, and spinal fluid Investigation. Nerve conduction velocity can be determined disorder.
- Yellow fever Vaccine(Yfvax), Zastavax (Zoster vaccine), Pneumovax (Pneumococcal vaccine), Gardasil (Vaccines for cervical cancer) is used for first-line treatment[27-29]

MICROCEPHALY[30-36]

- In pregnant women, first-trimester Transplacental infection of the NPCs in developing foetus. Zika virus infects human fetal brain cells.
- Microcephaly is he outcome of fetal brain disturbance progression, in which, after fairly ordinary brain raise in the trimester, the collapse of the fetal skull follows he destruction foetal brain issue.
- The elevated rates of microcephaly between infants born to mothers with established precursor severe ZIKV infection, provide strong roof associated with microcephaly of maternal Zikairus infection.

VACCINES &TREATMENT[37,29,43]

- In ZIKV disease, persons should have sufficient water drinking, plenty of rest, and care for pain and fever with liquid solutions. If the symptoms aggravate, they should look for counselling and therapeutic consideration.
- There are no exact medications or vaccine accessible to care for or stop ZIKV infections till now; only medications for the indicative release can be careful such as paracetamol to relieve pain and fever associated with this infection.
- Non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided and individuals should seek medical advice before taking additional medication if they are previously taking medicines for another medical condition.
- Homeopathy is a valuable healing option in ZIKV infection as it proved to be successful in Japanese encephalitis virus which is integrated into the same genus like Zika virus.
- Eupatorium is a naturally occurring pharmaceutical homeopathic complex efficient aligned with the symptoms of ZIKV disease, so it can be utilized as prophylactic treatment against ZIKV infection.
- Eupatorium perfoliatum, Rhustox, and Atropa belladonna the homeopathic prescription that may be utilized for ZIKV illness. These medicinal agents are effective aligned with the symptoms of ZIKV infection,
- During epidemics, homeopathic pharmaceuticals are more effective in reduction of mortality and morbidity as compared to the conventional system of medicines. One of the utmost momentous features of the ayurvedic structures is that they are usual substances and free from side effects and there is no technical evidence of danger for human use. It is a primordial medical science that contains herbal medicines of natural origin with a minimum side effect.
- *Tinospora cordifoliaisa* herb and utilize for years as a possible immune modulator and effective natural medicine for a viral illness of any nature. It boosts up the immune system and makes the body resistant enough to fight against infections. These herbs potentiate the phagocytic abilities of macrophages. Intestinal sickness, urinary tract infections, dengue, and swine infection are effectively treated by the astringent uniqueness of these ayurvedic plants so their capacity also is efficient for the Zika virus.
- Besides homeopathic and Ayurveda medicines, engineering approaches were also practical to build up peptide therapeutics and hold the (Way of a brain-penetrating peptide to treat neuro tropic viral infections. Therapeutic treatment protected against mortality and evidently lessened symptoms, neuro inflammation, and viral loads, furthermore mitigated microgliosis, neurodegeneration, and brain damage.

- However, ZIKV treatments and vaccines are in development. In 2016, WHO enlist all publicly affirmed commercial, government, and academic led projects focused on ZIKV interventions, together with vaccines. The list encompasses numerous approaches, comprising vaccines via purified inactivated virus, Virus-like particles, protein subunits, DNA and live recombinant attenuated viruses. Since April 2019, no vaccines have been allowed for medical usage, though extreme was in the medical stage of development.

STEPS TAKEN[38]

Enhanced Surveillance

Community based Surveillance

- Integrated Disease Surveillance Programme (IDSP) through its community and hospital-based data gathering mechanism would track clustering of acute febrile illness and seek primary case, if any, among (those who travelled to area with current broadcast in the 2 weeks preceding the onset of illness.
- IDSP would also counsel its State and District level unit to look for a cluster of cases of microcephaly among newborns and coverage of Gillian Barre Syndrome.
- The affectionate and Child Health partition (under NHM) would also give an opinion
- It's a field unit to look for a cluster of cases of microcephaly along with new born.

International Airports

- All the worldwide airport/port will demonstrate billboards/ signage providing information to travellers on Zika virus disease and reporting to (institution authorities if they are frequent from affected countries and) and suffering from febrile illness.
- The Airport Health Organization would have quarantine/isolation facility in identified Airports.
- Directorate broad of Civil Aviation, Ministry of Civil Aviation will be asked to tutor all global airlines to follow the suggested aircraft disinfections guidelines.

Rapid Response Teams

- Response Teams would be activated at globally surveillance units. Each team would comprise an epidemiologist/public health authority, microbiologist and a medical/paediatric Rapid professional and other experts (entomologist) to travel at short notice to inspect the suspected outbreak.
- National Centre for Disease Control, Delhi would be the nodal organization for analysis of epidemic in any part of the country.

Laboratory Diagnosis

- NCDC, Delhi, and National Institute of Virology (NIV), Pune, have the capacity to give laboratory opinion of Zika virus disease in the sensitive febrile stage.
- These two institutions would be the peak laboratories to support the outbreak inquiry and for verification of laboratory diagnosis. Tenextra laboratories would be strengthened by ICMR to expand the scope of laboratory diagnosis.

RT-PCR test would remain the standard test. As of now, there is no commercially available test for Zika virus disease. Serological tests are not recommended.

Risk Communication

- The States/ UT Administrations would create increased awareness among clinicians including obstetricians, pediatricians, and neurologists about Zika virus disease and its probable linkage with undesired pregnancy out comes. There should be improved observation to take note of travel records to the affected countries in the prior two weeks.
- The public needs to be free from worry that there is no cause for unnecessary distress. The Central/ State Government shall take all compulsory steps to address the test of this illness working closely with technical institutions, professionals, and global health partners.

Vector Control

- There would be enhanced integrated vector management. The measures under taken for organizing dengue/hemorrhagic fever will be further augmented. The guidelines for the integrated vector control will stress on vector supervise on (both for mature and larva), vector management through environmental modification/manipulation personal protection, biological and chemical control at household, community, and institutional levels. Details area Annexure-I.
- States where dengue broadcast is going on at present due to conducive weather situation (Kerala, Tamil Nadu, etc) should ensure extra vigil.

Travel Advisory

- Dispensable travel to the affected countries to be delayed/cancelled
- Pregnant women or women who are trying to become loaded should defer/ cancel their travel to the affected areas.
- All travellers to the precious countries/ should firmly follow entity defensive measures, particularly during the day time, to avoid mosquito bites (use of mosquito repellants, covers most of the body parts).
- Persons with co-morbid conditions (diabetes, hypertension, chronic respiratory infection, resistant disorders, etc) be supposed to seek advice from the bordering health facility, prior to travel to aprecious country
- Travellers having fever is within two weeks of arrival from an the affected areas should report to the near health facility.Pregnant women who have travelled to areas with the zikavirus the spread should state about their travel during ante-natal visits in order to be assessed and monitored appropriately.

Non-Governmental Organizations

- Ministry of Health/ State Health departments should work relatively with non-Governmental Organizations such as country/State
- Medical Associations, Professional bodies, etc to sensitize clinicians both in government and private sector about Zika virus diseases

Co-ordination with International Agencies

- National Centre or Disease control, Delhi central position for International Health regulations (IHR), would seek/ share information with the HR central position of the pretentious countries and be in even touch with World Health Organization or an update on the developing epidemic.

Research

- Indian council of Medical Research should recognize the research priorities and take appropriate action.

Monitoring

- The condition should be monitored by the combined monitoring group under Director - General of Health services on regular basis. The guidelines will be efficient from time to time as the rising condition demands.

CONCLUSION

The epidemic of ZIKV and its experimental consequences resulted in a speedy research reply, which has to begin to give answers as to why this virus transitioned from obscurity to notoriety. The scientific community is now answering questions associated with viral evolution, structure and function, virulence, tropism, and immune response, which begin to give details on how ZIKV causes congenital disease. Unanswered questions remain with regard to transmission dynamics, viral persistence, cross-immunity with associated viruses, as

well as the neuro-developmental sequelae of congenital infection. Zika virus has been gone and vaccines have been distributed and injected hopefully before a new epidemic. The lessons we have learned from ZIKV may be relevant to other viruses that cause future unexpected clinical syndromes.

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Table 1.IMPORTANT OUTBREAKS [17]

Date	Transmitted Countries	Major Report
22 Feb 2014	Chile	New virus outbreak;40 Suspected cases
25 march 2015	Chile, Brazil	18 cases of unknown illness, reported flushing, pruritus, fever and pain in body
26 march 2015	Chile, Brazil	7 suspects were positive by RT-PCR for ZIKV (369-bp fragment)
15 may 2015	Chile, Brazil	16 cases in Brazil: 8 cases in Bahia State, 8 cases in Rio Grande do Norte State.
30 may 2015	Chile, Brazil	health authorities of the State of Rio de Janeiro have reported the first case(conformation of zika virus)
11 June 201528 Oct 2015	Chile, Brazil	Above 100 cases are conformed and suspected
28 October 2015	Chile, Brazil Colombia	Cases reported in 5 regions in Colombia (239 cases)
8 November 2015	Guatemala Chile, Brazil Colombia	First case confirmed in Zacapa, Guatemala
18 November 2015	Colombia, Guatemala Chile, Brazil Colombia	reports 393 cases
27 November 2015	Colombia, Guatemala Chile, Brazil Colombia, Mexico	First death reported in Brazil

03 December 2015	Colombia, Guatemala Chile, Brazil Colombia, Mexico, panama	first 3 confirmed cases in Panama, Ustupu island in GunaYala
11 January 2016	Chile, Brazil, Colombia, Suriname, El Salvador, Mexico, Panama, Venezuela, Honduras, French Guiana, Martinique, Puerto Rico	3,836 cases confirmed in El Salvador
26 January 2016	With above Bolivia, Saint Martin, Haiti, Barbados, U.S. Virgin Islands, Dominican Republic	6 imported cases in Australia reported in 2015; Recent traveler to South America is confirmed case in Virginia, United States
13 February 2016	Withabove Nicaragua, Jamaica, Curacao, Costa Rica, United States	In Colombia: Cases of the virus total 31,555, among them 5,013 pregnant women.
March 2014, 2016	With above, France, New Zealand, Canada	cases in New Zealand has risen to 61 after reporting 14 new confirmed cases this week; More than 42,700 cases of Zika, including 7653 pregnant women were registered in Colombia, nearly 5,700 new cases in a week
March 14, 2016	With above New Caledonia, Sint Maarten, Laos, Philippines, Italy*, Cuba, Dominica	Colombia reports 55724 Zika cases. Spain has reported five new imported cases in the past week, bringing the country's tally to 43.
July, 2016	With above Bangladesh, Vietnam, Saint Lucia, Belize, Papua New Guinea, Portugal, Republic of auru, Grenada, Peru, Saint Barthélemy, Germany	Germany has confirmed its first case of sexually transmitted Zika virus

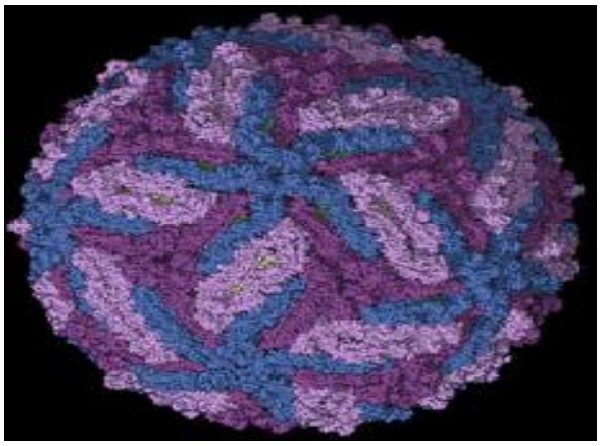

Fig.1.Zika virus

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RESEARCH ARTICLE

An Impact of Brand Positioning On Consumer Learning and Consumer Loyalty

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ABSTRACT

This study is descriptive and explanatory research in order to study on Impact of brand positioning on consumer learning and brand loyalty. For research both primary and secondary data is collected. I have also explored the demographic characteristics of respondents and then effective degree of factors influencing brand positioning, customer loyalty and consumer learning is measured. A convenience sample of approximate 201 respondents is taken for ascertaining and giving ranking to the factors influencing brand positioning, consumer learning and consumer loyalty.

Keywords: Brand Positioning, Customer Loyalty, Consumer learning.

INTRODUCTION

Impact of brand positioning on consumer learning and brand loyalty with the increase inincome levels, easy availability of finance, increase in consumer awareness, and introductionof new models, the demand for consumer durable has increased significantly. This in turn is leading to a strong competition among the different consumer durable brandsavailable in the nation as well as the price gap between the same consumer goods of different companies are narrowing down. Recently, the rising of consumer consciousness has made consumers choose to purchase their familiar and favourable brand. Complete projects onImpact of Brand Positioning on Consumer Learning and Brand Loyalty research isconducted to see an impact of brand positioning strategies on consumer's perception.The research basically revolves around 3 strategies of positioning that is beneficialpositioning, surrogate

positioning (Psychological) , Competitive positioning. As the study isconducted to examine the impact of brand positioning and its strategies on consumerperception in this research, the study revolves around 3 brand positioning strategies, that isbeneficial positioning, surrogate positioning, competitive positioning and what is its impacton consumers ' perception of whether it is positive or negative and what makes consumersbuy the product more frequently.

The basic identification and correspondence of the positioning of the product is based on thedistinction, rectifiable quality, and benefit of the brand over others. Copycat / imitatorproduct positioning works only if the company offers its products to the other rival at asignificant discount. Having a brand on a point that it should be at is very important to makesure that the branding is made so well as if it were incredibly viewed by the customer that itwill inspire them to buy the product of the particular brand and that they will then continue torecommend it to their fellow beings, and that is how the positioning of certain products isthriving and it is getting great success in the market.

LITERATURE REVIEW

According to CalinGurau (2012), the aim of this study is to compare the brand loyalty habits of five customer groups: three Millennial and two Generation X consumers. To stop generalisations that are reductionist, the research considers a variety of market-related scenarios, including three types of goods and two types of services, as well as the disparities in consumer loyalty profiles between two European Union countries with varying levels of economic growth. According to Yongmin Chen (2010), a theory of dynamic pricing states that companies can charge different prices to different customers depending on their previous purchases. A copula admitting different degrees of positive dependency describes brand preferences over two years. When committing to future rates is impossible, each firm offers its rival's customers lower prices. Consumer loyalty is rewarded as companies can commit to future prices if preference dependence is low, but tempting brand switching occurs if preference dependence is large.

Megan Divett (2003) claims that this research looks at a different way of effectively influencing customer loyalty and subsequent purchasing behaviour. The intervention improved consumer perceptions of approachability and responsiveness to customer feedback. Initial findings suggested that greater perceived approachability and responsiveness resulted in greater theatre loyalty and purchase behavior. According to Elena Delgado – Ballester (2001), the current literature on brand loyalty has primarily concentrated on the roles of perceived quality, brand credibility, and, in particular, satisfaction, since these factors summarise consumers' knowledge and experiences, guiding their subsequent behaviour. In this context, the change in focus to relational marketing has resulted in a significant amount of effort being dedicated to a Examine how other factors, such as confidence, influence future intentions.Many customer satisfaction studies have concluded that there is a substantial relationship between customer satisfaction and loyalty, according to Alison Dean (2001), but this conclusion has been challenged because most studies concentrate on assessing the cognitive aspect of customer satisfaction.The cognitive component is included in this analysis, but the affective component is the subject. It investigates the role of emotions in satisfaction before contrasting the cognitive and affective elements' ability to predict satisfaction.

According to Richard. L. Oliver (1999), happy customers are more likely to be loyal, but satisfaction does not always translate into loyalty. The author examines what part of the customer satisfaction response has consequences for loyalty and what portion of the loyalty response is due to this satisfaction dimension to understand the satisfaction-loyalty conundrum.Satisfaction is a necessary step in the

development of loyalty, but it becomes less important as loyalty develops by other mechanisms, according to the findings. The functions of personal Determinism ("fortitude") and social bonding at the institutional and personal levels are among the processes that are currently overlooked in current models. When these extra considerations are taken into consideration;Ultimate loyalty is the result of a synergistic effect of perceived product dominance, personal fortitude, and social bonding. The capacity for loyalty erodes when each fails to be achieved or is unattainable by individual firms serving consumer markets.

RESEARCH METHODOLOGY

Objectives

Primary Objective

- To study the impact of brand positioning on consumer learning and consumer loyalty.

Secondary Objective

- To study whether the brand positioning and other variables can influence different age groups and gender.
- To analyses consumers comparative mean value for switch brand, followed by promotion, emotional satisfaction, brand trust, customer loyalty.

Scope of Study

This research one can come to the point that in future aspect the research can be pursued regarding what are the parameters on which consumer accept or reject the brand. Moreover, how they perceive a new brand in the market and what are their expectations from a brand. The question regarding how positioning triggers the consumer to buy product of particular brand could also be answered in future researches.

Need for Study

Impact of brand positioning on consumer learning and brand loyalty, the increase in income levels, easy availability of finance, increase in consumer awareness, and introduction of new models, the demand for consumer durable has increased significantly. This in turn is leading to a strong competition among the different consumer durable brands available in the nation as well as the price gap between the same consumer goods of different companies are narrowing down. Recently, the rising of consumer consciousness has made consumers choose to purchase their familiar and favourable brand. Therefore, if businesses want to defeat their competitors, they have to make consumers love to buy their products and brands. Even though consumers familiarize and are willing to purchase a product, brand positioning is still an important factor to influence loyalty and purchase decision. The purpose of this study is when consumers want to buy a product, and a brand name can come to their minds at once, it reflects that product has higher brand positioning. Customers satisfaction, brand loyalty and consumers purchase intention can be influenced if a product has higher brand positioning.The analysis technique used is one sample t test and the software used is SPSS.

Research Design

In this study the research questions are developed. Research strategies are designed and research questions are answered accordingly. The qualitative approach emphasizes on processes and meanings that are not measured in terms of quantity, amount, intensity or frequency. The qualitative approach provides a deeper understanding of the phenomenon within context (Guba and Lincoln, 1994). On the other hand, quantitative researchers emphasize the measurement and analysis of casual relationships between variables. After comparing two research approaches in this study, quantitative approach is chosen. The current study, considers many factors related to impact of brand positioning on consumer learning and consumer loyalty.

Data Collection

Primary Data

A structured questionnaire is developed to measure the satisfaction of customers at restaurants. The questionnaire consisted of questions concerning customer satisfaction at restaurants and demographic information of respondents.

Secondary Data

Detailed review of literature from secondary sources is used as the base for identifying the domain, selection, designing and inclusion of various measuring variables in the questionnaire for the study. We also used various sources of secondary data which include:Information on internet, E- journals and different research papers.

Tools Used for Analysis

The collected data is analysed by Ms-office software in which the Ms-excel is used for coding the responses received. The collected data is also analysed using SPSS software. The software is further used for probable statistical techniques. To assess the impact of Brand positioning on consumer learning and brand loyalty, secondary data is collected and various analyses were applied.

Data Analysis and Interpretation

Demographics

45.3% of the respondents are in the age between 15-20years, 50.2% of the respondents are between 20-30 years, 2% of the respondents are between 30-40 years and 2.5% are above 50 years of age. 14.9% of the respondents are male and 85.1% of the respondents are female. This sample has a higher percentage of female (85.1%) than male (14.9%) which represents the population. From the table 2 it is clear that among the 201 respondents 91 respondents are between 15-20 years of which 3 are male and 88 are female. Of the 101 respondents from age group between 20-30 years, 25 are male and 76 are female. Among the 4 respondents in the age group of 30-40 years 1 is male and 4 are female. Only 5 respondents are above 50 years of age which comprises 1 men and 4 women. It could be inferred that women are more in age groups between 15-20 years, 20- 30 years, 30-40 years and above 50 years when compared to men. This could be due to the reason that in recent years more women are giving importance to brand due to the quality and quantity of the product.

Chi Square

It could be inferred from the above table that there is significant association ($\chi 2 = 17.794a$, $p < 0.000$) between Gender and Location of Residence. As the chi-square sig. value ($p < 0.000$) is less than 0.05, it indicates that the association between gender and Location of Residence is significant..

ANOVA

Null Hypothesis H01: There is no significant difference in the mean perception of respondents of different age groups with regard to Brand Trust, Emotional Satisfaction, Customer Loyalty, Promotion, Switch Brand. Table 2 reveals respondents age between 20-30 years have high perception regarding Brand Trust (M=1.8340) compared to respondents age between 15-20 years (M=1.8022), respondents age between 30-40 years (M=1.8000) and respondents age above 50 years (M=1.6400). This could be due to the reason that the respondents shows interest on brand which gives them experience. They would have tried various brands available in the market and hence people have Brand Trust.Respondents age between 15-20 years of age have high mean perception regarding Emotional Satisfaction (M=2.0714) compared to respondents age between 20-30 years (M=1.8960), respondents age between 30-40 years (M=1.3750) and respondents age above 50 years (M=1.8000). Respondents age between 15-20 have perceived high Emotional satisfaction were the companies produce brand product based on understanding individual hidden feeling.

Respondents above 50 years of age have high mean perception regarding Customer Loyalty (M=1.6000) compared to age between 15-20 years (M=1.3626), respondents age between 20-30 years (M=1.4307), respondents age between 30-40 years (M=1.3750). The customer would be loyal to the brand only when they are fully satisfied with that brand. Respondents above 50 years of age have high mean perception regarding Customer Loyalty when the brand satisfies customer need then there will be Customer Loyalty.

Respondents above 50 years of age have high mean perception regarding Promotion (M=2.5000) compared to age between 15-20 years (M=2.0824), respondents age between 20-30 years (M=2.1139), respondents age between 30-40 years (M=2.2500). Respondents above 50 years of age have high mean perception regarding Promotion is one of the way were it helps the customer to know about the product better than what they know about it. It would help the customer to get satisfied their needs.

Respondents above 50 years of age have high mean perception regarding Switch Brand (M=2.8000) compared to age between 15-20 years (M=2.7802), respondents age between 20-30 years (M=2.6238), respondents age between 30-40 years (M=2.5000). Switching Brand is one way used by the customer to get better result in the product they buy. Respondents above 50 years of age have high mean perception regarding Switch Brand if people are not satisfied with the product, if it is not effective, if it does not gives the customer's expected result will Switch Brand.

t-test

Testing at 5% level of significance, when the p value under Levene's Test for Equal variances yields a value of < 0.05 with respect to study variables, it indicates that there is significant difference in the perception of respondents and the group variances are not equal, hence in the column Levene's Test for Equality of variances the values in the second row (Equal variances not assumed) is to be considered. On the other hand when the p value under Levene's Test for Equal variances yields a value of > 0.05, it indicates that significant difference does exists in the perception of respondents and the group variances are equal, hence in the column Levene's Test for Equality of variances the values in the first row (Equal variances assumed) is to be considered. Table 3 reveals that significant difference exists in the perception of male and female respondents for the variable Brand Trust (p=0.071), There is no significant difference in the perception of male and female respondents for the variables namely Emotional Satisfaction (p=0.529), Customer Loyalty (p=0.568), Promotion (p=0.423) and Switch Brand (p=0.10). Female respondents score a high mean value compared to male respondents for Switch Brand, followed by Promotion, Emotional Satisfaction, Brand Trust, Customer Loyalty.

Testing at 5% level of significance, when the p value under Levene's Test for Equal variances yields a value of < 0.05 with respect to study variables, it indicates that there is significant difference in the perception of respondents and the group variances are not equal, hence in the column Levene's Test for Equality of variances the values in the second row (Equal variances not assumed) is to be considered. On the other hand when the p value under Levene's Test for Equal variances yields a value of > 0.05, it indicates that significant difference does exists in the perception of respondents and the group variances are equal, hence in the column Levene's Test for Equality of variances the values in the first row (Equal variances assumed) is to be considered. Table 4 reveals that significant difference exists in the perception of male and female respondents for the variable Emotional Satisfaction (p=0.221), There is no significant difference in the perception of male and female respondents for the variables namely Promotion (p=0.825), Switch Brand (p=0.251), Brand Trust (p=0.197) and Customer Loyalty (p=0.598). Unmarried respondents score a high mean value compared to married respondents for Switch Brand, followed by Emotional Satisfaction, Brand Trust, Customer Loyalty and only Promotion the mean value is high in married respondents when compared to unmarried respondents.

Correlation

Among the variables considered, highest correlation exists between Brand Trust and Emotional Satisfaction (r=0.308, p<0.000),followed by association between Brand Trust and Customer Loyalty (r=0.289, p<0.000) and the correlations

are moderate (Cohen, 1988). This implies that respondents place more value on Brand Trust than switch brand and other variables. The reason could be the respondents give more important to Brand Trust, Emotional Satisfaction, Customer Loyalty when compared to Promotion and Switch Brand.

Regression

Adjusted R square value is 0.101. This implies that 10.1% variability in the dependent variable i.e. Customer Loyalty is being predicted by the independent variables Brand Trust and Emotional Satisfaction. The value of Durbin Watson is 1.960.

Suggestions

This research suggest that they should seek an umbrella where they can make a strategy in a way that will be an innovative and exclusive thing in the market because these days the consumers are really conservative about the quality, brand name , brand image and the promise the brand do with their consumers so there is a roam available is a market and for that being a marker one should try to fill that gap in the industry which are missing this study can really help out to implement and to think out of the box one cannot be as a copy cat this research can create a certain image In the mind of the consumer that what position exemplifies as a new brand In a market one can implement this study and take a deep help out of it.

CONCLUSION

The findings of this research really enlightened the positioning of the brand and its importance as the findings showed that Consumer Showed positive behaviour and perception when they have seen television commercials of certain brands and they tend to be positive on the surrogate positioning which revolves on human psychology they perceive on a positive note for these positioning of the brand whereas the competitive positioning which always showed the brands strategy which always ends in a fighting and to prove one another brand best of the best consumers perception for them is negative or may be neutral to some extend same is the case with the case with the beneficial positioning where the marketers more emphases on selling products to masses regardless of the quality and customer loyalty. The conclusion revealed that as a marketer one should think holistically and to make consumer remember their products and brands for decades they should sell the quality and to gain the confidence of the consumer so as many giant brands are doing in the world and they have phenomenal rating when comes to the brand positioning as a brand the company must spend time on the R&D and educate the consumers in their ads whether print or visual that what the brand is for them for this companies must keep on educating the employees to win the consumers as it is made for them.

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Table 1 : Chi square test

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	17.794[a]	3	.000
Likelihood Ratio	20.493	3	.000
Linear-by-Linear Association	12.105	1	.001
N of Valid Cases	201		
a. 1 cells (8.3%) have expected count less than 5. The minimum expected count is 3.77.			

Table 2 : ANOVA – Age and Study Variable

		N	Mean	Std. Deviation	F	Sig.
Brand Trust	15-20 years	91	1.8022	.42635		
	20-30 years	100	1.8340	.41395		
	30-40 years	4	1.8000	.65320	.371	.774
	50 above	5	1.6400	.60663		
	Total	200	1.8140	.42698		
Emotional Satisfaction	15-20 years	91	2.0714	.66488		
	20-30 years	101	1.8960	.67940		
	30-40 years	4	1.3750	.47871	2.231	.086
	50 above	5	1.8000	.83666		
	Total	201	1.9627	.67996		
Customer Loyalty	15-20 years	91	1.3626	.40870		
	20-30 years	101	1.4307	.36763		
	30-40 years	4	1.3750	.25000	.883	.451
	50 above	5	1.6000	.82158		
	Total	201	1.4030	.39911		
Promotion	15-20 years	91	2.0824	.63798		
	20-30 years	101	2.1139	.63985		
	30-40 years	4	2.2500	.64550	.752	.522
	50 above	5	2.5000	.35355		
	Total	201	2.1119	.63337		
Switch Brand	15-20 years	91	2.7802	.71184		
	20-30 years	101	2.6238	.71905		
	30-40 years	4	2.5000	1.00000	.896	.444
	50 above	5	2.8000	.44721		
	Total	201	2.6965	.71585		

Table 3 : t – Test – Gender and Study Variable

Variable	Gender	N	Mean	SD		Levene's Test for Equality of Variances		t-test for Equality of Means		
						F	Sig.	t	df	Sig. (2-tailed)
Brand Trust	male	30	1.6933	.33521	EVA	3.301	.071	-1.687	198	.093
	female	170	1.8353	.43858	EVNA			-2.033	48.410	.048
Emotional Satisfaction	male	30	1.7167	.55216	EVA	.397	.529	-2.168	199	.031
	female	171	2.0058	.69237	EVNA			-2.540	46.601	.014
Customer Loyalty	male	30	1.4000	.33218	EVA	.327	.568	-.044	199	.965
	female	171	1.4035	.41058	EVNA			-.051	46.064	.959
Promotion	male	30	1.9500	.67403	EVA	.644	.423	-1.523	199	.129
	female	171	2.1404	.62371	EVNA			-1.442	38.220	.157
Switch Brand	male	30	2.4333	.89763	EVA	6.691	.010	-2.204	199	.029
	female	171	2.7427	.67160	EVNA			-1.801	34.918	.080

Table 4 : t – Test – Marital status and Study Variables

Variable	Marital status	N	Mean	SD		Levene's Test for Equality of Variances		t-test for Equality of Means		
						F	Sig.	t	df	Sig. (2-tailed)
Brand Trust	married	16	1.7750	.51575	EVA	1.675	.197	-.390	195	.697
	unmarried	181	1.8188	.42306	EVNA			-.330	16.832	.746
Emotional Satisfaction	married	16	1.9063	.58363	EVA	1.506	.221	-.405	196	.686
	unmarried	182	1.9780	.68694	EVNA			-.464	18.853	.648
Customer Loyalty	married	16	1.3750	.50000	EVA	.281	.597	-.301	196	.763
	unmarried	182	1.4066	.39270	EVNA			-.246	16.667	.809
Promotion	married	16	2.1563	.62500	EVA	.049	.825	.199	196	.842
	unmarried	182	2.1236	.62837	EVNA			.200	17.773	.844
Switch Brand	married	16	2.5000	.81650	EVA	1.325	.251	-1.112	196	.267
	unmarried	182	2.7088	.71126	EVNA			-.990	17.062	.336

Table 5 : Correlation analysis

		Brand Trust	Emotional Satisfaction	Customer Loyalty	Promotion	Switch Brand
Brand Trust	r	1	.308**	.289**	.126	-.116
	Sig. (2-tailed)		.000	.000	.076	.102
Emotional Satisfaction	r		1	.235**	.227**	.059
	Sig. (2-tailed)			.001	.001	.407
Customer Loyalty	r			1	.043	-.139*
	Sig. (2-tailed)				.543	.050
Promotion	r				1	.257**
	Sig. (2-tailed)					.000
Switch Brand	r					1
	Sig. (2-tailed)					

**. Correlation is significant at the 0.01 level (2-tailed)

* . Correlation is significant at the 0.05 level (2-tailed)

Table 6 : Regression Analysis

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	F	Sig.	Durbin-Watson
1	.289[a]	.084	.079	.38181	18.085	.000	
2	.331[b]	.110	.101	.37733	5.727	.018	1.960

a. Predictors: (Constant), AVGBT

b. Predictors: (Constant), AVGBT, AVGES

c. Dependent Variable: AVGCL

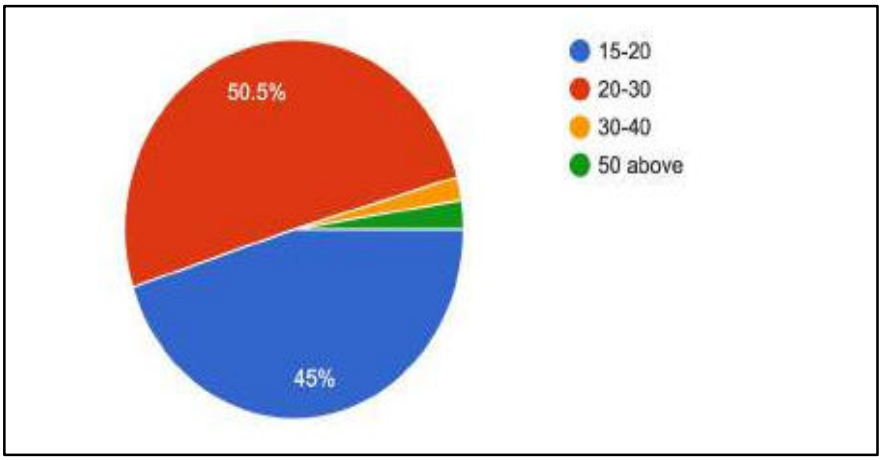

Figure 1: Age of the Respondents

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RESEARCH ARTICLE

On Some Properties of Metallic Ratios

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ABSTRACT

Among several interesting class of special numbers that exist in mathematics, sequence of metallic ratios plays an significant role in providing various ideas and applications. The familiar golden ratio and silver ratio are special cases of metallic ratios. In this paper, I will describe the metallic ratios in general and provide some elementary properties related to them by considering the expression for metallic ratio as a continuous function.

Keywords: Metallic Ratio, Recurrence Relation, Summation, Derivatives, Riemann Integral

INTRODUCTION

The study about golden ratio, silver ratio has fascinated mathematicians from ancient times to modern time. The use of golden ratio in the Greek Parthenon temple and silver ratio in determining paper sizes are significant applications of metallic ratios. Nature too exhibits these numbers in various forms. Hence the study of metallic ratios has not only been an enriching experience but it provides useful applications too. In this paper, I will try to prove some of the elementary new results regarding metallic ratios by considering the closed expression for metallic ratio as a continuous function.

Definitions

Metallic Ratios are sequence of numbers defined through the recursive relation $M_{n+2} = nM_{n+1} + M_n \quad (2.1)$.

In particular, the nth Metallic Ratio M_n is defined to be the positive root of the quadratic equation $x^2 - nx - 1 = 0 \ (2.2)$.

With above definition, we get $M_n = \frac{n+\sqrt{n^2+4}}{2}$ (2.3) and $-\frac{1}{M_n} = \frac{n-\sqrt{n^2+4}}{2}$ (2.4).

If we consider n = 1, 2, 3 respectively in (2.3) then the numbers obtained are defined as Golden, Silver and Bronze Ratios respectively. Thus, the golden ratio, silver ratio and bronze ratio are special cases formimg the first three terms of the most general class of numbers called Metallic Ratios.

By considering n = 1 in (2.3), the golden ratio is given by $M_1 = \frac{1+\sqrt{5}}{2}$ (2.5)

By considering n = 2 in (2.3), the silver ratio is given by $M_2 = 1+\sqrt{2}$ (2.6)

By considering n = 3 in (2.3), the bronze ratio is given by $M_3 = \frac{3+\sqrt{13}}{2}$ (2.7)

In view of exploring elementary and new properties related to metallic ratios, I am going to consider the expression for the nth metallic ratio M_n from (2.3) as a continuous function of n.

Summations Related to Metallic Ratios

In this section, I will determine sum up to n terms of certain expressions related to metallic ratios.

Theorem 1

If M_k is the kth metallic ratio then

$$\sum_{k=1}^{n} \frac{{M_k}^2 - 1}{M_k} = \frac{n(n+1)}{2} \quad (3.1)$$

$$\sum_{k=1}^{n} \left(\frac{{M_k}^2 + 1}{M_k} \right)^2 = \frac{n(2n^2+3n+25)}{6} \quad (3.2)$$

Proof: Adding (2.3) and (2.4), we get $M_k + \left(-\frac{1}{M_k}\right) = \left(\frac{k+\sqrt{k^2+4}}{2}\right) + \left(\frac{k-\sqrt{k^2+4}}{2}\right) = k$

Hence, $\sum_{k=1}^{n} \left(M_k - \frac{1}{M_k} \right) = \sum_{k=1}^{n} k$ from which $\sum_{k=1}^{n} \frac{{M_k}^2 - 1}{M_k} = \frac{n(n+1)}{2}$

Subtracting (2.3) and (2.4), we get $M_k - \left(-\frac{1}{M_k}\right) = \left(\frac{k+\sqrt{k^2+4}}{2}\right) - \left(\frac{k-\sqrt{k^2+4}}{2}\right) = \sqrt{k^2+4}$

Hence, $\sum_{k=1}^{n} \left(\frac{{M_k}^2 + 1}{M_k} \right)^2 = \sum_{k=1}^{n} (k^2+4) = \frac{n(n+1)(2n+1)}{6} + 4n = \frac{n(2n^2+3n+25)}{6}$

This proves (3.1) and (3.2) and hence completes the proof.

Derivatives of Metallic Ratios

Considering the expression for metallic ratio as a continuous function, I will derive closed expressions for its first three derivatives in this section.

Theorem 2

If M_n is the nth Metallic ratio, and assuming the expression for M_n as function of n, we have

$$M_n' = \frac{M_n}{2M_n - n} \quad (4.1),\ M_n''\left(M_n\right)^3 - 2\left(M_n'\right)^3 = 0 \ (4.2),\ M_n'''\left(M_n\right)^5 + 6n\left(M_n'\right)^5 = 0 \ (4.3)$$

where M_n', M_n'', M_n''' are first, second and third derivatives of M_n respectively.

Proof: By treating M_n as a function of n in (2.3) and differentiating, we get

$M_n' = \frac{1}{2}\left(1 + \frac{n}{\sqrt{n^2+4}}\right) = \frac{M_n}{\sqrt{n^2+4}}$. But from (2.3), we have $2M_n - n = \sqrt{n^2+4}$.

Hence, $M_n' = \frac{M_n}{2M_n - n}$ proving (4.1)

Now differentiating (4.1) using quotient rule, we get

$$M_n'' = \frac{\left(2M_n - n\right)M_n' - M_n\left(2M_n' - 1\right)}{\left(2M_n - n\right)^2} = \frac{M_n - nM_n'}{\left(2M_n - n\right)^2}$$

Now substituting the value of M_n' from (4.1), we get $M_n'' = \frac{M_n - n\left(\frac{M_n}{2M_n - n}\right)}{\left(2M_n - n\right)^2} = \frac{2M_n\left(M_n - n\right)}{\left(2M_n - n\right)^3}$

Using (2.3) and (2.4), we have $M_n - n = \frac{\sqrt{n^2+4} - n}{2} = \frac{1}{M_n}$. Substituting this in previous expression we get $M_n'' = \frac{2}{\left(2M_n - n\right)^3}$. Now from (4.1), we have $2M_n - n = \frac{M_n}{M_n'}$. Hence, we obtain $M_n''\left(M_n\right)^3 - 2\left(M_n'\right)^3 = 0$ proving (4.2)

Now differentiating (4.2) we get $\left(M_n''\right)\left(3M_n^2 \times M_n'\right) + \left(M_n\right)^3\left(M_n'''\right) - 6\left(M_n'\right)^2 \times M_n'' = 0$

Substituting the value of M_n'' in first and third terms from (4.2) we get

$$\left(M_n\right)^3\left(M_n'''\right) + \frac{2\left(M_n'\right)^3}{\left(M_n\right)^3}\left(3M_n^2 \times M_n' - 6\left(M_n'\right)^2\right) = 0$$

$$\left(M_n\right)^6\left(M_n'''\right) + 6\left(M_n'\right)^4\left(M_n^2 - 2M_n'\right) = 0$$

Now by definition (2.2), it follows that $M_n^2 = nM_n + 1$. Also, using (4.1) in the last factor of the second term of previous equation we get

$$\left(M_n'''\right)\left(M_n\right)^6 + 6\left(M_n'\right)^4 \times \left(nM_n + 1 - 2 \times \frac{M_n}{2M_n - n}\right) = 0$$

$$\left(M_n'''\right)\left(M_n\right)^6+\frac{6n\left(M_n'\right)^4}{2M_n-n}\times\left(2M_n^{\,2}-nM_n-1\right)=0$$

$$\left(M_n'''\right)\left(M_n\right)^6+\frac{6n\left(M_n'\right)^4}{2M_n-n}\times M_n^{\,2}=0$$

Now substituting for $2M_n-n$ from (4.1), we get $\left(M_n'''\right)\left(M_n\right)^6+6n\left(M_n'\right)^5\times M_n=0$

From this, we obtain $\left(M_n'''\right)\left(M_n\right)^5+6n\left(M_n'\right)^5=0$ proving (4.3)

This completes the proof.

Integrals of Metallic Ratios

In this section, I will consider the Riemann integral of the *k*th metallic ratio M_k considered as a continuous function taken over a closed bounded interval.

Theorem 3

If *n* is some natural number and if M_k is the *k*th Metallic ratio, then the Riemann integral of M_k taken over the interval $[0,n]$ is given by $\int_{k=0}^{n} M_k\,dk=\frac{nM_n}{2}+\log_e\left(M_n\right)$ (5.1)

Proof: Using (2.3), we have

$$\int_{k=0}^{n} M_k\,dk=\int_{k=0}^{n}\left(\frac{k+\sqrt{k^2+4}}{2}\right)dk$$

$$=\frac{1}{2}\left(\frac{k^2}{2}\right)_{k=0}^{n}+\frac{1}{2}\left(\frac{k\sqrt{k^2+4}}{2}+2\log_e\left(k+\sqrt{k^2+4}\right)\right)_{k=0}^{n}$$

$$=\frac{n^2}{4}+\frac{n\sqrt{n^2+4}}{4}+\log_e\left(n+\sqrt{n^2+4}\right)-\log_e 2$$

$$=\frac{n}{2}\left(\frac{n+\sqrt{n^2+4}}{2}\right)+\log_e\left(\frac{n+\sqrt{n^2+4}}{2}\right)=\frac{nM_n}{2}+\log_e\left(M_n\right)$$

This completes the proof.

Corollary

The Riemann integral of *k*th metallic ratio M_k over the intervals [0,1], [0,2], [0,3] are given by

$$\int_{k=0}^{1} M_k\,dk=\frac{1+\sqrt{5}}{4}+\log_e\left(\frac{1+\sqrt{5}}{2}\right) \qquad (5.2)$$

$$\int_{k=0}^{2} M_k\,dk=1+\sqrt{2}+\log_e\left(1+\sqrt{2}\right) \qquad (5.3)$$

$$\int_{k=0}^{3} M_k\,dk=\frac{3\left(3+\sqrt{13}\right)}{4}+\log_e\left(\frac{3+\sqrt{13}}{2}\right) \qquad (5.4)$$

Proof: Substituting $n = 1, 2, 3$ in (5.1) and using (2.5), (2.6), (2.7) we get

$$\int_{k=0}^{1} M_k \, dk = \frac{M_1}{2} + \log_e\left(M_1\right) = \frac{1+\sqrt{5}}{4} + \log_e\left(\frac{1+\sqrt{5}}{2}\right)$$

$$\int_{k=0}^{2} M_k \, dk = M_2 + \log_e\left(M_2\right) = 1+\sqrt{2} + \log_e\left(1+\sqrt{2}\right)$$

$$\int_{k=0}^{3} M_k \, dk = \frac{3M_3}{2} + \log_e\left(M_3\right) = \frac{3\left(3+\sqrt{13}\right)}{4} + \log_e\left(\frac{3+\sqrt{13}}{2}\right)$$

This completes the proof.

CONCLUSION

By considering the sequence of metallic ratios as a continuous function, I had proved several new properties in this paper. In particular, in theorem 1 of section 3.1, I had two closed expressions for determining sum up to n terms of sum and difference of certain expressions related to metallic ratios. In theorem 2 of section 4.1, I had derived three expressions related to first, second and third derivatives of metallic ratios respectively. One can try to generalize them by determining higher order derivatives and look for some pattern behind those equations. Since the sequence of metallic ratios is considered as a continuous function, the kth metallic ratio is Riemann integrable over any closed and bounded interval. Making use of this fact, I had derived a nice expression in theorem 3 of section 5.1. Based on this I had presented the corresponding integral values for golden, silver and bronze ratios as corollary in section 5.2. These new results will certainly provide insights to already known properties regarding metallic ratios.

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RESEARCH ARTICLE

Mapping of Groundwater Potential Zones in Pulampatti Watershed, Dharmapuri District – A Geospatial Approach

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ABSTRACT

The estimation of groundwater resources for the district has shown that under over exploited category. Hence, there is a need for demarcation of potential groundwater zones. The present study deals with the utilization of GIS based analytical hierarchy process (AHP) technique for identification of the groundwater potential zones in Pulampatti watershed, Dharmapuri district. Various thematic layers that influence the groundwater occurrence in an area are lithology, geomorphology, lineaments density, drainage density, slope, landuse/land cover, soil, and elevation. All these themes and their individual features are then assigned weights according to their relative importance in groundwater occurrence and the corresponding normalized weights were obtained based on the analytical hierarchy process. Finally, all the thematic layers were integrated using weighted overlay analysis in GIS environment to generate a groundwater potential map of the study area, viz., good, moderate and poor. It has been concluded that about 629.79 km^2 area has good groundwater potential which is 37.20% of the total study area. However, the area having moderate and poor groundwater potential is about 58.33 km^2 and 1005.02 km^2 respectively. Finally, the groundwater potential map was verified using the well yield data of 39 pumping wells with average potential yield value of ≥44 m^3/h, and the result was found satisfactory. The produced groundwater potential map could be used to formulate an efficient groundwater management plan for the study area so as to ensure sustainable utilization of scarce groundwater resources.

Keywords: Groundwater Potential Zone, analytical hierarchy process, GIS, Pulampatti watershed.

INTRODUCTION

Groundwater is one of the most valuable natural resources, and supports human life, economic development and ecological diversity. The main source for ground water is precipitation resulting in drainage flows through fracture

zone on the earth surface. In the world scenario, the availability of groundwater is reducing gradually due to over exploitation, and the lack of groundwater management. In India, more than 90% of the rural and nearly 30% of the urban population depend on groundwater for meeting their drinking and domestic requirements (Reddy et al., 1996).Hence, it is necessary to understand the methods and way to approach towards groundwater potential zones and surface water conservation and to improve the groundwater level at the national, regional, and local scale for sustainable livelihood. Groundwater studies have become crucial not only for targeting groundwater potential zone, but also for monitoring and conserving this vital resource.

Geospatial technology, with its advantages of spatial, spectral and temporal availability of data covering large and inaccessible areas within a short time, has emerged as a very useful tool for the assessment, monitoring and management of groundwater resources (Singh et al. 2013). Geospatial techniques provide a rapid and cost effective tool for generating valuable geo-data (geology, geomorphology, landuse/land cover, lineaments/structures and slope, etc.) both directly and indirectly, that can be used in deciphering groundwater potential zones (Dar et al. 2011; Singh et al. 2014).Recently, there are several research study were conducted on groundwater targeting with successful results through different methodologies. Remote sensing and GIS techniques have been effectively utilized as a tool to delineate groundwater potential zones in various parts of India (Ramasamy et al. 1989; Anbazhagan et al. 2001; Neelakantan and Yuvaraj 2012; Gnanachandrasamy et al. 2018). Multi-criteria decision analysis (MCDA) is effective tools for providing a framework for groundwater resource management (Pietersen 2006; Madruccietal.2008; Jha et al. 2010). The AHP method is one of the most widely used MCDA models, which has also been to obtain spatial plan, resource allocation etc. Additionally, the AHP tool is a suitable technique for evaluating the consistency of the result, consequently reducing the bias in the decision making process (Saaty 1990). AHP has been accepted by the international scientific community as a very useful tool for dealing with complex decision problems. Its major innovation was the introduction of pair-wise comparisons. AHP technique analyzes the multiple datasets in a pair-wise comparison matrix, which is used to calculate the geometric mean and normalized weight of parameters (Omid Rahmati et al. 2015; Vijay Prabhu et al. 2016; Aenumula Mallikarjun et al. 2018; Arulbalaji et al. 2019). The AHP has been successfully applied in several studies of water resource management by integrating MCDA with RS and GIS techniques (Shashank Shekhar and Arvind Chandra Pandey 2014; Muralitharan and Palanivel 2015; Jothibasu and Anbazhagan 2016; Domingos Pinto et al. 2017; Biswajit Das et al. 2018). In the present study, analytic hierarchy process and GIS technique used to determine the ground water potential zones in pulampatti watershed. Development of groundwater in the study area is through construction of dug wells. The groundwater is being continuously exploited for drinking and irrigation purposes, it is essential to delineate the groundwater potential zones. Therefore, the various thematic layers, such as geomorphology, lithology, drainage density, lineament density, landuse/land cover, slope, soil, and elevation were prepared using remote sensing and GIS technique and identifying groundwater potential zones.

Study area

Pulamapatti watershed is located in Dharmapuri district, Tamil Nadu with an area of 1,701.69 km^2. It is located between 78°00' to 78°35'E longitude and 12°00' to 12°31'N latitude and covers SOI toposheets 57L/2, L/3, L/4, L/7, L/8 and L/12 on 1:50,000 scale (Fig.1). The main River is Ponnaiyar and split into Pulampatti and Semmandakuppam River at near Kambainellur. The River originates and flowing towards south eastern side of watershed. Physiographically the study area is covered by undulating plain and upland plateau. The watershed is predominantly covered with Archaean crystalline formations of Charnockite and gneissic rocks. The average annual rainfall is around 978mm. The lowest temperature is reached in January is about 19°C. April and May are the hottest months of the temperature of about 37°C.

Methodology

To identify the groundwater potential zone in the study area, thematic layers of geomorphology, lithology, lineament density, slope, landuse/land cover, drainage density, soil and elevation were generated using topographic maps, satellite image, existing maps and field data in GIS environment.

Groundwater parameters

Geomorphology: Geomorphology of an area is one of the most important features in evaluating the groundwater potential and prospect. The geomorphology, as such, controls the surface water and subsurface movement of the groundwater. The geomorphologic features of the study area identify the IRS LISS III satellite imagery by visual interpretation techniques (Fig.2). The major geomorphologic features of the study area include shallow buried pediment, flood plain and buried pediment, which are potential zones for groundwater storage.

Lithology: The lithology map published by Geological Survey of India (1995) is referred in the present study (Fig.3). Geologically, the watershed consists of Charnockite, Epidote-hornblende gneiss and Pink migmatite of the Archaean age.

Lineament Density: Lineaments represent the zones of faulting and fracturing resulting in increased secondary porosity and permeability. Areas with high lineament density are good for groundwater potential zones (Haridaset al.1998). Lineament density is classified as very high followed by high, medium and low categories (Fig.4). Very high lineament density is in the southeastern part of the study area with a value range from 117.75 to 157 km/km^2.

Slope (Degree): Slope determines the rate of infiltration and run-off of surface water (Nassif and Wilson, 1975). The slope map of the study area is produced using the SRTM data with 90m resolution. On the basis of slope, the study area is divided into four classes, which are 0–10.72º, 10.72–21.44º, 21.44-32.16º and 32.16–42.88º. The study area is dominated by slope of >10º, which indicates almost flat topography and runoff is slow, allowing more time for rainwater to percolate and consider good groundwater potential zone (Fig.5).

Land use / Land cover: The fundamental approach to any watershed planning is to determine the present situation of land use / land cover pattern. Different land use / land cover patterns obstruct the run-off, reduce evaporation of surface and ground water and hence have an impact on groundwater resources. Agricultural land has very good groundwater potential because of enough void space for groundwater recharge and built up area showing very low groundwater potential because of very low groundwater recharge. The land use/land cover map was created using LISS-III satellite image by visual interpretation technique and classified it into eleven classes. The study area is almost covered by crop land and land with scrub in all directions. Classification of land use/land cover for weighted analysis was decided based on the land use type and properties to infiltrate water, and their characteristics to hold water on the ground surface (Fig.6).

Drainage density: Drainage density is an inverse function of permeability, and therefore it is an important parameter in evaluating the groundwater zone. The drainage map prepared from the SOI published toposheets of the study area is used for obtaining the drainage density map. Higher weightage were given to low drainage density regions causes more infiltration and results in good groundwater potential zones as compared to a high drainage density region. High drainage density values are favorable for run-off, and hence indicates low groundwater potential zone. Drainage density value was classified into four classes viz; low (0-97.61 km/km^2), moderate (97.61-195.21 km/km^2), high (195.21-292.82 km/km^2) and very high(292.82-390.42 km/km^2) groundwater potential respectively (Fig.7).

Soil: The movement of ground water and infiltration of surface water into ground is based on the porosity and permeability of soil. Therefore the study of soil is important to determine the amount of ground water of Pulamapatti watershed. The soil data were collected from soil survey and landuse board and the same data was digitized in GIS platforms. The soil for the watershed reveals three main soil categories namely red gravelly soil, red loamy soil and red sandy soil (Fig.8).

Elevation: Water tends to store at lower topography rather than the higher topography. Higher the elevation lesser the ground water potential and vice versa (Hammouri et al. 2012), for the present study elevation data having 90 meter spatial resolution has been created from the SRTM image. The study area's elevation ranges between 295 meters to 1237 meters from the mean sea level, these values have been classified equally into four classes (Fig.9).

Multi criteria decision analysis using GIs techniques

AHP is used to demarcate the potential groundwater zones and this technique was proposed by Saaty (1990). In this study, the AHP pair-wise matrix was developed by input values of scale weights of themes and their features based on relative influence on groundwater occurrence and expert opinion (Table1&2). Thereafter, a pair-wise comparison matrix was constructed using the Saaty's analytical hierarchy process (Saaty, 1980) to calculate normalized weights for individual themes and their features. The AHP method allows assessing the geometric mean (Eq. 1), followed by allotting a normalized weight (Eq. 2) to various themes for finalizing the decision process. The normalized weights were assigned to various thematic layers which include lithology, geomorphology, lineament density, slope, landuse/land cover, soil, drainage density and elevation provides certain clue for the groundwater potential. The pair-wise comparison for the eight layers were given based on the comparison between the layers and their relative importance towards groundwater prospects and an8×8 matrix was formed. Based on the comparison matrix the following steps were carried out to calculate the normalized weight. In step 1 each thematic layer of the column were divided by their corresponding sum of the row to form the relative weight matrix. In step 2 the geometric mean was obtained by averaging across the rows and normalized weight was obtained by dividing each geometric mean thematic map with sum of geometric mean is shown in Table 2.

Geometric Mean

The geometric mean is derived from the total sum of score of a specific parameter known as total scale weight divided by total number of parameter; this is expressed as:

$$\text{Geometric Mean} = \frac{\text{Total Scale Weight}}{\text{Total number of parameter}} \quad (1)$$

Normalized Weight

The normalized weight was derived from the assigned weight of a parameter feature class divided by the corresponding geometric mean. The formula is represented as:

$$\text{Normalized weight} = \frac{\text{Assigned weight of a parameter feature class}}{\text{Geometric Mean}} \quad (2)$$

RESULTS AND DISCUSSION

Groundwater Potential Zones

On the basis of normalized weights for individual themes and their corresponding categories, all the eight thematic layers are integrated (Fig.10) in the GIS environment. The normalized weighted map is an indicator of potential groundwater zone that was classified into three classes as high, moderate and poor potential zone. The class with maximum weight is considered as high suitable zone and least weighted class is poor or unsuitable zone for groundwater.

Validation of groundwater potential map

The groundwater potential zone map delineated in the present study was verified using the available well yield data of 39 pumping wells with average potential yield value of ≥44 m^3/h. Mean discharge of the existing pumping wells in individual groundwater potential zones was computed and compared. In addition, cumulative frequencies of the wells falling in individual groundwater potential zones were plotted against well yields.

CONCLUSION

The application of integrated geospatial technology and AHP has proven to be a better tool for the identification of potential groundwater zones in Pulampatti watershed. The present study demarcates the groundwater potential zones by integration of the groundwater influencing factors. Each factor was assigned appropriate weight based on expert knowledge and finally groundwater potential map of the study area was produced. The results indicated that good, moderate and poor potential zones occupying an area of 629.79km^2 (37.20%), 58.33km^2 (3.44%) and 1005.02km^2(59.36%). The study area that buried pediment, low slope angle (0-10°), crop land, very high lineament density (117.75-157) and granitoid gneiss have high infiltration ability which is helps to development of the high potential zone. The validations of groundwater potential map with well yield data, the accuracy of the verified model is 72%, which gives satisfactory result. The findings of this study can be used to watershed development programme and proper sustainable management of groundwater resources.

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Table 1 Weights assigned to the thematic layers

Theme	weight
Lineament Density	7.5
Lithology	7
Landuse/Land Cover	6.5
Slope	5.5
Drainage Density	6
Geomorphology	8
Soil	5
Elevation	4.5

Table 2 AHP–pairwise matrix analysis of thematic layer's scale weight for geometric mean

Parameters	LD	LI	LU-LC	SL	DD	GEOM	SO	EL	Total value	Geometric Mean
LD	7.5/7.5	7.5/7	7.5/6.5	7.5/5.5	7.5/6	7.5/8	7.5/5	7.5/4.5	9.94	1.24
LI	7/7.5	7/7	7/6.5	7/5.5	7/6	7/8	7/5	7/4.5	9.27	1.16
LU-LC	6.5/7.5	6.5/7	6.5/6.5	6.5/5.5	6.5/6	6.5/8	6.5/5	6.5/4.5	8.61	1.08
SL	5.5/7.5	5.5/7	5.5/6.5	5.5/5.5	5.5/6	5.5/8	5.5/5	5.5/4.5	7.29	0.91
DD	6/7.5	6/7	6/6.5	6/5.5	6/6	6/8	6/5	6/4.5	7.95	0.99

GEOM	8/7.5	8/7	8/6.5	8/5.5	8/6	8/8	8/5	8/4.5	10.6	1.33
SO	5/7.5	5/7	5/6.5	5/5.5	5/6	5/8	5/5	5/4.5	6.62	0.83
EL	4.5/7.5	4.5/7	4.5/6.5	4.5/5.5	4.5/6	4.5/8	4.5/5	4.5/4.5	5.96	0.75

LD = Lineament Density; **LI** = Lithology; **LU-LC** = Landuse / land cover; **SL** = Slope; **DD** = Drainage Density; **GEOM** = Geomorphology; **SO** = Soil; **EL** = Elevation

Table 3 Assignment of weight for the feature classes of individual parameter and normalized weight calculation

Name of the parameter	Feature class	Assigned weight (AW)	Geometric mean (G)	Normalized weight (N=AW/G)
Lineament density	Low (0-39.25)	3	1.24	2.42
	Moderate (39.25-78.5)	5		4.03
	High (78.5-117.75)	7		5.64
	Very High (117.75-157)	8		6.45
Drainage density	Low (0-97.61)	7	0.99	7.07
	Moderate (97.61-195.21)	5		5.05
	High (195.21-292.82)	3		3.03
	Very High (292.82-390.42)	1		1.01
Slope (in degree)	0-10.72	7	0.91	7.69
	10.72-21.44	5		5.49
	21.44-32.16	3		3.30
	32.16-42.88	1		1.10
Soil	Red gravelly soil	6	0.83	7.23
	Red sandy soil	4		4.82
	Red loamy soil	2		2.41
Landuse / land cover	Crop land	8	1.08	7.41
	Forest plantation	7		6.48
	Tank/Reservoir	6		5.55
	Upland	5		4.63
	Fallow land	5		4.63
	Sandy area	4		3.70
	River	4		3.70
	Land with scrub	3		2.78
	Scrub forest	3		2.78
	Built-up land	2		1.85
	Barren rocky/stony waste	1		0.92
Geology	Granitoid gneiss	6	1.16	5.17
	Hornblende-biotite gneiss	5		4.31
	Epidote-hornblende gneiss	5		4.31
	Ultramafics	4		3.45
	Pink migmatite	4		3.45
	Anorthosite	3		2.59
	Syenite complex	3		2.59
	Charnockite	2		1.72
	Carbonatite	1		0.86

	Pyroxene granulite	1		0.86
Elevation (M)	295-530	4	0.75	5.33
	530-766	3		4.0
	766-1001	2		2.67
	1001-1237	1		1.33
Geomorphology	Buried pediment	9	1.33	6.77
	Shallow buried pediment	8		6.01
	Flood plain	7		5.26
	Tank/Reservoir	6		4.51
	Valley fill	6		4.51
	Structural hill	5		3.76
	River	4		3.01
	Residual hill	3		2.25
	Inselberg	3		2.25
	Denudational hill	2		1.50
	Linear ridge/dyke	1		0.75

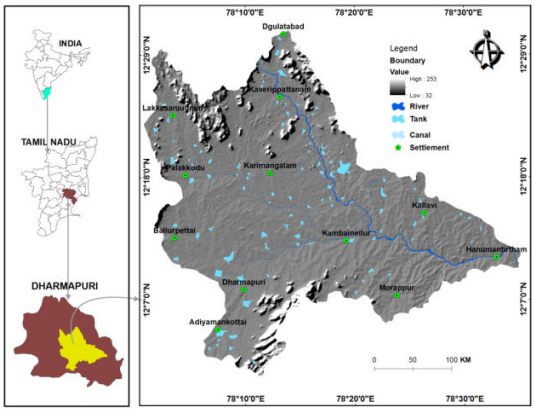

Figure 1 Location of the study area

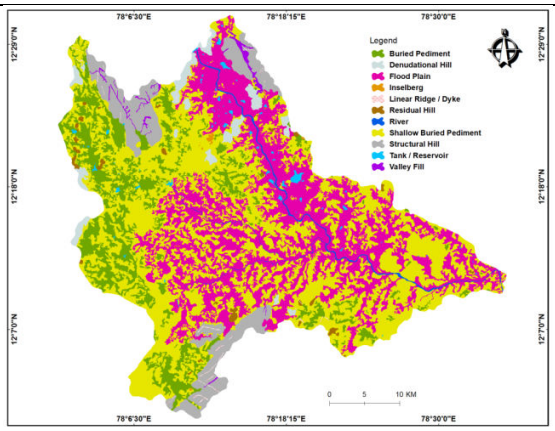

Figure 2 Geomorphology of the study area

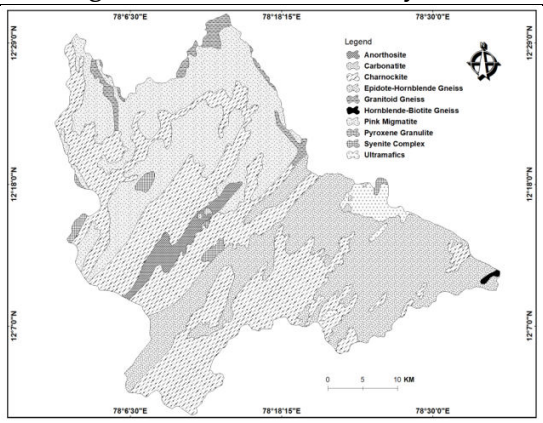

Figure 3 Lithology of the study area

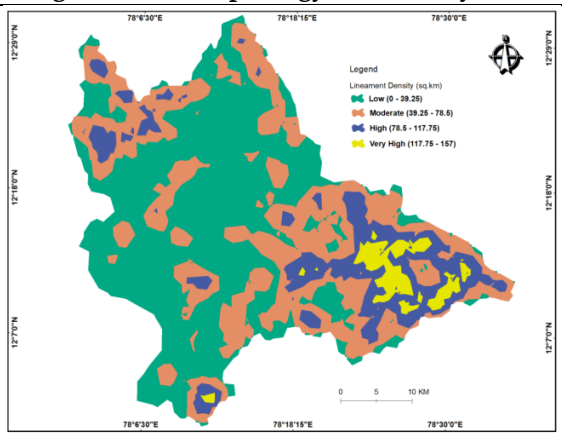

Figure 4 Lineament density of the study area

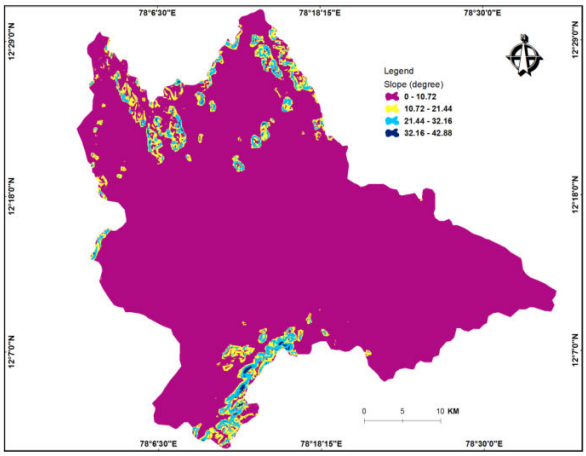

Figure 5 Slope (Degree) of the study area

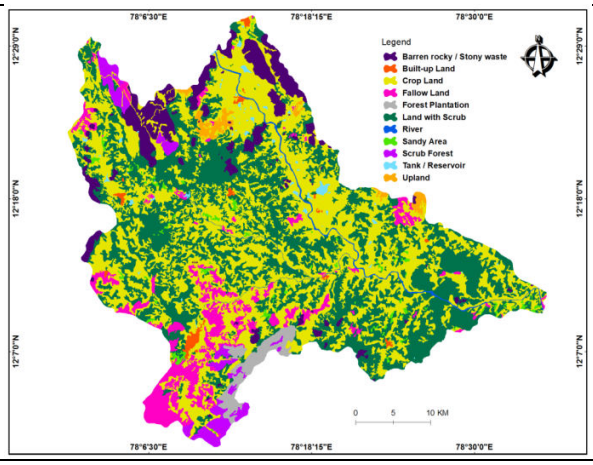

Figure 6 Land use / Land cover of the study area

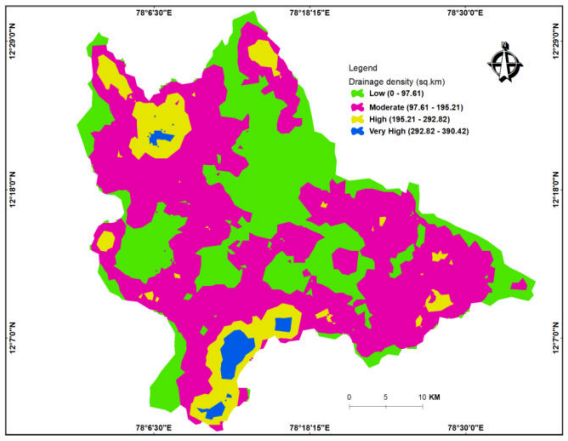

Figure 7 Drainage density of the study area

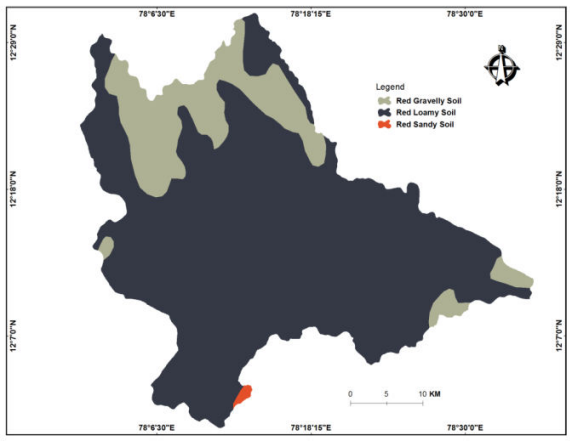

Figure 8 Soil of the study area

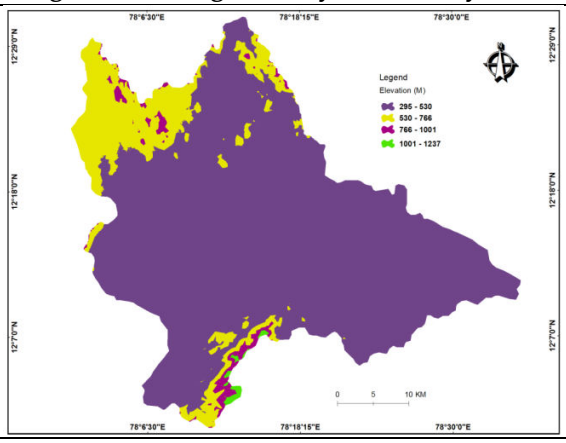

Figure 9 Elevation of the study area

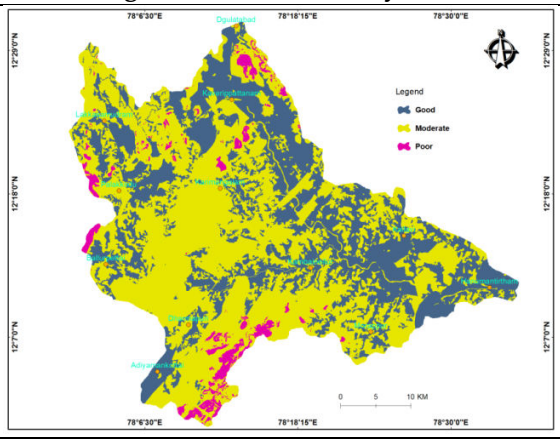

Figure 10 Groundwater potential zones in the study area

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REVIEW ARTICLE

A Review on Stent Therapies

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ABSTRACT

A stent is a small tube that can be placed into a blocked area. It's used to replace the flow of blood and other fluids. Stent are made up of metal or plastic, either it made up of specialized fabric materials and also coated with medications which helps to closing the blocked artery. Types of stent are cardiac stent, Heart angioplasty and stent, Peripheral angioplasty and stent, Drug eluting stent, Esophageal stent, Intracranial stents, Bronchial Stents, Urethral stents, Biliary stent. Methods of stent preparation and suitable polymers are given below. The insertion of stent is done by using a minimally invasive procedure; there will make a small cut using a catheter to guide specific tools into our blood vessels to reach the place where it needs a stent. Finally the incision will be closed and dressed, and then the patient will be taken to a recovery room for observation. A catheter is a diagnostic tool used in the treatment for certain types of heart disease. The surgeons gives Catheter procedures an in-deep look at the arteries well known to the heart and also allow them to cure structural problems such as irregular fatigue, rhythms and other potentially risking symptoms. A catheter procedure is Cardiac catheterization, Catheter ablation. The stent have some benefits of substantially improve our blood flow. It helps to prevent further damage to your heart muscle. It can also improve symptoms, such as angina chest pain and breathing difficulty.

Keywords: Stent, Blood vessels, Angiogram, Catheter.

INTRODUCTION [1,2,3].

A stent is a small tube that can be placed into a blocked area. It's used to replace the flow of blood and other fluids. Stent are made up of metal or plastic, either it made up of specialized fabric materials and also coated with medications which helps to closing the blocked artery.

Plaques are made up of cholesterol and other substance which block the blood vessels. An artery of a heart called a coronary artery if the coronary artery is blocked then the stent is place a catheter this will allow them to develop like a balloon. Then angioplasty allows to open a blockage after that leave the stent in a artery to keep the vessel open.

Stents are also used to prevent aneurysms from splitting in our brain, aorta, or other blood vessels.

Apart from that blood vessel, stents can open any of the following pathways:

1. Bile ducts, which are tubes that carry bile to and from digestive organs
2. Urethras, which are tubes that carry urine from the kidneys to the bladder
3. Bronchi, which are small airways in the lungs

These tubes are blocked just like blood vessels.

Stent Performance [4,5,6].

There are several ways to place a stent. The insertion of stent using a minimally invasive procedure, there will make a small cut using a catheter to guide specific tools into our blood vessels to reach the place where it needs a stent. This cut is generally in the groin or arm. Some of these tools having a camera at the end that helps to guide the stent. During this procedure, we can use an imaging technique called an angiogram. It will help the stent to move through the vessel. Using the necessary tools, locate the blocked vessel and install the stent. Then the instruments will remove from our body and close the cut.

Instruction to be Followed After a Stent Insertion [7,8].

After an insertion feel a bit of soreness at the site of incision. To treat these problem Mild painkillers is used. Anticoagulant medication is used to prevent clotting. The doctor will typically want patient to remain in the hospital overnight. To ensure there are no complications. Patient might need to stay even longer if patient needed the stent because of a coronary event, such as a heart attack or stroke. After return home, drink plenty of fluids and restrict physical activity for some time.

Types of Stents

Cardiac Stent [9,10,11].

An oxygen high level of blood supply by Coronary arteries to the heart muscle, over time, cholesterol can be developed in coronary arteries. Due to this limit blood flows to the heart. This is known as coronary heart disease [CHD].. It can damage heart muscle and gives risk of having a heart attack. A cardiac stent is used to treat blocked or a risk coronary arteries, it can also used to improve blood flow immediately. Cardiac stents are expandable coils and it made up of metal mesh.

There are 5 type of cardiac stent depending on the surgery,

Dual Therapy Stent: [12,13,14].

Dual therapy stenting is a form of heart stent surgery that has shown huge results in clinical trials throughout the world. In Dual therapy stents, the polymer all over the stent is coated with medication to ensure that the walls of the arteries do not close down and the high-flown region is provided with the medication essential to improve the process of cell generation. The insides of the stent are coated with EPC technology that uplift the growth of healthy tissue and provides speedy recovery in the coverage of the stent structure.

Bioresorbable Vascular Scaffold: [15,16,17].

Bioresorbable Vascular Scaffolds are made by modern medicine for the latest technological advancements in the field of heart stent surgery. It is made up of natural elements in the body, thereby making it dissolvable over time. Using bare-metal stents is a widely adopted practice, but is now being replaced by BVS as it does not pose the risk of long term stent thrombosis.

Bio-Engineered Stent: [18,19,20].

Bio-engineered stents first get approval in Europe and have been under goes global adoption ever since. A Bio-engineered stent used in heart stent surgery which is a new form of alternative. It consists of cobalt and chromium mesh and it is thinner and more flexible. It enables to heal the closure area which comes with endothelial progenitor cell **[**EPC**].** technology and raise its cell walls in due course of time. These Bio-engineered stents is element for a Dual-helix stent design and make them choice for a longer duration. EPC also forms shelter against thrombosis and modular rest enosis.

Drug-Eluting Stent: [21,22].

Drug-eluting stents are stents coated with medication that keep the blood clot from occurring again. These stents are used to treat the narrowing of heart arteries. It releases a sequence of blood into the bloodstream. This is not suggested for a patient who are suffered from clotting and bleeding problems.

Bare Metal Stent [23,24,25].

Bare-metal stents are present no outer coating and it is made up of aluminum, stainless steel and nickel. This stents are used to removing the clots from an artery and keep the cell walls of the arteries from subsiding. After a bare metal stent heart surgery, the cell wall turns to grow around and keep in place. Although, this lead to the overgrowth of scar tissue around the stent.

Heart Angioplasty and Stent [26,27,28,29].

Angioplasty with stent placement is a short procedure used to open narrow or blocked arteries. This procedure is suitable for different parts of body; it requires only a small incision on the area of the affected veins.

Angioplasty involves in the use of a small balloon to enlarge the artery. A stent is a small wire-tangle tube that your doctor inserts into the artery. The stent halt in a heart to prevent the artery from closing. A surgeon consistently to perform both procedures at the same time,

Peripheral Angioplasty and Stent [30,31,32].

Peripheral arteries disease is caused by atherosclerosis. Atherosclerosis means high cholesterol levels or plaque attach to the walls of arteries. This reduces the flowing space for blood in veins.

Plaque can rise in any parts of our body, including the veins in our arms and legs. These veins and other veins outermost from heart are called peripheral arteries. This is the treatment options for peripheral artery disease **[**PAD**].** and it involves in the narrowing of arteries in limbs. If medication and other treatments don't help for PAD, then the doctor preferred for angioplasty and stent placement. It's also used as an urgency procedure if the patient having a heart attacks or stroke.

Drug Eluting Stent [21,22,33].

A drug-eluting stent is coated with extended release medicine. That medication is gradually released into the blood vessel to prevent from plaque blocked again. Coronary artery disease **[**CAD**].** means Coronary arteries become narrowed by plaque.This condition can break the flow of blood to heart. If the heart cannot get enough oxygen-rich blood, then the patient at greater risk of having a heart attacks. During this stage the physician advised to use stent treatment and the stent procedure called a coronary angioplasty, a physician will insert a stent into coronary artery at the place of damage. A stent is a small tube made of metal tangle. This is designed to carrier artery walls to

prevent the blocks formed by plaque and help to flow the blood more freely to the heart. According to review issued in American Family Physician, after angioplasty surgery without a stent about 40 percent of people have experienced an artery becomes narrowed again called rest enosis. After this can be drops to about 30 percent while using a bare stent. It drops to less than 10 percent while using a drug-eluting stent.

Esophageal Stent [34,35,36].

An esophageal stent is a tube which is placed on esophagus **[**that means throat**].** to keep open a blocked area. This tube helps to swallow solid and liquid materials. Esophagus is the muscular tube connecting the back of our mouth to stomach. The muscles of esophagus contract when we swallow any solid and liquid materials. It propels the solid and liquid materials into our stomach. The medical term of dysphagia means a portion of esophagus can partly block. That can make it difficult to swallow. It may produce a pain when we swallow or feel like food is get stuck in our chest portion or a food may come back up after we swallow. An esophageal stent can help reopen the blocked esophagus. The procedure take place under general anesthesia to feel like no pain. During the procedure, the surgeon places a long thin tube **[**catheter**].** down the back of the mouth and into the esophagus. Then the surgeon places a folded-up stent over the catheter in the correct position across the blockage. The stent give support and expands against the walls of esophagus. After that removes the catheter and leaves the stent in esophagus.

Intracranial Stents [37,38,39,40]

Intracranial Stents is a blocking of an artery in the brain and reducing the blood flow to the organ. When plaque-causing agents block the carotid artery and reduce the flow of oxygen-rich blood reaching the brain. The symptoms of this condition are blurry vision, giddiness and nausea. If this condition is untreated, then it can be lead to strokes. At this condition intracranial stent is placed in the area of plaque developed in carotid artery near the neck either a veins in a brain. The procedures involved in the treatment of intracranial stenosis are difficult, time-consuming as the arteries in the brain are small and placed in a number of loops via the brain.

Bronchial Stents [41,42,43].

Bronchial stents are used to keep bronchial openings in lungs. Bronchial stents are also called Airway stents. Bronchial stents are used when tumour blocks the blood flow in the bronchi either when the bronchi are trembled caused by the natural reasons, lymphoma or other metastasizing diseases. Airway stents are placed via an incision in the neck or inserted orally. The stent helps the smooth flow of air in and out of the lungs.

Urethral Stents [44,45,46,47].

Urethral stenting is done when the blood clots in urethra or kidney stones or infection or other reasons. The urethra is a long thin tube that connects the kidneys to the urinary bladder. Its function is to discharge the toxic substances filtered by the kidney via the bladder. In this condition urethral stent is used and it does not involve an incision through the skin. But a stent is placed in the urethral tubes for removing the clotting agents in the affected area.

Biliary Stent [48,49,50].

Biliary stent is used for the treatment of intructive jaundice. This condition is a formation of bile in the liver causes a tumor. Bile is a substance made up of Bilirubin and its inadequate formation that cause jaundice. If it is untreated then it becomes very dangerous. In a biliary stent is placed in the affected area of the blood vessel to keep the steady flow and prevent the further formation of bile in the liver.

Stent Manufacturing Design Process [51,52,53,54,55].

Mechanical Properties

Stent's mechanical properties are interrelated and sometimes contradictory, requiring careful compromise between geometrical and material aspects.

- The geometrical aspects are coil, helical spiral, woven, individual ring and sequential ring.

- The material aspects are coil EsophaCoil, Closed cell Palmaz-Schatz and open cell smart.

Manufacturing Process

Five techniques has been used to manufacture stents: etching, micro-electro discharge machining, electroforming, die-casting and laser cutting.

Additional Properties

Although it constitutes the final layer of the stent manufacturing, additional properties cover a range of modifications to stent designs that sometimes become crucial. The additional properties are Radiopacity markers, drug release.

Polymes Used in Stent Preparation [56,57,58,59].

Non-degradable and fully degradable polymers are used is give in table 1. Most common polymer coating techniques in stent manufacturing industries are Dip coating, Electro-treated coating, Plasma treated coating and Spray coating. Polymers are commonly used to prepare stent.

Common Procedure for Stent Placement

Stent Procedure [4,5,6,60,61,62,63].

Stent placement is a minimal procedure but it may take longer time if stents need to be placed in more than one artery. First give a local anesthetic to the patient that helps them to relax body and mind or feel like sleepy. Most people are awake during this procedure, but they don't feel any pain. There are several steps to the procedure:

Making the Incision

Stent placement is a small invasive procedure that is done by making a small incision, usually in heart, arms, legs, groin or hip. The goal is to create an incision to access the blocked area or narrowed artery that causing a health issues.

Locating the Blockage

Through that incision, the surgeon will insert a thin & flexile tube known as a catheter. With the help of angiogram guide the catheter through arteries to the blockage. During this step, view the arteries using a special X-ray called a fluoroscopy. And the doctor may use a dye to identify and locate the blockage.

Placing the Stent

Next the surgeon wills ravine a small wire through the catheter. If the procedure is a placement of angioplasty with stent then the surgeon will place the second catheter. Then the catheter is attached to a small balloon will come after the guide wire. It will be bloated, once the balloon reaches the blocked artery. This pressures the artery to open the blocks and allows blood to flow return. The stent will be inserted at the same time and expands with the balloon. After that the surgeon will remove the catheter once the stent is protected and assure that the stent is in place.Some stents are coated in medicine that slowly releases into artery called drug-eluting stents. This keeps the veins smooth and open, and it helps prevent futher blockages.

Closing the Incision

Finally in the stent placement, the incision will be closed and dressed, and then the patient will be taken to a recovery room for observation. A nurse will monitor blood pressure and heart rate of the patient. Most stent placements need an overnight visit to assure that there are no problems.

Catheter Procedure [64,65,66].

A catheter is a diagnostic tool used in the treatment for certain types of heart disease. The surgeons gives Catheter procedures an in-deep look at the arteries well known to the heart and also allow them to cure structural problems such as irregular fatigue, rhythms and other potentially risking symptoms.

Types of Catheter Procedures

Cardiac Catheterization [67,68,69,70].

Cardiac catheterization is a procedure that gives overly detailed pictures of coronary arteries. It allows to determine the type of illness and to treat the problem. A catheter is a thin, ravine tube that inserts into a blood vessel and guides toward heart. They'll generally use a vessel in groin, neck, or arm. It may be insert with dye and the catheter help to make the arteries and blood vessels more visible. Cardiac catheterization examines pressure, flow rate and oxygen level in blood. During this procedure take a blood samples and a biopsy of heart muscle.

Catheter Ablation [71,72,73].

Catheter ablation is a procedure that can act to treat some heart arrhythmias, which are called irregular heartbeats. The catheter ablation is done when medications don't control arrhythmia. Other reasons for catheter ablation include:

1. Ventricular tachycardia, which is a life-threatening rapid heartbeat that reduces the blood flow to your body
2. Ventricular fibrillation, which is irregular electrical activity in your heart that leads to life-threatening cardiac arrest
3. An accessory pathway, which is a congenital condition in which additional pathways exist between the heart's atria and ventricles, causing an irregular beating pattern
4. Arterial fibrillation which is a rapid, flutter-like heartbeat due to extra electrical impulses

Risk Associated With A Catheter Procedure [74,75,76].

Heart catheter procedures done in a hospital setting, the patient takes fasting for at least eight hours before catheterization preparation. Risks are uncommon but may include:

- Blood clots.
- Excessive bleeding.
- An allergic reaction to the contrast dye.
- Low blood pressure readings.
- An accumulation of fluid between your heart and its outer covering.
- A stroke.
- A heart attack.

RISK ASSOCIATED WITH STENT PROCEDURE 977,78,79,80].

- An allergic reaction to medication during the procedure
- Breathing problem caused by using anesthesia
- Blood clotting
- Infections of the vessels
- Kidney stones formed by using the stent in urethera
- Bleeding
- A blockage of the artery
- Irregular heart beats
- Kidney failure
- Mild chest pain
- Rare side effects include seizure
- Rapture of artery

- Rare in scare tissues form after stent
- Pain in esophagus or new hole in esophagus
- Heart burns
- Movement of stent.

Prevention [81,82,83].

While stent placement observed an individual blockage, it doesn't spot the intrinsic cause of the blockage. To prevent other blockages and reduce risk form by other medical conditions, so the patient can make particular lifestyle changes, such as

- Eating a healthy diet for heart by limiting intake of saturated fat, sodium, and refined foods.
- Quitting smoking if you smoke because it increases risk of PAD.
- Managing stress.
- Getting regular exercise.
- The long-term use of anticlotting drugs.

Benefits of Stents [84,85,86].

- Stenting has a positive impact on quality of life for many people.
- The lifesaver of coronary heart disease is called combination of angioplasty and stenting, especially performed right after a heart attack.
- It can substantially improve our blood flow.
- It helps to prevent further damage to your heart muscle. It can also improve symptoms, such as angina chest pain and breathing difficulty.
- Stenting may eliminate need for coronary bypass surgery, in some cases.
- Drug-eluting stent can help to avoid plaque form again.
- The procedure to insert a stent is much less occupied than bypass surgery, which is generally advised for people who have more than two blocks. Compare with coronary bypass surgery most people recover faster using drug eluting stent.

CONCLUSION

Stent is a treatment of choice for the patient with a high risk of plaque form in a body. For this purpose the surgeons use various types of stents like cardiac stent, Heart angioplasty and stent, Peripheral angioplasty stent, Drug eluting stent, Esophageal stent, Intracranial stents, Bronchial Stents, Urethral stents, Biliary stent. Compared with bypass surgery most of people recover faster while using stent treatment. It helps to prevent re-formation of plaque. To overcome the limitations, there have been many reports as the treatment option of choice for stent design is more benefits than bypass surgery. The stent treatments have a major application in cardiology and now it developed to next level with some technologies.

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TABLE 1:

POLYMERS	**EXAMPLES**
Non-degradable	316 stainless steels **[**SS316**].** Chromium Nickel Molybdenum alloy of steel Nitinol
Fully degradable	Magnesium **[**Mg**].** Magnesium Poly-l-lactide acid **[**PLLA**].** Renewable resources, such as corn starch Polycaprolactone **[**PCL**].**

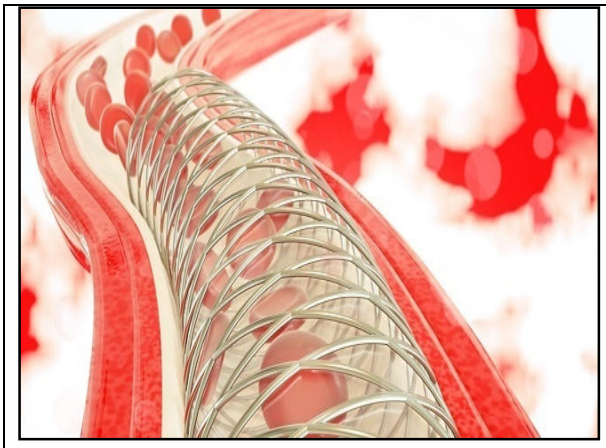

Fig:1 Stent

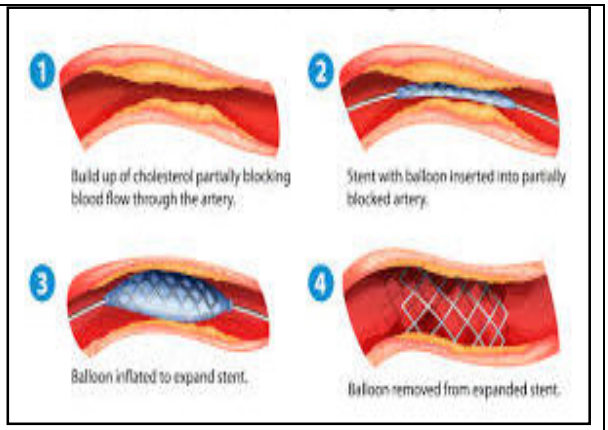

Fig: 2 stent placement

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REVIEW ARTICLE

Study on Impact of Work from Home on Work Life Balance of IT-Employees During COVID-19

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ABSTRACT

Work from has now become the new normal all over the world, many private and public organization now offer work from home as an alternative way of working. Working from remote has both benefits and drawbacks for employee and employers when it is compared to office working. The primary objective of the study is to analyse the impact of work from home and work life balance in pandemic situation with special reference to software industry in Coimbatore district. The data required for the study is collected through questionnaire. The factors of work from home that have a significant impact on work life balance have also been analysed and insights have been obtained.

Keywords: Work from home, COVID-19, IT - Employees

INTRODUCTION

World is witnessing the impact of Covid-19 on all aspects of life, in all countries and in almost all the industries. No one is sure about how much and how long the impact of the pandemic will last on the world's economy. New normal "Work from Home" is followed by Indian IT industry as per government's rule during the lockdown. As a result, more number of employees worked from home with 65% of them from metros and rest 35% from small towns. During the lockdown, the IT industry transitioned to Work from Home model, smoothly providing business deliverables to clients without lowering quality or productivity, surprising industry leaders and customers.

Manpower is the base of IT companies, IT sector totally depends on humans and are not able to operate due to restriction in movement of people arising from lockdown and quarantine. Consequently, some are not able to deliver the project on time, and also result in declining of project. To better understand, the implication of work from home including readiness of different sectors, cities, and occupations, the suitability of diverse occupations to work from home in India was measured. Workplace culture is typically defined by a number of factors such as the organizational structure, management practices, company policies, company's mission, vision and values, the type of people that are employed in a business and how they interact and importantly workplace environment. The new environment for work is home and online. Interaction is via collaboration tools, in which some employees are facing issues.

Need For the Study

Work from Home

Work From home is a concept where the employee can do his/her job from home in their own flexible time. Connecting remotely gives flexible working hours to the employee as well as the job for the employer is done with ease. Work from home is helpful to delivering work life balance to the employee, and also helps the company to get the work done as usual. However not all are comfortable with this new normal. The following points can help workers who are new to remote working – or who are having trouble staying productive from work from home: control your environment, manage your time, prevent distractions, work securely, combat feeling of isolation

Work Life Balance

Work life Balance play a significant part in all lives. It is no easy way to achieve work-life balance in today's life. It is becoming more difficult to separate work from personal lives, prime reason being that we are increasingly growing through technology and social media. Maintaining a healthy work-life balance will improve employees productivity and their performance. Some of the best ways to achieve work life balance are, taking time off between break, proper planning, encouraging a healthy lifestyle, time management, paid vacation time , encouraging work from home.

Conceptual Framework

REVIEW OF LITERATURE

Parida (2012): Work life balance of the employees needs to be considered by an organization, as now-a-days lives of both the male and female employees is consumed of personal and family responsibilities and other interests. Gupta and Charu (2013): Chi-square calculation has be used to mention the work life balance and burnout which affects the job satisfaction among employees in IT sector. The data for this study is collected from 100 working employees using the convenience sampling method. Friedman (2014): The author highlights on the value that "to know what matters" - needs to be known by all. "Four circles" representing four domains "work, home, community and self". He suggests modifying the sizes of each circle to reflect how much you value each. This helps to know the values, goals, interests, actions and results of each domain and whether the latter are compatible or opposed to each other.

Derek Thompson (2020): He suggests ways to deliver results and avoid stir-crazy environment assome employees will be working from home environment for the first time, point out how to stay on working task in a new environment that may not lend itself to productivity. Chris Walker (2020): Remote work was accelerating in the U.S even before the pandemic. Two of the facts are obvious that made remote work peak in US, the share of the labor force that works from home tripled in the past 15 years, according to the Federal Reserve. Those two facts are living costs in metros with the highest density of knowledge workers, and technology, such as Slack and Microsoft Teams, that moves collaboration and gossip online.

RESEARCH METHODOLOGY

The study has a major objective to understand the perception on work from home and work life balance of employees in IT company In order to meet this major objective, the objective of study are simplified into two as listed below,

Primary Objective

To analyse the impact of work from home and work life balance in pandemic situation

Secondary Objective

1)Toanalyse how employees from different background, handle the work from home.
2)Toanalyse the communication, distraction, stress factors of work from home employees.
3) To offer suggestions to handle the imbalance between pandemic and work from home.

Research Design

The study chooses a descriptive research design where primary data is collected through a online survey form with the intension of meeting the study objectives. And the sampling techniques used here is Census Survey

Data Collection

The data needed for the study was collected as primary data through online survey from 152 working employees in an organization. For this purpose the questionnaire based on Likert 5 Point Scale was used and the same was transformed into electronic survey forms using Google Forms platform**.**

Data Interpretation

Reliability Analysis

Reliability Analysis was conducted to test the consistency of the scales used in the questionnaire. Cronbach's Alpha Value was used for the purpose, greater the value of alpha greater is the consistency of scale used. The following tables describes the main part of the whole study where the data collected from various sources are presented and analyzed in detail,

Interpretation

The Cronbach's alpha is .716 for working environment, .812 for communication, .880 for Distractions, .844 for Stress Factors and .853 for Work Life Balance which indicates a high level of internal consistency for our scale with its specific sample.

Percentage Analysis

Percentage Analysis was conducted to study the demography of the collected primary data through online survey forms. Below are the table of results for the percentage analysis conducted for the study

This study contains five major demographic variable they are listed below,
1. Gender of the Respondent
2. Age of the Respondent
3. Marital status of the Respondent
4. Experience of the Respondent
5. Designation of the Respondent

The interpretation for the percentage analysis done are as follows,

Percentage Analysis – Gender of the Respondent

Interpretation

Out of the 152 respondents, 60.5% are Male, that is 92 respondents are Male and 39.5% are Female, that is 60 respondents are Female..

Percentage Analysis – Age of the Respondent

Interpretation

Out of 152 respondents, 39.5% of the respondents belong to the age category of 21-25 Years, 31.6% of the respondent belong to the age category of 26-30 Years, 20.4% of the respondents belong to the age category 31-35 Years, 6.6% of the respondents belong to the age category of 36-40 Years, 2.0% of the respondents belong to the age category of Above 40 years.

Percentage Analysis – Marital Status of the Respondent

Interpretation

Out of the 152 respondents, 46.1 % are Married, that is 70 respondents are Married and 53.9% are unmarried, that is 82 respondents are Unmarried. The result shows the internal employee demography of marital status in the organisation**.**

Percentage Analysis – Experience of the Respondent

Interpretation

Out of the 152 respondents, 36.2 % of the respondents have a work experience of 0-5 Years, 27.0% of the respondents have a work experience of 6-10 Years, 27.0% of the respondents have a work experience of 11-15 Years, 6.6% of the respondents have a work experience of 16-20 Years, 3.3% of the respondents have a work experience of More than 20 Years. The result shows the internal employee demography of work experience in the organisation.

Percentage Analysis –Designation of the Respondent

Interpretation

Out of the 152 respondents, 38.8% of the respondents are Associate software engineers, 27.0% of the respondents are senior software Engineer, 13.8% of the respondents are Team Leader, 11.2% of the respondents are Associate Manager, 6.6% of the respondents are Senior Manager, 2.6% of the respondents are Manager. The result shows the internal employee demography of Designation in the organisation**.**

Correlation Analysis

Pearson Correlation measures a degree of the linear relationship of a two variable. By of a linear relationship, we mean that the relationship can be well characterized by a straight line. Correlation will range from -1.0 to +1.0, Pearson correlation is given by the letter r, Factor having correlation value +1 are said to be highly correlated with each other, value -1 are said to be weakly correlated with each other. The table of results for the correlation Analysis conducted on the data of the study is as follows**,**

Interpretation

From the coefficients given in the above table it is clear that there is a significant correlation between all the factors that has an impact on work from home. It can be inferred that the effect of change in one factor will influence the other factor positively. Therefore, a change in the factor work life balance will affect all other factors working environment, communication, distractions and stress factors

Regression Analysis

Regression Analysis is one of the important and widely used statistical tool for finding a relationship between a, dependent variable and one or more independent variable. As far this study is concerned linear regression

techniques using analysis of variance (ANOVA) has been used to identify the relationship between the dependent and independent variable

Hypothesis are to be set to conduct the analysis and infer the result, two hypothesis are set, namely Null Hypothesis (H0) and Alternate Hypothesis (H1). If the result are significantly significant, then Null Hypothesis is rejected and Alternate Hypothesis(H1) is accepted and vice versa if results are not significantly significant.

a. predictors(constant): Working Environment, Communication, Distraction, Stress Factor

b. Dependent Variable: Work life Balance

Interpretation

1. From the table, R value represents the simple correlation and is 0.671 which indicates a high degree correlation.
2. R square 0.451 indicates how much of the total variation in the dependent variable can be explained by independent variables.
3. The statistical significance of the regression which is higher than 0.5 indicates that over all regression model statistically predicts the outcome variable

Analysis Of Variance Anova

The five factors of work from home impacting the employees were taken to test whether there was any influence of the demographic profile of the respondents on pandemic situations. Keeping this as an objective, the data was collected and worked out for the testing of the hypothesis at 5% level of significance using the Analysis of Variance.

One-Way Anovabetween the Demographic Profile and the Factor Work Life Balance

H0 : There is no significant difference between the demographic profile of respondents and the factor work Life Balance

H1: There is a significant difference between the demographic profile of respondents and the factor Work Life Balance

Interpretation

The result shows that the obtained significance value is 0.933, 0.258, 0.286, 0.830, 0.924, which is greater than 0.05, provided that the level of significance is at 5%. Therefore the data is not statistically significant, which means that Null Hypothesis (H0) should be accepted and Alternate Hypothesis (H1) should be rejected.

Limitations ofthe Study

The study also has a few limitations, the limitation of the study are because of the following factors listed below,

1.The study results are based on the data from only 152 respondents

2. The study has been conducted for a particular software company only

3. The study would be relevant only to present situation

4. Limited number of samples was selected for study and this sample may not be a true representation of the entire population because the sample's view might deviate from the view of population

Findings

1. From the Percentage Analysis, it was found that people between the age of 21-25 are maximum work from home

2. Majority of the Respondents are Male

3. Majority of work from home employees are Unmarried

4. Majority of the respondents have the work Experience of 0-5 Years

5. Majority of the respondents Designation is Associate Software Engineer

6. By using One-way Anova it was found that the demographic profile of the respondents i.e. age, gender, marital status, Work Experience, designation add an effect on the factor work life balance

7. By using the Correlation Analysis, it was found that an effect of change in one factor will affect the other factors positively and vice versa.

Suggestions

1.The IT companies need to follow the government rules in pandemic situations.
2.Employees need to adopt the work from home culture to balance the work life.
3.The companies need to give proper training to all the employees to work from home.
4.Both employers and employees must learn effective technology to work from home.
5.Companies need to provide the equipment to the employees or the employees can use their finance to buy equipment and can be claimed from the company.
6.Monthly claim for Internet can be provided for the employees may be 1000 per month, that should be sufficient.
7.Daily scrum or team call (using zoom, Microsoft teams …) can be made with teams so that freshers having queries can be cleared, this also helps the TL to track the work of employees
8.Awareness programs can be conducted for employees about work life balance
9.Yoga class and online fun activity can be conducted twice a week which might relax the employees

CONCLUSION

From the above study it can be concluded that work from home has a statistically significant impact on work life Balance. As it depends on various factors such as working environment, communication, distractions, stress factors and work life balance. But in this pandemic situation the employees need to adapt the work from home culture for financial growth of the family and company

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Table 1. Reliability statistics for the factor working environment, Communication, Distraction, Stress Factor and Work Life Balance:

Reliability Statistics			
Factors	**Cronbach's Alpha**	**Cronbach's Alpha Based on Standardized Items**	**No. of Items**
Working Environment	.727	.716	7
Communication	.812	.812	8
Distractions	.880	.880	4
Stress Factor	.844	.847	6
Work Life Balance	.853	.853	5

Table 2. Percentage Analysis – Gender of the Respondent

PERCENTAGE ANALYSISC-GENDER OF THE RESPONDENT					
	Component Analysed	**Frequency**	**Present**	**Valid percent**	**Cumulative Percent**
Valid Responses	Male	92	60.5	60.5	60.5
	Female	60	39.5	39.5	100.0
	Total	152	100.0	100.0	

Table 3. Percentage Analysis – Age of the Respondent

PERCENTAGE ANALYSIS – AGE OF THE RESPONDENT					
	Component Analysis	**Frequency**	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid Responses	**21-25 Years**	**60**	**39.5**	**39.5**	**39.5**
	26-30 Years	**48**	**31.6**	**31.6**	**71.1**
	31-35 Years	**31**	**20.4**	**20.4**	**91.4**
	36-40 Years	**10**	**6.6**	**6.6**	**98.0**
	Above 40 Years	**3**	**2.0**	**2.0**	**100.0**
	Total	**152**	**100.0**	**100.0**	

Table 4. Percentage Analysis – Marital Status of the Respondent

PERCENTAGE ANALYSISC-MARITAL STATUS OF THE RESPONDENT					
	Component Analysed	Frequency	Present	Valid percent	Cumulative Percent
Valid Responses	Married	70	46.1	46.1	100.0
	Unmarried	82	53.9	53.9	53.9
	Total	152	100.0	100.0	

Table 5. Percentage Analysis – Experience of the Respondent

PERCENTAGE ANALYSIS – EXPERIENCE OF THE RESPONDENT					
	Component Analysis	Frequency	Percent	Valid Percent	Cumulative Percent
Valid Responses	0-5 Years	55	36.2	36.2	36.2
	6-10 Years	41	27.0	27.0	63.2
	11-15 Years	41	27.0	27.0	90.1
	16-20 Years	10	6.6	6.6	96.7
	More than 20 Years	5	3.3	3.3	100.0
	Total	152	100.0	100.0	

Table 6. Percentage Analysis –Designation of the Respondent

PERCENTAGE ANALYSIS – DESIGNATION OF THE RESPONDENT					
	Component Analysis	Frequency	Percent	Valid Percent	Cumulative Percent
Valid Responses	Associate Software Engineer	59	38.8	38.8	38.8
	Senior Software Engineer	41	27.0	27.0	65.8
	Team Leader	21	13.8	13.8	79.6
	Associate Manager	17	11.2	11.2	90.8
	Senior Manager	10	6.6	6.6	97.4
	Manager	4	2.6	2.6	100.0
	Total	152	100.0	100.0	

Table 7. Correlation Analysis

		WORKING ENVIRONMENT	COMMUNICATION	DISTRACTIONS	STRESS FACTOR	WORK LIFE BALANCE
Working Environment	Pearson correlation	1	.566**	.380*	.450**	.406*
	Sig (2 tailed)		.000	.000	.000	.000
	N	152	152	152	152	152
communication	Pearson correlation	.566*	1	.655*	.712**	.526**
	Sig (2 tailed)	.000		.000	.000	.000
	N	152	152	152	152	152
Distractions	Pearson correlation	.380**	.655**	1	.724**	.577**
	Sig (2 tailed)	.000	.000		.000	.000
	N	152	152	152	152	152
Stress Factor	Pearson correlation	.450**	.712**	.724**	1	.649**
	Sig (2 tailed)	.000	.000	.000		.000
	N	152	152	152	152	152
Work Life Balance	Pearson correlation	.406*	.526**	.557**	.649**	1
	Sig (2 tailed)	.000	.000	.000	.000	.000
	N	152	152	152	152	152

** correlation is significant at the 0.01 level(2-tailed)

Table 8. Regression Analysis

Model Summary					
Model	**R**	**R Square**	**Adjusted R square**	**Std. Error of the Estimate**	**Durbin - Watson**
1	.671	.451	.436	.75945	2.052

a. predictors(constant): Working Environment, Communication, Distraction, Stress Factor

b. Dependent Variable: Work life Balance

Table 9. One-way Anova between the demographic profile and the factor work Life Balance

ANOVA						
		Sum of square	**df**	**Mean Square**	**f**	**sig**
Gender of the Respondent	**Between Groups**	2.575	21	.143	.542	.933
	Within Groups	34.599	131	.264		
	Total	37.173	152			
Marital Status of the Respondent	**Between Groups**	3.761	21	.209	1.215	.258
	Within Groups	22.532	131	.172		
	Total	26.293	152			
Age of the Respondent	**Between Groups**	8.941	21	.497	1.181	.286
	Within Groups	55.119	131	.421		
	Total	64.060	152			
Experience of the Respondent	**Between Groups**	3.515	21	.195	.676	.830
	Within Groups	37.845	131	.289		
	Total	41.360	152			
Designation of the Respondent	**Between Groups**	2.478	21	.138	.557	.924
	Within Groups	32.382	131	.247		
	Total	34.860	152			

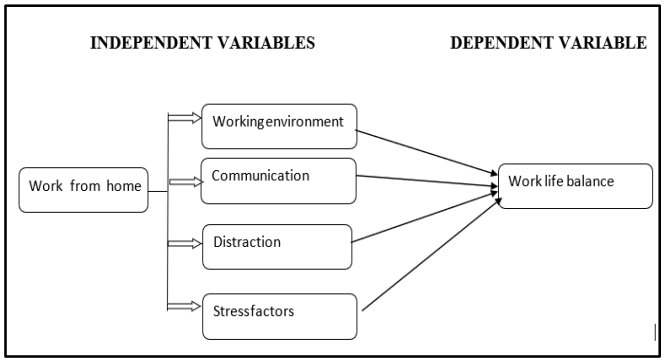

Fig.1.Conceptual Framework

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RESEARCH ARTICLE

Dermatoglyphics: A Predictive Tool for Determination of Criminal Tendency- A Case-Control Study

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ABSTRACT

Dermatoglyphics is unique and individualistic and is a valuable tool for identification. These are friction ridges of the skin and are formed in the uterus and stay unchanged until the end of a person's life. Many researchers believe that genetics play an important role in the formation of dermatoglyphics. The main aim of this research is to ascertain the association between digital dermatoglyphics and criminal tendency by studying fingerprint patterns in the normal population and criminal group. It is also done to detect the frequency of occurrence of digital dermatoglyphics on each digit and their comparison and to establish the predictive role of dermatoglyphics. For this purpose, 1800 fingerprints were obtained through the inking method and analyzed. Statistical methods as Arithmetical mean, percentage, chi-square were done to compute the results of the study. Whorl patterns were found more in cases than in the control group. The study indicates that dermatoglyphics is linked to criminal tendency and establishes it is non-invasive, easy to apply, and economical tool for predicting criminal tendency.

Keywords: Criminal tendency, arch, whorl, Loop, Genetics, Dermatoglyphics, Predictive tool

INTRODUCTION

Our palmar and plantar skin is composed of elevations and depressions. Dermatoglyphics, a Greek word, means scientifically studying elevations and depressions on friction ridge skin. The ridges are formed in the 12 to 13th week of the development of an embryo and are fully formed by the sixth month. It is a general belief that brain cell

formation and dermatoglyphics formation happened together and hence any kind of gene modification is reflected in the dermatoglyphic formation. [Solhi *et al.*2010; Madan *et al.* 2011; Yang *et al.* 2016]. Many researchers utilized the potential of dermatoglyphics as a predictive tool in clinical medicine. Diseases as Cancer [Sakineh Abbasi,2006], schizophrenia [Bramon,2005], diabetes [Desai & Hadimani, 2013], heritable Multiple intelligence [Adekoya *et al.* 2013], Leprosy[Gupta, and Tutakne, 1986],] & Hypertension [Shirali *et al.,* 2018] were studied and found dermatoglyphics played an important role. Vogel & Motulsky,[1986] observed that tendency to commit crimes is hereditary in their study on twins. Pricilla *et al* [2018] noted that differences exist in dermatoglyphic traits between controls and female convicted criminals. Yarovenko [2015] found a greater number of whorls in dermatoglyphics of a person who killed 19 people. Karim *et al.,* [2019] in their study on fingerprint patterns in sexual offenders observed a decrease of the ulnar loop in both hands [right and left]. Most research was conducted to link dermatoglyphics and diseases but not much work has been done to determine the role of hereditary criminal tendency and its association with dermatoglyphics.

Objectives of the Present Study

The objectives of this research are:

- To study fingerprint patterns of criminal group and control group
- To detect the frequency of occurrence of patterns on each digit in each case
- To ascertain the association between digital dermatoglyphics and criminal tendency by comparing the patterns in both cases.

MATERIALS AND METHODS

Research Methodology Design

The research design selected was a case-control study. For detecting criminal tendency, for study purposes, the normal population and criminals group were selected for a case-control study.

Type and age of Participants

The participants were criminals and control groups in the age group of 18-70. As the research involved the study of fingerprints bilaterally [samples of all fingers of both hands], a sample size of </= 100 was considered.

Data Acquisition

For the study, 1800 handprints samples were collected and observed from the control and criminals' group. Ten-digit samples of rolled & plain prints were acquired. The objective was explained and prior consent was obtained. Materials used magnifier with light, scale, black ink with roller and pad, forms for taking prints, cleansing solution, moisturizer.

a] Omission/Exclusion:

1. Improper prints as scarred or damaged were not considered.
2. Fingerprints of people not willing were not taken.

b] Admittance/Inclusion:

1. Age of samples was between 18 yrs to 70yrs.
2. All sexes were treated equally

Sample Collection

To acquire the handprints, all participants were asked to clean and wash their hands well with soap and water. Next, they dried their fingers well before inking. The hands were rolled on the inking pad which was prepared by spreading ink uniformly and rubbed by roller. The inked digits were rolled on format sheets one by one from radial

to ulnar side, all ten of them. Then they washed hands again with a cleansing solution and applied moisturizer. The details of the contributor were noted on the sheets.

Data Entry: The formats of handprints so obtained were categorized and manually sorted. Each criminal and control group was given different nomenclature. The control group samples had 'SHS' and the criminal had 'CHA' as part of their code. The fingerprint patterns on format slips were studied using an LED magnifier and the number and the type of fingerprint pattern were noted. All details were entered systematically into Excel spreadsheets.

Statistical Analysis: As is common with observations, all the data was arranged for a qualitative and quantitative study. Arithmetic calculations as addition, deletion, percentage, etc were done on excel worksheets. All statistical calculations as chi-square- test of independence were done and a value of $p< 0.05$ was considered significant.

RESULT AND DISCUSSION

A total of 1800 fingerprints from 180 human subjects [case and control] were analyzed. The results so obtained were tabulated in various tables given below [Table: 1, 2, 3, & 4].
Table: 1. Fingerprint pattern frequency on individual digits-RH
Table: 2. Fingerprint pattern frequency on individual digits-LH
Table: 3. Individual Fingerprint occurrence in 10 digits of the criminal group
Table: 4.Individual Fingerprint occurrence in 10 digits of the control group

DISCUSSION

From the tables above, it can be observed that loops are the most occurring, followed by whorls and then arches. Arches are occurring more on the left hand and loops and whorls more on the right hand. Arches are the highest on the index finger of both hands in each group and least on the ring finger. This is supported by a study conducted by Ojo *et al.,*[2020].In the control group, loops occur more in the middle finger and less in the ring finger in RH whereas the little finger dominates in LH with the ring finger coming up last. In the criminal group, the little finger shows more occurrence in both hands. Whorls are found more in the case group than in the control group whereas loops are less in the case group than the control group in both hands, except little finger [Table1&2]. This study is supported by research done on dental caries in school children by Sharma *et al.* [2018], wherein whorls patterns were more prominent in the individuals with dental carries (WDC) group than caries free (study) group and loops were more in the study group than WDC group.

It has been observed in Table 3, 4 that in a criminal group, the occurrence of 7 loops was highest whereas 8 &9 loops were more in the control group. Repetition of 9 & 10 whorls and 1 loop were least common in control whereas 6,7,9 &10 whorls and 1 and 4 loop repetition were least frequent in criminals. It can also be seen that the criminal group had a greater number of whorls than the non-criminal /control group. This is found to agree with the study conducted by Matyas [1999] on male criminals.

CONCLUSION

The results of this current study indicate that there is a possibility of interrelation between criminal tendency and dermatoglyphics. It supports the hypothesis that there exists a genetic connection between criminal tendency and dermatoglyphics. The authors acknowledge that further studies involving many more parameters as ridge counts, ATD angle, ABRC, TFRC, and others should be employed and done on a bigger group for confirmation. Findings so obtained are useful to create a forensic model of criminals to develop preventive methods and to help children who

are ''at risk' of becoming criminals. Dermatoglyphics can be utilized as the predictor tool as they are easy to apply and do not change over the lifetime of an individual.

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Abbreviations

RT[Right thumb], RI[right index], RM[right middle], RR[right ring], RL[right little], LT[left thumb], LI[left index], LM[left middle], LR[left ring], LL[left little], RH[right hand] and LH[left hand].

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Table: 1 Fingerprint pattern frequency on individual digits-RH

PATTERNS	GROUPS	Pattern frequency [Highest to lowest]				
Arch	control	Index-8.9	Thumb-2.22	Middle-2.22	Little-1.11	Ring-0
	Criminal	Index-11.1	Thumb-1.11	Middle-1.11	Little-0	Ring-0
Loop	control	Middle-78.9	Little-77.8	Index-58.9	Thumb-57.8	Ring-52.2
	Criminal	Little-82.2	Middle-71.1	Index-40	Thumb-36.6	Ring-33.3
Whorl	control	Ring-47.8	Thumb-40	Index-32.2	Little-21.1	Middle-18.8
	criminal	Ring-66.6	Thumb-62.2	Index-48.8	Middle-27.7	Little-17.7

Table: 2 Fingerprint pattern frequency on individual digits-LH

PATTERNS	GROUPS	Pattern frequency [Highest to lowest]				
Arch	control	Index-14.4	Middle-4.44	Thumb-3.33	Little-1.11	Ring-0
	Criminal	Index-12.2	Thumb-5.55	Middle-3.33	Little-2.22	Ring-0
Loop	control	Little-76.6	Middle-73.3	Thumb-63.3	Index-56.6	Ring-54.5
	Criminal	Little-82.2	Middle-72.2	Ring- 54.4	Index-45.5	Thumb-42.2
Whorl	control	Ring-45.5	Thumb-33.3	Index-28.8	Middle-22.2	Little-22.2
	criminal	Thumb-52.2	Ring-45.5	Index-42.2	Middle-24.4	Little-15.5

Table: 3 Prevalence of Individual Fingerprint Patterns in 10 digits of the criminal group										**Total**
A1-10	A2-7	A3-4	A4-0	A5-0	A6-0	A7-0	A8-0	A9-0	A10-0	21
U1-5	U2-11	U3-7	U4-5	U5-9	U6-12	U7-18	U8-8	U9-12	U10-7	94
W1-11	W2-7	W3-15	W4-11	W5-8	W6-5	W7-5	W8-12	W9-5	W10-5	84
A= Arch U= Loop, W= Whorl										

Table: 4 Prevalence of Individual Fingerprint Patterns in 10 digits of the control group										**Total**
A_1-10	A2-6	A3-2	A4-1	A5-0	A6-2	A7-0	A8-0	A9-0	A10-0	21
U1-3	U2-5	U3-5	U4-5	U5-7	U6-14	U7-13	U8-15	U9-15	U10-14	96
W1-16	W2-14	W3-12	W4-10	W5-6	W6-4	W7-4	W8-4	W9-3	W10-3	76
A= Arch, U= Loop, W= Whorl										

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RESEARCH ARTICLE

Low Energy N-Ion Irradiation Effects on Cadmium-Telluride (CdTe)

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ABSTRACT

This manuscript includes a Monte-carlo simulation of irradiation of low energy nitrogen ions on the surface of cadmium telluride by using SRIM. We explore the variation in surface properties of this compound with effect of the radiation. Where we discuss the atomic distribution and different energy recoils with respect to the effect of radiation.

Keywords: Cadmium telluride, energy recoils, Nitrogen ions

INTRODUCTION

Cadmium Telluride being a known novel compound to shine in efficient thermal and electrical properties [1,2]. Subsequent discovery of CdTe by Margottete and Fabre lead to put this material in lime light for several years. Then the current researchers are exploring to find the new usage and application of different cadmium based compounds. Simple preparation methods of CdTe is being a hallmark since the time of discovery [3]. This compound has a wide application in photocells since this pertain a high photosensitive behavior. It is well known that CdTe is an efficient semiconductor as compared to the other chalcogenides of cadmium. The high mobility and simple control on conversion of conductivity from P to N type semiconductors, makes it more reliable to use in semiconductor devices like diodes and transistors [4,5]. Since this is sensitive to visible as well as infrared and X-ray radiations, this can be used in photodiodes, infrared telescopes, photo-electric cells etc. In the present context, we perform a Monte-carlo simulation using SRIM [6-9] for irradiating low energy alkali ions on CdTe surface to predict the change in behavior and properties [10-12]. Where, the atomic distribution and energy recoils are discussed in detail. We use the widely used package of SRIM for this purpose and Nitrogen atom with 500 KeV energy is used for irradiation.

RESULTS AND DISCUSSION

We perform a SRIM calculation of N-ion irradiation of energy 500 KeV on the target atom, where the back scattered and transmitted atoms are observed [13]. This calculation is displayed in Fig. 1.This represents the path distribution of recoiled Cd and Te atoms along with the Nitrogen ion and the vacancy produced after the N-ion is irradiated to the CdTe target. The blue dots represent the recoiled atoms and the red line represents the path followed by those atoms and ions after collision. The N-ion range and distribution is illustrated in Fig. 1. When the N-ion with energy 500 KeV is projected to CdTe surface it penetrates to the surface up to a micrometer length and displace the atoms by creating the vacancy. Few Cd and Te atoms recoils after the collision, which leads to the surface modification of this compound. The atomic distribution of Cd and Te is represented in the left panel of Fig. 2, where the cyan and orange color signify the Te and Cd atoms respectively. The lateral distribution is shown in the right panel of the same Fig. Where the radial and projected displacement is clearly significant. The radial and projected straggled atoms are displayed in red and cyan colors respectively. Fig. 3 justify the collision events and impact on target atoms. Here, the target displacement, target vacancies and collision replacement are shown in red, blue and green respectively. We can easily interpret that the replacement collision is very less as compared to the displacement and vacancies. In the left panel of Fig. 4, the energy recoils of Cd and Te atoms are represented in orange and cyan color respectively. The right panel shows that negligible atoms are sputtered with the ion bombardment with energy distribution less than 1.6 KeV. The energy loss after collision are displayed in Fig. 5, where the blue and red colors stand for the energy loss of recoiled atoms and the bombarded ions respectively after ionization. The ionization is more in the N ions as compared to the recoils. The right panel shows that the phonon vibrations are more in the recoils as compared to the ions.

CONCLUSION

We studied the surface modifications of CdTe compound by irradiating with nitrogen atoms of 500 KeV energy. We discuss the displacement and recoils of surface atoms in the target compound. We found the energy of the bombarded ion is sufficient to penetrate upto a micrometer depth in the target surface. The SRIM calculation provided a significant inference of energy distributions and ionization data and tempt the options to open for further studies.

ACKNOWLEDGEMENT

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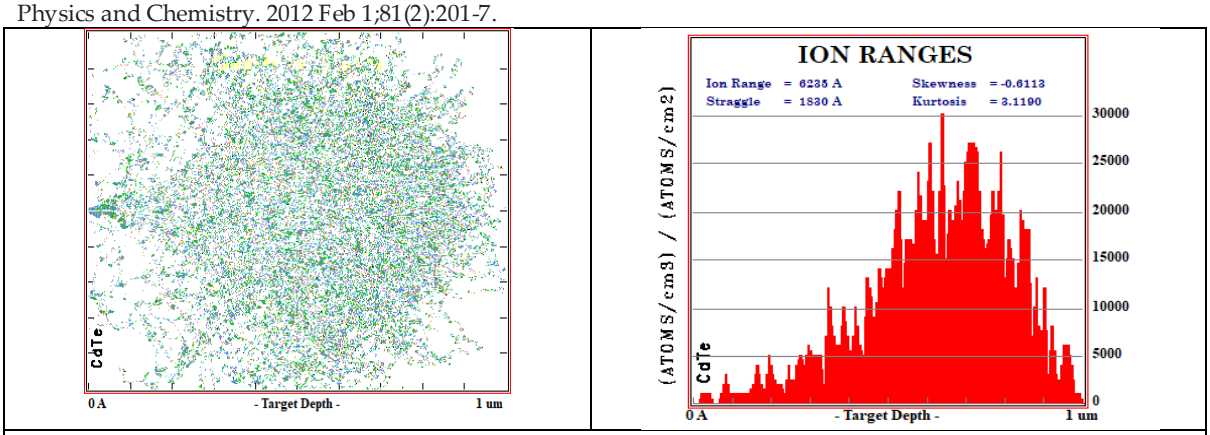

Fig 1. SRIM calculation for 500 KeV Nitrogen irradiation and Ion distribution presented in 2D

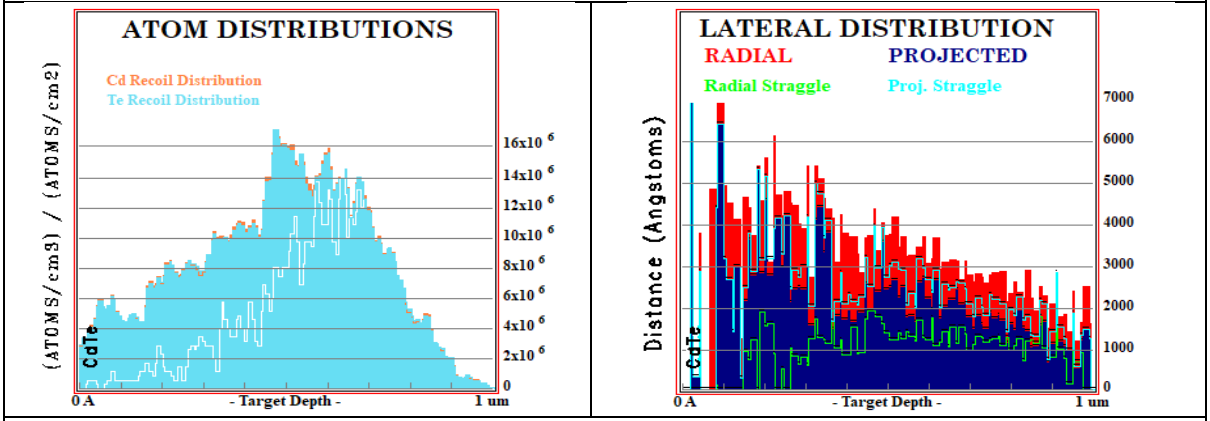

Fig 2. Atomic distribution of Cd and Te atoms after collision

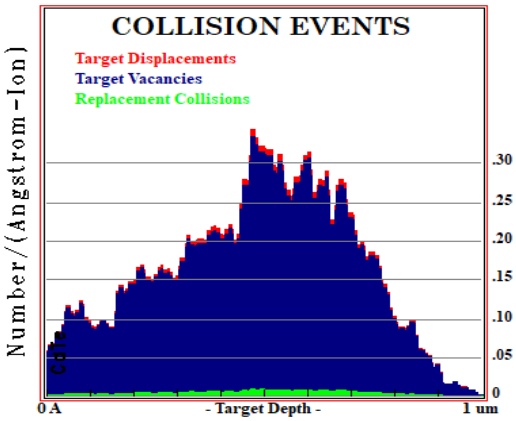

Fig 3. Collision events for N-ion bombardment on CdTe surface

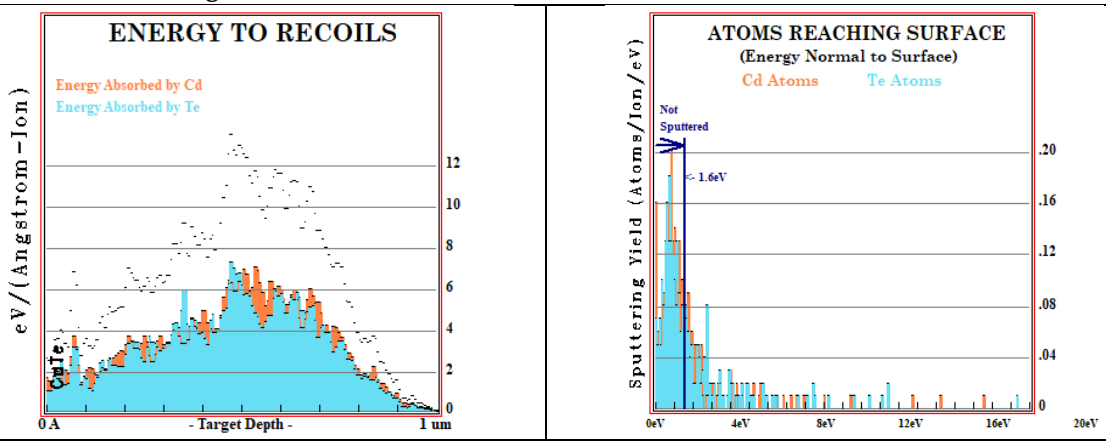

Fig 4. Energy recoils of CdTe after collision

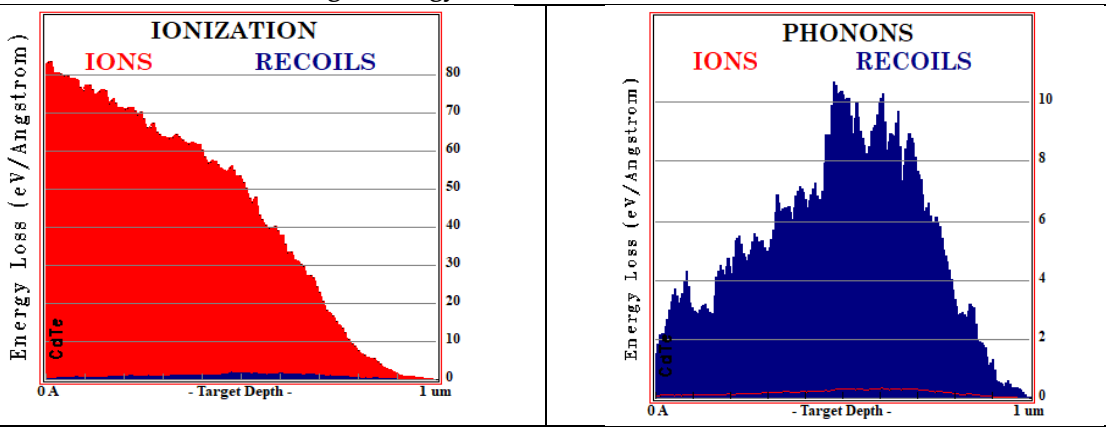

Fig 5. Ion and phonon recoils after the irradiation

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RESEARCH ARTICLE

Assessment of Treatment Strategies and Management of Tinea Infections in a Tertiary Care Teaching Hospital of Salem District

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ABSTRACT

Tinea infections are fungal infections of the skin caused by dermatophytes. It is estimated that 10% to 20% of the world population is affected by fungal skin infections. Sites of infection vary according to geographical location, the organism involved, and environmental and cultural differences. Both Tinea corporis, also referred to as 'ringworm' and Tinea cruris or 'jock itch' are conditions frequently seen by primary care doctors and dermatologists. The diagnosis can be made on clinical appearance and can be confirmed by microscopy or culture. A wide range of topical and oral antifungal drugs are used to treat these superficial dermatomycoses, but it is unclear which are the most effective. The present study is aimed to assess the treatment strategies and management of Tinea infections among the patients. We searched the following databases for Six months in a tertiary care hospital of Salem district, Tamil Nadu. Randomised people with proven Tinea infection of all over the body were selected with 150 participants met the inclusion criteria and found 4 types of tinea these are *T.Corporis, T.Cruris, T.Versicolor* and *T.Incognito.* Treatment duration varied from one week to 6 weeks. The study concludes with the importance of treatment strategies and management of Tinea infections which were evaluated and

analysed. This show the frequently used medications are topical formulation like candid cream and oral formulation Itraconazole were utilised more when compared to the other drugs prescribed.

Keywords: Tinea infections, Itraconazole, Candid cream, Tertiary care hospital

INTRODUCTION

Skin is the largest organ in the body and covers the body's entire external surface. It is made up of three layers, the epidermis, dermis, and the hypodermis, all three of which vary significantly in their anatomy and function. The skin's structure is made up of an intricate network which serves as the body's initial barrier against pathogens, UV light, and chemicals, and mechanical injury. It also regulates temperature and the amount of water released into the environment [1].

Tinea Infections

Tinea is the name of a group of diseases caused by a fungus. Superficial dermatophyte infection has been identified with a variety of terms through the ages although the term "Tinea" has persisted as the most common. Dermatophytes are taxonomically classified into three genera: Trichophyton, Microsporum, and Epidermophyton [2]. Dermatophytes require keratin for growth. Due to this they usually affect hair, nails, and superficial skin that invade and multiply within keratinized tissues causing infection [3]. (It's estimated that 10% to 20% of the world population is affected by fungal skin infections).

Diagnosis

They typically present as a red annular, Scaly, pruritic patch with central clearing and an active border. Lesions may be single or multiple and the size generally ranges from 1 to 5 CM, but larger lesions and confluence of lesions can also occur. Tinea Corporis may be mistaken for many other skin disorders, especially eczema, psoriasis, and Seborrheic dermatitis. A Potassium hydroxide (KOH) preparation is often helpful when the diagnosis is uncertain based on history and visual inspection worsening after empiric treatment with topical steroid should raise the suspicion of a dermatophyte infection. Tinea Corporis, ringworm of the body [4].

Pharmacological Treatment

- The medication may be in the form of powder, ointment or cream. It is applied directly to the affected areas of the skin. There are various types
- Clotrimazole: apply 2-3 times a day for at least four weeks.
- Miconazole: apply twice a day and continue for 10 days after the skin is back to normal
- Econazole: apply twice a day until the skin is back to normal
- Ketoconazole: apply once or twice a day and continue for a few days after the skin is back to normal. Cannot be used for children.
- Terbinafine: apply once or twice a day for one to two weeks. Cannot be used for children.

Non-Pharmacological Treatment

- Avoid sharing towels, hats, hairbrushes, and clothing with someone who has the infection.
- After a shower, dry your skin well- especially between the toes where skin touches skin, such as in the groin and armpits.
- Be sure to maintain good personal hygiene around other people and avoid scratching the affected areas of your skin.

METHODOLOGY

The Prospective Observational study was conducted on Assessment of treatment strategies and management of Tinea infection on Tinea patients in Vinayaka mission's Kirupananda Variyar Medical College and Hospital of Salem District, for a period of 6 months from October 2019 to March 2020. All kinds of information of Tinea patients were collected from the hospital a total of 150 cases was recorded and analysed.

RESULTS AND DISCUSSION

The gender wise classification was made among 150 patients; the female patients were more prone to Tinea infections when compare with male patients. Distribution were made based on the age group 21-40: 63% (95) and followed by 41-60: 30 (20%) and least percentage was found between age groups of 0-20: 23 (16%) and 61-80: 2(1%). The patients were classified according to types of Tinea infection, out of 150 patients the majority of patients were affected with Tinea corporis 68(45%) followed by Tinea versicolor 34(23%) and the least percentage was found Tinea cruris 30(20%) and Tinea incognito 18(12%). Distribution based on occupational status of the affected patients were made who affected the patients were classified based on who affected by Tinea infection was house wife 56(37%) followed by students 40(27%) labour 25(17%), farmer 18(12%) and others 11(7%).

CONCLUSION

The study concludes with the importance of treatment strategies and management of Tinea infections which were evaluated and analysed. This show the frequently used medications are topical formulation like candid cream and oral formulation Itraconazole were utilised more when compared to the other drugs prescribed. Economically candid cream were low cost when compare to other prescribed creams and Itraconazole was slightly high cost when compare to other prescribed drugs, but according to the aggressiveness of the infection new generation drug like Lulibrut and Terbinafine which are higher in cost are prescribed for the better result and cure for the patient. This type of treatment strategies will be decreasing the duration of treatment. Therefore as the cost of drug increases, the duration of treatment decreases and the therapeutical effect of the drug increases which results in better cure in short duration.

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Table 1: Distribution based on the types of Tinea infection

S.No	Types of Tinea	Number of patients (n=150)	Percentage(%)
1	*Tinea corporis*	68	45
2	*Tinea cruris*	30	20
3	*Tinea incognito*	18	12
4	*Tinea versicolor*	34	23
Total		**150**	**100**

Table 2: Distribution based on Duration of Tinea infection

S.No	Duration of infection	Number of patients (n=150)	Percentage(%)
1	Past 10 Days	44	29
2	Past 2 weeks	84	56
3	More than 1 month	22	15

Table 3: Distribution based on Affected Parts

S.No	Affected parts	Number of patients	Percentage(%)
1	Scalp	14	9
2	Trunk	90	60
3	Upper limb	41	27
4	Back	93	62
5	Groin	41	27
6	Lower limb	67	45
7	Foot	16	11
8	Nails	14	9

Table 4: Distribution based on the Illness

S.No	Illness	Number of patients	Percentage(%)
1	Itching	137	91
2	Plaques	91	61
3	Patches	86	57
4	Scaling	94	63
5	Sweating	108	72

Table 5: Distribution based on treatment of Tinea infection

S.No	Treatment	Number of Patients(n=150)	Percentage(%)
1	Oral	0	0
2	Topical	39	26
3	Oral + Topical	111	74
Total		150	100

Table 6: Distribution of drugs based on *Tinea corporis*

S.No	Drugs	Number of Patients	Percentage(%)
1	Oral. Fluconazole	10	8
2	Oral. Itraconazole	11	9
3	Oral. Terbinafine	10	8
4	Candid cream	54	43
5	Ketostar cream	10	8
6	Lulibrut cream	4	3
7	Keto soap	6	5
8	Scalp E shampoo	2	2
9	Candid powder	18	14

Table 7: Distribution of drugs based on *Tinea cruris*

S.No	Drugs	Number of Patients	Percentage(%)
1	Oral. Fluconazole	4	5
2	Oral. Itraconazole	12	16
3	Oral. Terbinafine	14	18
4	Candid Cream	13	17
5	Ketostar cream	13	17
6	Lulibrut cream	3	4
7	Keto soap	4	5
8	Scalp E shampoo	5	7
9	Candid powder	8	11

Table 8: Distribution of drugs based on *Tinea incognito*

S.No	Drugs	Number of Patients	Percentage (%)
1	Oral. Fluconazole	2	5
2	Oral. Itraconazole	15	36
3	Oral. Terbinafine	1	2
4	Candid cream	4	10
5	Ketostar cream	7	17
6	Lulibrut cream	7	17
7	Keto soap	1	2
8	Scalp E shampoo	4	10
9	Candid powder	1	2

Table 9: Distribution of drugs based on *Tinea versicolor*

S.No	Drugs	Number of patients	Percentage (%)
1	Oral. Fluconazole	22	25
2	Oral. Itraconazole	6	7
3	Oral. Terbinafine	7	8
4	Candid cream	12	14
5	Ketostar cream	11	13
6	Lulibrut cream	9	10
7	Keto soap	8	9
8	Scalp E shampoo	2	2
9	Candid powder	10	11

Table 10: Distribution based on Oral drugs

S.No	Drugs	Fluconazole	Percentage (%)	Itraconazole	Percentage (%)	Terbinafine	Percentage (%)
1	*Tinea corporis*	10	26	11	25	10	31
2	*Tinea cruris*	4	11	12	27	14	44
3	*Tinea incognito*	2	5	15	34	1	3
4	*Tinea versicolor*	22	58	6	14	7	22

Table 11: Distribution based on Topical drugs

S. No	Drugs	*Tinea corporis*		*Tinea cruris*		*Tinea incognito*		*Tinea versicolor*	
		No.of Patients	Percentage (%)	No.of Patients	Percentage (%)	No.of Patients	Percentage (%)	No.of Patients	Percentage (%)
1	Candid Cream	54	57	13	28	4	17	12	23
2	Ketostar cream	10	11	13	28	7	29	11	21
3	Lulibrut cream	4	4	3	7	7	29	9	17
4	Keto soap	6	6	4	9	1	4	8	15
5	Scalp E shampoo	2	2	5	11	4	17	2	4
6	Candid powder	18	19	8	17	1	4	10	19

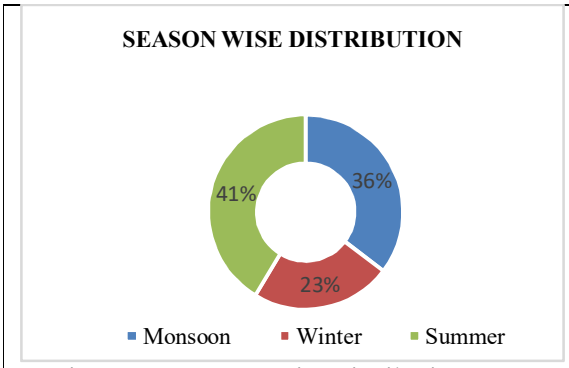

Figure.No.1: Season Wise Distribution

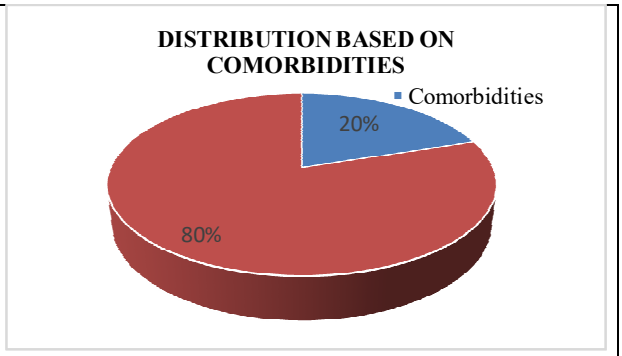

Figure 2: Distribution based on Comorbidities

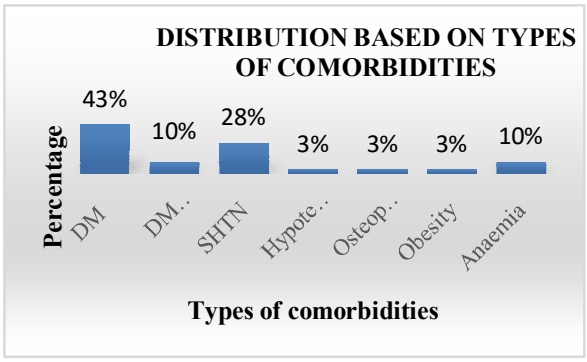

Figure 3: Distribution based on types of Comorbidities

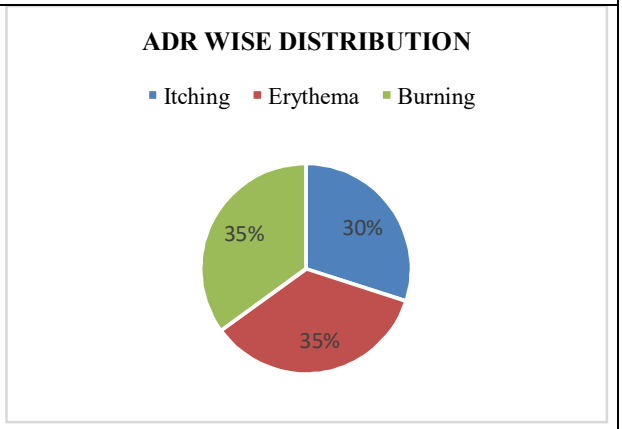

Figure 4: ADR Wise Distribution

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RESEARCH ARTICLE

Green Chemistry Approach for the Functionalization of Reduced Graphene and TiO_2 as Efficient Super Capacitor Application

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ABSTRACT

In order to enhance the capacity of graphene as high performance super capacitor, various graphene composites such as metal oxides/graphene and polymer/ graphene is proposed to incorporate pseudo capacitance with EDLC of graphene. In addition to grapheme composites, organically functionalized graphene is also tested as the super capacitors electrode with pseudo capacitance. TiO_2functionalized graphene shows dramatic increase in the specific capacitance values. However, to the best of our knowledge, there has been no report on the TiO_2 functionalized graphene as super capacitor electrode. Amine functional group in TiO_2 is an electron donating group which could donate electrons to graphene, an electron acceptor which could accept multiple electrons due to its 2D expanse network. Such electron transfer is expected to produce charge differential that yields pseudo capacitance. Herein, The phase structure and micro morphology were characterized XRD, SEM and FT-IR. It was found thatTiO_2nanoparticles were embedded in the grapheme sheets and form a composite structure. The electrochemical properties of the material were tested. The results show that the incorporation of graphene and Titanium dioxide acted as an electrode material. The results concluded that the TiO_2/RGO composite has excellent cycle stability, after 2000 cycles the average specific capacitance retention remains 80%. This is benefit from the introduction of graphene sheets and TiO_2 uniformly load between the sheets of graphene.

Keywords: Titanium dioxides, Graphene, Specific Capacitance, Composites, Nanoparticles

INTRODUCTION

A modern technological society demands the storage of energy on a large scale. In the context of energy storage, a high performance energy storage device is expected to supply energy at a fast rate. A conventional energy storage device such as a capacitor and battery could not full the increasing techno- logical demands as the capacitor is limited by low energy density where as a battery is limited by low power density. In this context, super capacitors are promising energy storage devices with higher energy density than capacitors and deliver energy a higher rate than batteries [1-6]. A super capacitor could be fully charged or discharged in seconds; therefore attracting worldwide research interests due to diverse applications. There are two types of charge storage mechanisms in super capacitors: electrochemical double layer capacitance (EDLC) and pseudo capacitance. In EDLC, electric energy is stored through the accumulation of electric charges at an electrode/electrolyte interface, without Faradaic reaction. Therefore, EDL Care highly stable as they do not involve any phase changes during charge storage process. Carbon such as activated carbon and carbon nano tubes are popular choice for EDL Celectrode. On the other hand, charge storage mechanism of pseudo capacitance is based on Faradaic process where a redox reaction occurs at the electrode surface. Metal oxides and conducting polymers are the common electrode materials with large pseudo capacitance effect. Pseudo- capacitance is generally higher than EDLC due to Faradaic process; however, at the expense of the long term stability of the electrode. Therefore, the integration of both EDL Candpseudo capacitance in a super capacitor could be a solution to fabricate high performance super capacitor with long term stability.

MATERIALS AND METHODS

Graphite powder (fine powder, extra pure) as the starting material was obtained from Merck. Concentrated hydrochloric acid (HCl, 37%), hydrogen peroxide (H_2O_2, 30 wt%), concentrated sulphuric acid (H_2SO_4, 99.9%), potassium permanganate ($KMnO_4$), phosphorus pentoxide (P_2O_5), potassium persulfate ($K_2S_2O_8$), were obtained from Sigma-Aldrich *Azadirachta indica,* commonly known as neem, was collected from Trichy district and extract prepared in our laboratory. All the chemicals were used without further purification.

Synthesis of Grapheme Oxide (GO)

By Hummer's process, GO was synthesized. Graphite powder (1.5 g) was slowly poured to the 1000 mL beaker, which already contains a mixer of sulphuric acid and phosphoric acid (9:1 volume) and slowly stirred until well combined. Potassium permanganate (8 g) was progressively added with continued stirring for 1 h. The temperature was steadily raised to 60 °C and kept under agitation for 12 hours. With 700 ml of ice water and 1 ml of 30 percent H_2O_2 added to prevent the reaction, the substance was slowly diluted. It was demonstrated by a change in colour from brown to yellow. The obtained product was washed with 10% HCl solution and deionized water until the pH was neutralized, then the resulting product was washed with ethanol and dried for 12 h in hot air at 60 ° C. The dark brown GO powder was obtained.

Preparation of *Azadirachta indica* Leaf Extract

Fresh *Azadirachta indica* leaf (10 g) was collected from Kumbakonam, Thanjavur district. Leaf were washed with demineralized water and boiled in 200 ml of demineralized water for 30 minutes at 95 ^oC. The solution was filtered using whatman filter paper and extract was collected and stored in refrigerator at - 4 ^oC.

Preparation of *Azadirachta indica* Leaf Extracts

For the extracts, 10 g of fresh *Azadirachta indica* leaves were taken. The leaves were washed with demineralized water and were boiled for 30 minutes at 95^o C in 200 ml of demineralized water. The solution was filtered and extract was collected using whatman filter paper and placed at - 4 ^oC in the refrigerator.

Green Synthesis of Reduced Graphene Oxide (RGO) By *Azadirachta indica* Leaf Extract

100 mg of GO powder was taken and then 30 ml of demineralized water for 30 minutes was applied with 20 ml of *Azadirachta indica* leaf extract and reflux for 12 hours at 950 °C. The colour of the suspension solution changes from dark brown to dark black after reducing the *Azadirachta indica* leaf extract. By repeated washing with demineralized water until the absence of *Azadirachta indica* leaf extract, the suspension solution obtained was centrifuged at 2000 rpm for 10 minutes. In order to obtain black powder from reduced graphene oxide nano sheets, the final product was dried in a hot-air oven at 500 °C for 12 hours.

Synthesis of Zinc Oxide Doped With Reduced Graphene (ZnO/RGO)

1 gramTiO_2 and 5 g of urea were dissolved in a beaker with 50 mL of deionized water and sonicated for 2 h, then moved to the hydrothermal reactor and stored for 36 h at 90 °C. for 3 minutes, the hydrothermal reaction product was centrifuged at 8000 r/min and washed three times with ethanol to obtain the TiO_2 precursor.1 gram of RGO and 50 ml of 1.0 M TiO_2 solution were added drop wise into 30 ml of 2.0 M NH_4HCO_3 solution under constant stirring at 60°C in water bath for 1 h. The precipitate was separated by filter and washed for three times with double distilled water and ethanol, dried in a vacuum oven at 60°C for 24 h. Finally, the product was calcination at 1200°C for 1 h to obtain black powder of TiO_2/RGO

Sample Characterization

To investigate the microscopic morphology of the samples, scanning electron microscopy was used. The sample composition was analysed by x-ray diffractometry, X-ray photoelectron spectroscopy, Raman spectroscopy and Fourier transform infrared spectroscopy. The capacitance property characterization carried out by a electrochemical workstation (Metrohm-PGSTAT204, Switzerland).In order to prepare a solution of 5 mg/mL, the prepared TiO_2/rGO composite material was ultrasonically dispersed by deionized water, and then 0.5μL solution was pipetted out for applying the surface of a polished glass carbon electrode (with a diameter of 3 mm).After drying the electrode, it was used for the working electrode (with a load density of 0.300 mg/cm2).The counter electrode was used as a platinum mesh, Ag/AgCl is the reference electrode and 6 mol/L KCl solutions are the electrolyte. The potential window of the cyclic voltammetry test and the constant current charge and discharge potential window are −1.0V~0.2 V.

RESULTS AND DISCUSSION

UV–Vis Spectroscopy

Fig.2.shows the UV spectra for GO, rGOandTiO_2-rGO.TheGO exhibits a characteristic peak at 200 nm which could be attributed to the p–p* transition of the C = C bond. The p -conjugation network is restored during reduction process and the corresponding absorption peak is red-shifted to 221nm, as seen in the absorption spectrum of rGO.

X-ray Diffraction (XRD)

Fig. 3. shows the XRD powder diffraction results of RGO and TiO_2/rGO composites. Curve a is XRD spectrum of GO and the diffraction peak is not very obvious, indicating that the crystallinity is not good, and the precursor is inferior in crystallinity. The XRD spectrum of curve b shown that characteristic diffraction peaks appear at 36.96 (111), 43.08 (200), 62.56 (220),74.92 (311), 78.72 (222) position and the intensities are in agreement with the diffraction data of the RGO cubic crystal standard spectrum which proves a cubic structure of and has no other impurities. It can be seen from curve c that in the prepared composite material appeared the amorphous structure TiO_2-RGO. The crystalline structure was disappeared and Fig.1c,which proves a successful synthesisofTiO_2-RGOcomposite.[7-8]

Surface Morphology Analysis (FE-SEM)

Fig.3 a shown the zoom in image of grapheme oxide, it could observe that the pure grapheme oxide is a complex multilayer structure. Fig.3 bisthe SEM image of the synthesized pure TiO_2, as illustratedin the figure the TiO_2 structure contains many nanospheres. Although the agglomeration of TiO_2 organic material is obvious, the small nano- particles indicate that the Titanium dioxide synthesis process is generally successful. Fig.3 cisthe SEM image ofTiO_2-RGO composites. It could be observed that the nanoparticles are embed into the grapheme layers, this means that the grapheme surface and nitrogen contained organic material may have as strong coherent effect The interaction between the grapheme and nanoparticle Titanium dioxide might have an effect of inhibits the each one to another. From the SEM morphology result, it could conclude that the synthesis ofTiO_2-RGocompositesisquite effective, from a microstructure prospect[9-10].

Fig. 4(a&B)show that the Ny quist plots for both rGO electrode and TiO_2-rGO electrode. Both of them show similar trend: a semicircle at high frequency followed by near 90° linear line at low frequency region. The inset picture depicts the clear semicircle with intercept at the *x*-axis. The intercept represents the equivalent series resistance (ESR) of the electrode and it is approximated to be 0.6 U and 0.4 U for rGO electrode and TiO_2-rGO electrode, respectively. The relatively lower ESR value for TiO_2-rGO electrode is expected, due to the improved surface wett ability

CONCLUSION

In this work, we report on the structural and electrochemical properties of TiO_2 functionalized reduced graphene oxide (TiO_2-rGO) for its suitability as a supercapacitorelectrode.TheTiO_2-rGO is prepared by so nicating a suspension of rGO with Titanium dioxide and the filtered sediment is subjected to spectroscopy studies and electrochemical studies. were carried out. The microspic phase structure phase structure and morphology of the samples were characterized by SEM, TEM, XRD and and AC impedance test were used to study the electrochemical property and cycle performance of the TiO_2/rGO composite electrode. Spectroscopy studies reveal the successful unctionalization of Titanium dioxide ontoTiO2-rGO through p–pinteractions. Electro chemical analyses of TiO_2-rGO show a substantial increase in the specific capacitance for TiO_2-rGO (160 F g^{-1} at 5 mV s^{-1}) compared to the non-functionalized rGO (118 F g^{-1} at 5 mV s^{-1}).Furthermore, the TiO_2-rGO has 1.5 fold higher energy density than the non-functionalized rGO electrode, thereby making it suitable as a deployable super capacitor electrode.

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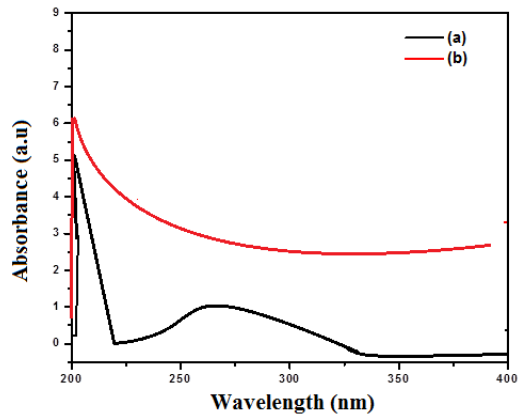

Figure 1. UV-visible absorption spectra of (a) GO and (b)RGO

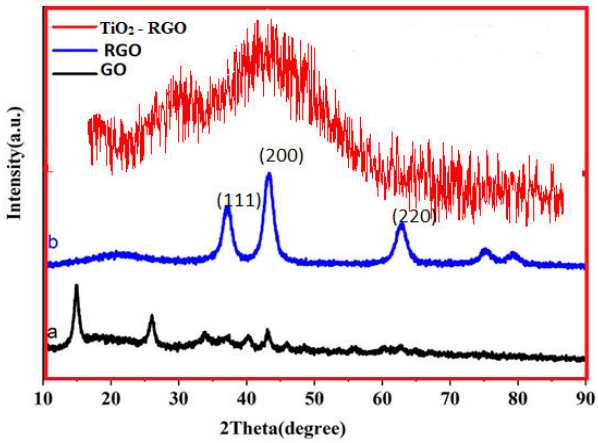

Figure 2. XRD spectra of(a) RGO (b) TiO_2(c)TiO_2/ RGO

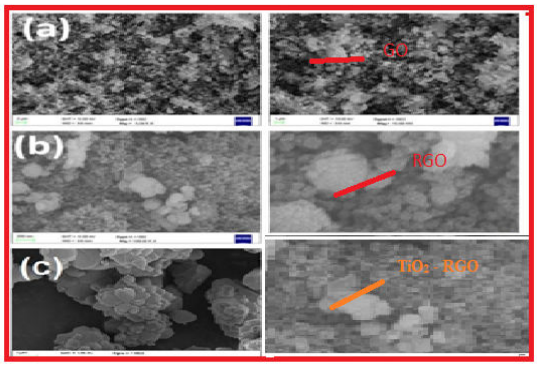

Figure 3. FE-SEM image of (a) GO, (b) RGO (c) TiO_2/RGO

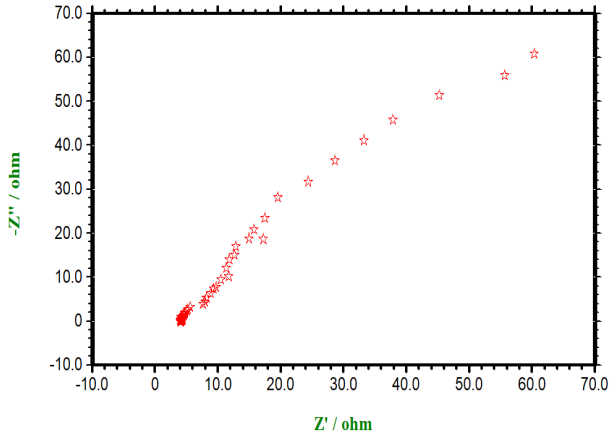

Figure 4. aNyquist plots for rGO electrode

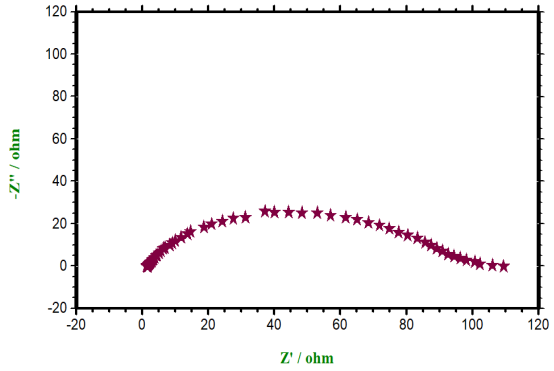

Figure 4 b. Nyquist plots for both TiO_2-rGO electrode

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REVIEW ARTICLE

Biosimilars- A Review on Biological Equivalents

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ABSTRACT

"Biologics", considered one among the fastest growing sectors, that has been introduced by many new treatments to life threatening and rare illnesses. As a result, research based and generic pharmaceutical companies alike are pursuing the prospect to develop "generic" substitutes for original biologics, herein mentioned as biosimilars, within the recent scenario, there's an increasing demand for biological drugs .This review plan to highlight the differences between biosimilars and chemical generics, development stages ,analysis of biosimilar, Regulatory aspects of biosimilars, guidelines of biosimilar in various country, problems with concern with the utilization of biosimilars and need of appropriate regulations for his or her approval. Generic approach isn't scientifically useful to manufacture biosimilars.

Keywords: Biosimilar, Biologics, Guidelines , Regulatory aspects

INTRODUCTION [1-17]

Biological medicines or biologics have shaped modern medicine by drastically changing the prognosis for several severe and life threatening diseases like cancers, diabetes and autoimmune diseases (rheumatoid arthritis, Morbus Crohn, MS , severe psoriasis) and rare diseases. Biologics are fundamentally distinct from conventional medicines in terms of nature or origin, structural complexity and variability, manufacturing process, side effects (immunogenicity), formulation, sensitivity, and regulatory aspects. But the crucial obstacle for accessing biologic medicines is their high cost, thanks to their lengthy and risky development process. Originator biologics are novel medicines that contains active substances made up of living cells or organisms and are manufactured through biotechnology, using complex system cells and recombinant deoxyribonucleic acid technology. To award research and innovation, but at an equivalent time to make the chance for market competition and access to therapies, novel biologics enjoy two mechanisms of protection: patents (which usually last up to twenty years), and a period of

knowledge exclusivity and market exclusivity (for up to 11–12 years). Hence, it doesn't necessarily mean that an already approved biosimilar can immediately seek the market. A biosimilar is released on the market and may be available to clinics only after its originator biologic reaches expiry of all patents, which sometimes are often issued after the originator is already in use by patients no matter various definitions, terminology and regulatory approaches for investigating and approving biosimilars, biosimilars are often defined as non identical copies of originator biologics, determined to be of comparable quality, safety and efficacy to them.

Since the biosimilar approval pathway has been abbreviated, biosimilars became available to patients at lower cost. Therefore, biosimilars have the potential to scale back overall medicine expenditures, but most significantly to extend access to biologic therapies, thereby improving patient outcomes. the value shouldn't be the first decision for healthcare professionals, and it's within their responsibility to prescribe safe and effective therapies of the specified quality. By leading on the establishment of general and product¬ specific guidelines for the event of biosimilars, updated over time, the ecu Medicines Agency (EMA) has approved the very best number of biosimilars to diverse active substances.Since 2006, the EMA has approved six biosimilars of trastuzumab, four of infliximab, 11 of adalimumab (two of those were withdrawn from the market, two of bevacizumab, at the request of the manufacturer), seven of rituximab, nine of filgrastim (two were withdrawn from the market at the request of the manufacturer),three of etanercept, seven of pegfilgrastim, three of epoetin alfas, two of enoxaparin, two of epoetin zeta, one among insulin lispro, one among insulin apart, three of insulin glargines (one withdrawn), two of teriparatide, two of follitropin alfas, and two of somatropin . In contrast to the EU, nearly a decade later, through the Biologic price war and Innovation Act of 2009, the US Food and Drug Administration (FDA) has approved the primary biosimilar Zarxio (Filgrastim¬sndz) in 2015, and so far , we've not seen the issuance of all product specific guidelines. Up to now, the FDA has approved five trastuzumabs, four infliximabs, two bevacizumabs, two rituximabs, six adalimumabs, two etanercepts, two filgastrims, four pegfilgrastims, and one epoetin alfa . the world Health Organization (WHO), by issuing several guidelines for biosimilars, keeps trying to align regulatory aspects for developing and approving biosimilars across countries. there are 95 approved biosimilars at 2019 all over the world. School of medicine , where healthcare professionals initially acquired knowledge on the principles of therapy, don't extensively include biologic medicines as a part of their curriculum. Therefore, many researchers have suggested that educating healthcare professionals who are involved in prescribing, dispensing biologics and biosimilars will play a important role within the acceptance of biosimilars in clinical practice. Having regard of the very fact that every country has its policies for purchasing and pricing of biosimilars, this review principally aims to explore the present knowledge, attitudes, and in 2018–2020 awareness of healthcare professionals involved in prescription of biosimilars . It also further extends the plan to converge the regulatory, clinical and scientific aspects of biosimilars.

Advantages of Biosimilars: [18,19,20]

- There's large market needs and growing affordability for biosimilars in global and domestic market.
- Production and Development of biosimilars are improved by existing manufacturing technology.
- Within the recent scenario, there's increasing demand for biological drugs.
- Due to competitive pricing advantages biosimilars are available at affordable prices on global market which they're typically sold at the discount up to 85 %.
- Due to no investment in phase I-II of clinical trials, biosimilars are available at cheaper prices than the reference products, so as that it's low market risk.

Disadvantages of Biosimilars: [21,22,23]

- The event and manufacturing process of biosimilars is more complex than that for small molecule drugs.
- Manufacture of biosimilars requires growing and harvesting of the merchandise from living cells which is extremely costly &time consuming process.

- The event of biosimilars is lengthy process & can take many months to supply .
- As compared to chemical drugs, biologics are often dozens to thousands of times larger, so as that development process is extremely critical.
- Traditional generic drugs must be shown to be the an equivalent because the reference drug; however, with modern science, follow on biologics or biosimilars can only be almost just like the reference or innovator biologic.

Quality, Safety, and Efficacy: [24-42]

The quality, safety, and efficacy of a biosimilar product must be approved by the relevant regulatory body before marketing approval are often gained, appropriate comparability exercise. The EMEA requires comparison of the biosimilar product with the innovator product to figure out absence of any differences. The standard comparison between the biosimilar and therefore the innovator product is crucial, because the standard of a protein product affects that biopharmaceutical manufacturing could also be a multistep process, selection of an appropriate cell expression system and involving cloning of the suitable genetic sequence into a carefully selected vector, scale up and purification, up to formulation of the final product[24]. Towards the particular process used, biopharmaceuticals variation in product quality, and exhibited in great sensitivity was commonly observed, even when the precise same producing was used.

The challenge that remains to assess and quantify these differences, determine whether the new product is as safe. Further, variability of source material has also been known to affect quality of the product. Thus the merchandise is affected both by the therefore the processing steps that follow. In addition, protein molecules are often degraded during processing steps and impurities created in these contribute to decreased potency and/ or increased immunogenicity. With the large number of quality attributes, acquiring a complete knowledge of the attributes on clinical safety and efficacy is not feasible[25]. However, the recent guidelines of the International Conference on Harmonization Q8 development[26], and the rollout of the Quality by Design[27] and Process Analytical Technology[28] initiatives from the FDA have improved understanding producing processes and their starting materials, on product quality.

Biochemical characterization of the protein product requires sophisticated analytical the chances of changes to the merchandise . Further, the characterization of the merchandise requires a spread of methods for various attributes or, orthogonal methods for the characterization of a given attribute, thus developing a comprehensive fingerprinting of a protein product[29,30]. However, remain that still require attention in the high complexity of the products, processes and raw materials that are a part of the manufacturing biotechnology products. Virtually all therapeutical proteins induce some level of antibody response, The immune reaction can vary from low affinity, IgM antibodies to a high titer, high affinity IgG response, low titer, with consequences ranging from none to severe or life threatening. Many factors determine immunogenicity, including patient characteristics and disease state, and therefore the therapy itself influences the generation of an immune reaction factors such as the molecule design, the expression system, posttranslational modifications, impurities, contaminants, formulation and excipients, as well as degradation products are all implicated[31]. It is fundamental to conduct preclinical and clinical studies to know the security , efficacy, and innovator product and biosimilar medicines.

Preclinical studies aren't yet capable of assessing the clinically relevant immunogenicity potential of those factors. Understandably, most of the focus has been on assessing immunogenicity of protein products by nonclinical studies[32-34]. Despite advances characterization and other nonclinical methods for assessment of immunogenicity, the unpredictability of the human system still necessitates detailed assessments, which can rely heavily on clinical trials. This is why clinical experience, through clinical trials and extensive pharmacovigilance programs, most reliable way to assess immunogenicity[35-37]. The suitable example of an unexpected things happening with protein drugs that have been well characterized biosimilar epoetin zeta (Retacrit®), which was approved by EMEA. Eprex®

(Amgen/Johnson & Johnson) is synthetic erythropoietin (epoetin alpha) replace the erythropoietin that is lacking in people who cannot make enough, usually because their kidneys are not working properly.

Epoetin alpha to treat people with cancer who develop anemia due to chemotherapy treatment. Although preapproval physicochemical, in vivo, and animal testing biosimilar to its innovator product epoetin alpha (Eprex), it had lower potency in clinical trials[38]. Accordingly, current analytical techniques are unable immunogenicity and potency. This is evident from the Eprex case which showed that one protein are often different from another in ways in which can't within the laboratory, but are seen only by the body's exquisitely sensitive immune system. If one change to a well established complex manufacturing by the manufacturer who has intimate knowledge of the method , can cause a drag with immunogenicity, surely the danger is even greater with an manufacturer and process – as with biosimilar[39]. Recently launched efforts, such as the EMEA concept paper on immunogenicity assessment of monoclonal antibodies intended for in vivo clinical use, are expected to provide further clarity on this topic[40].

Further, when the Committee for Medicinal Products (CHMP)/EMEA evaluations so far were examined, any difference in host cell expression system, purity, and formulation appears acceptable if the clinical negative effect[41]. Besides safety of an innovator product, evidence suggested that efficacy also can be a priority . The products were characterized the sorts of glyco forms present, the relative degree of unfolding, in vitro potency, presence of covalent aggregates, and presence of cleavage aggregates. Biochemical discrepancies between the different copy products were most likely caused by the differences in the manufacturing process and the cell lines[42].

Development Stages of Biosimilars: [43-46]

Development of biosimilars is a complex and tedious process that comprises four stages. The overall cost of under development new biosimilar product depends on stages changing with requirement and period involved to finish it. The period of time prolongs up to eight years for development of biosimilar products thanks to involvement of complex biotechnological process like preparation of cell banks, replication of host cells, method development, and scaleup for higher batch size and quality control testing.

Development of Product and Relative Analysis:[47] This stage contains the manufacturing of targeted protein from defined cell culture and evaluating its stability profile. The newly developed product must be highly similar to innovators product.

Development and Optimization of Process and Validation: [47] This stage can involve complete development and optimization of the process to improve the final yield of the biosimilar product. The scale up process should follow good manufacturing practice. The production process should be validated for reproducibility of yield.

Clinical Studies: [47] This is an important stage for biosimilars product. Clinical studies will be necessary for nearly all biosimilars product so as to validate bioequivalence to reference or innovator product.

Analysis of Biosimilars:[48-51]

To be registration of biosimilars drugs, "biosimilarity" want to be validated between the physiochemical parameters of biosimilar properties and originator batches. Is to be verify safety and efficacy of biosimilars as compared with reference or originator, preclinical and, clinical studies must be conducted as per regulatory guidelines from the EMA and therefore the FDA should approved . Also developing and validating the bioanalytical methods to support these requirements is extremely essential. ICH guidelines, ICH Q5E, and Q6B provide well defined in regulation on physiochemical and structural features that would be considered as appropriate within the assessment of compartability as listed below:

- aminoalkanoic acid sequence;
- aminoalkanoic acid composition;
- Terminal aminoalkanoic acid sequence;
- Peptide map;
- Sulfhydryl groups and disulfide bridges;
- Carbohydrate structure;
- Molecular weight;
- Isoform pattern ;
- Electrophoretic pattern;
- Liquid chromatographic patterns;
- Spectroscopic patterns.

The advanced analytical technique like mass spectrometers employed within the assessment of physiochemical parameters extremely sensitive to the concentration and sample matrix. Isolation or purification of a lively constituent from the reference formulation is administered by extraction method, therefore, there might be possibility to a change in physiochemical or structural properties of in active constituent and ultimately offers influence on comparability with along side to physiochemical and structural elucidation, quantification of product and process related impurities should also include within the evaluation of biosimilars.

Regulation Aspects of Biosimilars;[52-68]

A drug may be a much less costly copy of an innovator drug product. Generics are often produced when the patent on a drug has expired, for drugs which haven't held patent, in countries where a patent(s) is are not effective , and where the generic companies certify that the branded companies' patents are either invalid, unenforceable, or won't be infringed. drug manufacturers apply for marketing approval for generic drugs and newer drug under the Abbreviated New Drug Application (ANDA) pathway established by FDA. Moreover, drug applications are termed "abbreviated" because they're generally not required to Regulation aspects of biosimilars .A drug may be a much less costly copy of an innovator drug product. Generics are often produced when the patent on a drug has expired, for drugs which haven't held patent, in countries where a patent(s) is are not effective, and where the generic companies certify that the branded companies' patents are either invalid, unenforceable, or won't be infringed. A drug manufacturers apply for marketing approval of generic drugs under the Abbreviated New Drug Application (ANDA) pathway is established by FDA. Moreover the drug applications are termed "abbreviated" because they're generally not required to innovator products. These differences imply that biosimilars shouldn't be approved and controlled within the same way as conventional generic drugs. The regulatory pathway for approval of biosimilars is more complex than for the generic innovator product because the planning of a scientifically valid study to demonstrate the similarity of a highly process dependent product isn't easy.

Further, the analytical tests currently available aren't sophisticated enough to detect the slight but important structural differences between innovator and biosimilar products. Modest differences may have clinical implications and pose a big risk to patient safety. Therefore, it's needed that biosimilars must be assessed for clinical efficacy and safety by valid preclinical and clinical studies before marketing approval . The European Medicines Agency (EMEA) has moved before the remainder of the world during this direction, and issued variety of general guidelines that detail the wants for market approval. Additionally to those guidelines, product class specific guidelines are issued for the event of both biosimilars supported recombinant erythropoietin, somatotropin, human granulocyte colony stimulating factor, human insulin, recombinant IFNa, and low relative molecular mass heparins . Generally, the approval process varies consistent with the products, because significant differences exist between them, and permit products to be assessed on a case by case basis. In the US, after the approval of biosimilar Omnitrope in 2006, the FDA stated that no other biosimilar are going to be approved until a selected regulation has been issued. The

Pathway for Biosimilars Act of 2009 and therefore the Patient Protection and Affordable Care Act of 2010 have provided greater clarity, and a fairly clear mandiate from the Congress for the FDA to act and approved more openly and decisively on an abbreviated approval pathway for biological products. However, in Canada, the primary Subsequent Entry Biologic (SEB) Omnitrope™ was approved on April 20, 2009. Recently, Health Canada published its finalized guidance document for the approval of SEBs with the intention that this document would function an administrative aid to guide SEB decision making. In fact, the regulations covering the market approval of biosimilars are still evolving round the world. With progress within the US, Australia, Canada, Japan, Turkey, and other countries round the world already armed with a regulatory framework for biosimilar medicines, there's a requirement to succeed in global agreement on criteria and guidelines for such products. This objective is inspired by ethical and scientific principles also as economic considerations, and can have a big positive therapeutic impact for many patients living with life threatening and chronic diseases.

Guidelines for Biosimilar in Various Country: [69]

The use of biosimilars is increasing worldwide and several different international regulatory pathways have been developed to expedite entry of biosimilars into the global marketplace. The first wave of biosimilar use, specific to oncology, was in Europe and India in 2007. Oncology department biosimilars are now widely ranged marketed in many several countries in Europe, and in Australia, Japan, China, Russia, India, and South Korea. The striking exemption for the worldwide acknowledgment of biosimilars has been the United States, a number of regulatory and cost barriers to biosimilar approval appear to exist, as evidenced by the very first biosimilar not being approved by the US FDA until 2015.

World Health Organization – WHO: [70]

In April 2010, the WHO published their Guidelines on Evaluation of comparable Biotherapeutic Products. These guidelines aimed to supply a group of worldwide acceptable principles to approve biosimilar medicines that might assure quality, safety and efficacy. WHO suggested the rules might be adopted as an entire , partially, or might be the idea for developing a regulatory pathway.

European Medicines Agency – EMA:[71-75]

The European Union was the only region to line up a framework for the approval of biosimilars in 2003, which began with a directive providing the legal basis in 2001 because of inescapable patent terminations for a few biologics (somatropin, epoetin alfa, and filgrastim). The EMA has developed overarching, products pecific, quality, clinical and nonclinical issue guidelines for biosimilars. These are revised on a day to day by the Biosimilar Medicinal Products working party (BMWP) of the EMA to form sure they're up thus far and take into account experience with biosimilars and advances in science and technology. EMA guidelines support an shortened pathway for registration of biosimilar products, basing approval on preclinical and clinical studies that compare the product's efficacy, safety and immunogenicity to the first reference product. The regulatory guidelines are customised for various classes of biosimilar, including different data requirements for nonclinical and clinical studies of recombinant therapeutic proteins, recombinant erythro poietins, interferon b, and monoclonal antibodies. The EMA requires that the biological reference product has got to are authorized for marketing by the ECU Union for a minimum of 10 years. This provides a full decade of post marketing safety and efficacy information to be available for review. The biosimilar must have the same pharmaceutical form, administration route , and strength (eg. Injection or infusion) because the reference product. EMA guidelines examine manufacturing (quality comparability),toxicology, nonclinical pharmacology, pharmacodynamics , and pharmacokinetics .

Clinical considerations, immunogenicity and effectiveness are assessed in safety and efficacy studies using two or three comparative groups and a minimum of one equivalence trial, or an attempt that has the biosimilar, the reference biological, and a placebo, is required. Post approval pharmacovigilance (safety and monitoring after approval – more detail in Chapter 5) and risk management studies are required, because like all biologic products,

many toxic effects may only be detectable after several years. EMA does allow approval extrapolation to other indications (if the reference product works for condition x and y, then the biosimilar can also be used for condition x and y), but these are only considered on a case by case basis. The EMA approval process stresses the importance of rigorous analytical testing of biosimilars and requires that it's supported by appropriate confirmatory clinical evidence to guage the clinical impact of minor changes in structure compared with the reference product. An example of this was within the application of a biosimilar candidate (recombinant human interferon a2a). The EMA began its initial assessment of this product shortly after the appliance had been submitted in December 2003 during which the manufacturer claimed that analytical testing had shown the merchandise to be almost just like the reference product. However, the EMA assessors diligently insisted on further data and eventually determined that the products demonstrated different impurity profiles and therefore the candidate product was refused approval in 2006 supported incomplete and inconclusive data. As well, clinical trials of the proposed biosimilar revealed differences in pharmacokinetics and clinical efficacy (hepatitis C viral infection relapse rate) compared to its reference product.

United States Food and Drug Administration: [76-79]

In the US, the 2009 Biologics price competition and Innovation Act (BPCIA) set the FDA framework for biosimilar approvals. The BPCI Act was passed as a neighborhood of the Affordable Care Act that President Obama signed into law in March 2010 and A biosimilar may be a biological product that's highly almost like and has no clinically meaningful differences from an existing FDA approved reference product. An interchangeable product may be a biosimilar product that meets additional requirements outlined by the Biologics Price Competition and Innovation Act. This abbreviated licensure pathway, under section 351(k) of the overall public Health Service Act, permits reliance on certain existing knowledge base about the security and effectiveness of the reference product, and enables a biosimilar product to be licensed supported a but complement of preclinical and clinical data, specific thereto biosimilar product. The facilities where the biosimilar is being manufactured must also meet strict standards and thus the FDA will resolve any uncertainties associated with comparability using physiochemical and functional assays that provide the power to assess changes within the manufacturing process, and preclinical and clinical studies. Since 2010, the FDA has released several guidance documents related to the assessment of biosimilars within the US. They outline the approaches needed to assess the molecular structure, function, and toxic effects in preclinical animal studies, the type of human pharmacokinetic and pharmacodynamics studies which can sufficiently demonstrate safety, purity, and potency, and thus the wants for showing clinical efficacy, safety, and immunogenicity. All of this evidence are getting to be used to create a risk based assessment. Beyond their own requirements, the FDA does take into consideration the protein complexity, manufacturing processes, and studies comparing biosimilars with products that are licensed outside the USA, also because the pharmacovigilance post marketing safety concerns. The FDA does have the discretion to review the completeness of this information from other regions and determine if it's getting to leave some elements of the regulatory procedure to not be needed.

Guidelines in India: [80-83]

The Department of Biotechnology (DBT) was introduced "Draft Guidelines on Similar Biologics: Regulatory Requirements for Marketing Authorization in India," in June 2012. These guidelines state the premarketing and post-marketing regulatory requirements as well as necessities to the manufacturing process and quality control of similar biologics. These Indian guidelines are similar to biosimilar guidelines of EU and USA in numerous aspects. However, India accepted "sequential approach" that is similar to "stepwise approach" (US and EU) to market biosimilar product.now a days, India is one of the leading contributors in the world biosimilar market. India has demonstrated the greatest acceptance of biosimilars, which is reflected from over 50 biopharmaceutical brands getting marketing approval. Biosimilars have covered their way in India due to the regulatory authorities and regulatory guidelines coming into force.

The Purple Book:[84]
Biologic drugs, biosimilars, and interchangeable biologic drugs licensed by the FDA under the PHS Act are listed within the "Purple Book." The Purple Book lists biologic drugs, and, if applicable, its biosimilar drug, also as information on interchangeability for every drug. The Purple Book also provides information on any existing reference drug exclusivity protecting a reference biologic drug. the knowledge provided includes the date a biologic drug was licensed under 351(a) of the PHS Act, whether the FDA evaluated the biologic drug for reference drug exclusivity under section 351(k) (7) of the PHS Act, and whether a biologic drug licensed under section 351(k) has been determined by the FDA to be biosimilar to or interchangeable with its reference drug.

Current status of Biosimilars in India: [85-88]
India features a thriving biosimilar ecosystem as compared to other countries and since of that Indian pharmaceutical companies have risen because the worldwide market leaders in biosimilars. India certified its first biosimilar much before the us and Europe. hepatitis B was the first biosimilar approved and marketed in India in 2000, there was no specific guideline available at that time for the approval and marketing of biosimilar in India. whereas several biosimilars were developed and marketed in India by many biopharmaceutical companies. in recent times, an Indian biopharmaceutical company attained the USFDA's nod for marketing its novel biologic. Herceptin was the first biologic to be approved by FDA, which is used in certain stomach and breast cancer. it was also the first similar biologics manufactured by an Indian company, which got endorsement to plug within the us .Now a days , there are quite 100 Indian biopharmaceutical companies, which are involved in manufacturing and marketing of biosimilar.

Biosimilar is as "similar biologics" by the Indian regulatory agencies. No certain guideline was available for "similar biologics," although the undeniable fact that India was one of the first nations within the world to utilize it, and approval process of comparable biologics is more cumbersome and wish more data than other generic drugs. to deal with the issues and challenges associated with the event of comparable biologics, Central Drugs Standard Control Organization (CDSCO) along side the Department of Biotechnology (DBT) has developed "Guidelines on Similar Biologics; Regulatory Requirements for Marketing Authorization in India" in 2012 and has revised it in 2016. These guidelines address the regulation of manufacturing process also as quality, safety, and efficacy of comparable biologics. It also addresses the regulatory requirements pre and post marketing of similar biological preparations. DBT Through the review committee for genetic manipulation, it is responsible for event supervision and preclinical evaluation of the biology.

The similar biologics in India are managed according to Drug and Cosmetic Act (1940), Drug and Cosmetic Rules, 1945, and Rules for Manufacture, Use, Export, Import, and Storage of Genetically Engineered Organisms / Hazardous Microorganisms or Cells, 1989 (rules, 1989) notified under Environmental (Protection) Act,1986. CDSCO has brought some important changes in its earlier guideline, like earlier it had been essential for the reference biologic that biosimilar is to be developed possesses to be approved and marketed in India but it's now changed to either India or the opposite international council for harmonisation countries (i.e., European Union , Japan, us , Canada, and Switzerland). It also tries to align with other international agencies like EMA and thus the world Health Organization. consistent with Indian guideline, biologics are developed by the sequential approach to means the similarity of the molecular and quality characteristic of a biosimilar with reference products. Another difference between the 2012 guidance and thus the document issued in 2016 is that the stress on the post marketing studies, which CDSCO says are intended "to further decrease the residual difficulty of the similar biologic," CDSCO has made it fundamental for the biopharmaceutical company to conduct a phase IV clinical trials study with a minimum of 200 patients within 2 years of getting approval for marketing.

The regulator also added a replacement section on non comparative safety and efficacy studies, noting that if a product is found to be similar "in pre¬clinical, in vitro characterization having established PK (pharmacokinetic) methods and a PD (pharmacodynamic) marker that's surrogate of efficacy, the residual risk is significantly reduced

within the clinical test |phase I|clinical trial|clinical test"> phase I clinical trial clinical trial study if equivalence is demonstrated for both PK and PD. phase III clinical trial clinical trials of such a uniform Biologics product could even be waived...[and] where needed , an appropriate single arm study during a minimum of 100 evaluable subjects could even be administered within the foremost sensitive indication to affect any residual uncertainty." CDSCO also added new information on when a confirmatory clinical safety and efficacy study are often waived, noting: "In case the safety and efficacy study is waived all the indications approved for reference product could even be granted supported comparable quality, non-clinical also as convincing PK/PD data. Wherever the clinical test |phase III|clinical trial|clinical test"> phase III clinical trial clinical trial trial is waived, the immunogenicity should are gathered within the PK/PD study and may also need to be generated during post¬approval phase IV clinical trials clinical trials study."Indian companies are taking multiple steps to involve them in manufacturing and marketing to tap this huge potential. Biosimilars approved and utilized in India mainly contains the insulin, recombinant proteins, vaccines and monoclonal antibodies, . India has achieved the excellence of being the second largest supplier of vaccines within the world . Various biosimilars are approved by India to be used in several diseases.

Multidisciplinary Expert Perspectives: [87-105]

Gastroenterology: [87-92]

The recent approval of infliximab biosimilars for IBD has prompted significant debate within the field of gastroenterology. Physicians are generally unaware of the innovative licensing approach on which the approval of biosimilars is predicated. Misunderstanding among gastroenterologists may arise, especially , from an important reliance on robust disease specific clinical test data (eg, for Crohn's disease and UC) to measure clinical validity as may be a prerequisite for originator therapies, but could also be superfluous, time consuming, and dear in the case of biosimilars. Therefore, gastroenterologists should remember that there's an important distinction between the evaluation of originators and biosimilars therein preclinical research involving physicochemical, PK, and pharmacodynamic analyses drive the approval process for biosimilars, with existing or new clinical trials providing important supporting data. The licensing of CTP13 could also be a pertinent example of this process, which encompassed extensive physicochemical characterization supported batch to batch analysis, also as nonclinical and clinical studies and mechanism of action studies to verify similarity with the originator infliximab. This approach will expedite the introduction of biosimilars in real world practice.

From the attitude of the Czech Republic , the rapid and robust reduction (30%–40%) in costs related to biosimilars has facilitated earlier initiation of biologic therapy in those patients with IBD on treatment waiting lists, with 1000 more entering treatment in 2014 compared with the previous year. Emerging results from prospective observational studies, including interim data from a Hungarian nationwide cohort, support the short term clinical efficacy and safety of CTP13 in patients with IBD, including those infliximab. Although such results are promising, implementation of national registries of IBD patients on biologic therapy; prospective, long term real world data on clinical efficacy and safety; and better dissemination of the approval process are, among others, essential factors which can need to be addressed if biosimilars are to understand widespread acceptance in gastroenterology.

Nephrology: [93-97]

ESA markets for treatment of chronic kidney disease–associated anemia have proven to be highly country specific, and even across EU countries, the penetration rate of biosimilar epoetins varies significantly. The still unsatisfying acceptance of biosimilar epoetins is multifactorial, often because of a persistent lack of knowledge and expertise within the sector of biological agents. a scarcity of availability of biosimilar advocacy and policies, in conjunction with the sometimes confusing nomenclature, promotes further uncertainties. Despite such studies because the pan European, prospective MonitorCKD5 (Multilevel Evaluation of Anemia Treatment, Outcomes, and Determinants in Chronic renal disorder Stage 5) study of HX575,additional largesample, longterm observational studies are urgently needed. When reviewing the ESA class of biological products, a recent systematic analysis of adults with chronic kidney disease suggested that the currently available clinical evidence was markedly but that of the proprietary

ESAs. The marketing withdrawal of peginesatide, a longacting originator ESA, that was recalled in February 2013 after reports of severe hypersensitivity reactions in dialysis patients who received a primary dose, may be a warning example that strict post marketing surveillance is important. Additionally , nephrologists are encouraged to carefully observe developments worldwide including threshold countries, where often extensive practical experience with biosimilar ESAs exists. Longterm post marketing real world data demonstrating clinical effectiveness, safety, and eventually cost savings are required to finish the success story of biosimilar ESAs within the field of nephrology.

Oncology: [98-102]
Use of biosimilars in oncology thus far has been largely confined to supportive care therapy like filgrastim and ESA biosimilars, which, on the whole , are shown to be comparable in efficacy and safety to their originators. The clinical success of these supportive care agents in oncology invites the event of biosimilars for curative therapy. Institutions welcome the potential for significant reduction in costs with biosimilars also as oncologists, many of whom report that drug costs feature in their clinical decisions. Cost effectiveness and establishment of best practice and ongoing post marketing surveillance are researched within the routine clinical management of the oncology patient. (MONITORGCSF [Multilevel Evaluation of Chemotherapy induced Febrile Neutropenia Prophylaxis, Outcome, and Determinants with Granulocyte colony Stimulating Factor], NEXT, and ORHEO [Epoetin Alfa Biosimilar within the Management of Chemotherapy Induced Symptomatic Anaemia in Haematology and Oncology]) across European countries report long term efficacy and safety of the biosimilars filgrastim and epoetin for febrile neutropenia or chemotherapy induced anaemia, respectively, in real world patients with cancer.The cost reductions associated with biosimilar granulocyte colony–stimulating factor have resulted in a rise in access in most European markets (ranging from 2% in Belgium to an almost 100% share of the accessible market in Croatia, Czech Republic, Hungary, and Romania); this might be an indication of the "real value" of biosimilars.

Rheumatology: [103-105]
The infliximab biosimilar has already been introduced in some countries for rheumatic conditions. Additionally to ongoing studies on other anti–tumour necrosis factorα biosimilars (eg, adalimumab and etanercept), several rituximab biosimilars are in advanced stages of development, and a couple of are currently undergoing evaluation in clinical trials of patients with RA.50 Results from these studies, if positive, will contribute to existing clinical data for infliximab biosimilars in RA. There remain, however, pertinent and valid challenges to the introduction of biosimilars in rheumatology, not least is that the need for extra disease specific clinical trials and post marketing surveillance data. As for other areas of drugs , rheumatologists' awareness of biosimilars is lacking (when compared, for instance , with other biologic therapies), particularly among those physicians with less clinical experience. Encouragingly, rheumatology experts and organizations worldwide have taken a collective stance to tell and guide physicians on the clinical utility of biosimilars in rheumatic diseases. biosimilars, nevertheless, will within the appear the hay practicing rheumatologists and their trust within the evidence base for biosimilars in rheumatology.

CONCLUSION

Biological products are in market from last three decades and growing rapidly thanks to mainly intended within the treatment of incurable diseases. Biosimilar products aren't an artificial chemical drug or generic; biologics are high relative molecular mass and sophisticated than chemical drugs because they're derived biotechnologically from living cells. The generic method is technically not correct in the biosimilar products to bring them into the market. globally biosimilars problem are actively debatable at present . A critical evaluation is required for more efficient, cost effective widespread availability of biosimilars. Because biosimilar products are very complex molecules, factors just like the robustness of the manufacturing process, structure is similar to the parent molecule, level of understanding of the mechanism of action, quality of pharmacodynamic assays is utilized, demonstrated comparability in pharmacokinetics and immunogenicity, quantity of clinical data, and therefore the innovator's

experience with the parent product must be considered critically before marketing approval of biosimilars are often granted.

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RESEARCH ARTICLE

Influence of Hand Dominance on Shoulder Range of Motion in Young Non-Athlete Women

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ABSTRACT

The shoulder joint is one of the most commonly injured joints. Handedness is most often not a standard question of the musculoskeletal assessment form. But it may have an impact on developing musculoskeletal injury, especially in upper limb injury. There is paucity in studies correlating handedness and shoulder range of motion in young non athlete women. The aim of this study was to determine whether handedness influences active shoulder range of motion in young adult non athlete women. In this observational study, hundred healthy non athlete females of age group 18-24 were selected. Bilateral shoulder range of motion on all three planes for each female was measured by a qualified physiotherapist using a universal goniometer. The collected data was put into statistical analysis using paired t test.

Keywords: Shoulder range of motion, hand dominance, nonathlete adult women.

INTRODUCTION

The preference of hand usage while performing a particular task is referred to as hand dominance [1]. The functional ability and the performance of activities of daily living is greatly impacted by the hand dominance of the extremities, especially the upper extremity [2,3].Since the dominant hand is usually used for so many daily activities and for recreational activities, hand dominance is an important factor to be considered in motor skill performance [4]. Due to extensive practice and associated experience of using the dominant hand most often, better skill development and motor learning happens. This in turn results in superior speed, co-ordination and precision of the dominant hand over the non-dominant hand [1].Most often handedness is not a standard question featuring in the assessment form.

But it has to be understood that it has a definite impact on posture and risk of developing musculoskeletal injuries [5,6]. Muscle imbalance may result from repetitive movements, injuries, or habitual movement patterns. It may also result from surgeries and incomplete injury rehabilitation [5].Hand dominance could further impact these imbalances. A right-handed person can have inefficient posture that runs the length of the kinetic chain, from the hand to the foot. A right-handed person's stance will typically show a lower right shoulder with an adducted scapula, lateral pelvic tilt with adducted and medially rotated right hip joint and maybe even right foot pronation [5].

The shoulder is a joint that is designed to move. The proximal humerus and the humeral head articulate with the glenoid fossa of the scapula in the glenohumeral joint, which is part of the shoulder joint.Scapulothoracic joint is formed by the articulations of the scapula, humerus and the ribs. The shoulder joint being a ball and socket joint is capable of performing a variety of movements which includes flexion, extension, adduction, abduction, external and internal rotation. Hence it is a joint built for multidirectional mobility [7].

The ligamentous joint capsule and rotator cuff muscles that surround the glenohumeral joint are responsible for the joint's stabilisation. All gross shoulder motion is followed by scapula motion around the ribs as an accessory motion. Dominant arm is subjected to more constant stress in sports person when compared to non-dominant arm. Since an active person's dominant arm presents a different therapeutic challenge than a sedentary person's non-dominant shoulder, hand dominance is critical in treatment recommendations [8]. Gleno-humeral joint measurements are important for the prevention and the rehabilitation of the shoulder injuries. Measuring treatment progress and setting treatment goals is mostly dependent on range of motion measurements as far as health care of musculoskeletal disorders is concerned.

Some authors have hypothesized that there is a natural difference between the dominant and non-dominant sides [9,10]. If this is true, then using the opposite side as an estimate of preinjury ROM is inappropriate. This rationale for differences existing from side to side is related to usage. The idea is that the overuse of some joints could lead to overstress of the joint and, consequently, the development of micro injuries. These micro injuries would increase the deposit of scar tissue in the area leading to a decrease in the ROM, most commonly on the dominant side [11]. Though some authors have attempted determining the range of motion difference between body sides [12,13,14], at present the available literatures are insufficient, contradictory and mostly confusing. There is a paucity of literature in determining the clinical usage of hand dominance in the assessment of ROM of shoulder and in present available literature it is contradictory and confusing whether there is a significant difference between body sides exist. Therefore, this study is to verify the influence of hand dominance on shoulder range of motion (ROM) in nonathlete women to make reasonable protocols or preventive strategies in females who play a major role in the development of the society.

MATERIALS AND METHODS

This is an observational study. Hundred healthy non athlete women between the age group of 18-24 years who were all right dominant were selected. Care was taken in including only those who were not participating in any repetitive activities with upper limbs at the time of the study and not having any shoulder injury or pathology. The assessment was performed with a standard universal goniometer, for each subject by the same examiner. Flexion, extension and abduction movements were taken with the subject in standing position, the adduction (horizontal adduction) movements with the subject in sitting position and internal rotation (IR) and external rotation (ER) in lying position. The means of dominant and non-dominant sides were assessed using paired *t* test.

Data Analysis

One hundred females of age 20.25±1.59 were selected with a BMI of 21.45±3.63. The active range of motion (ROM) of right and left shoulders were assessed using a universal goniometer and the means of dominant and nondominant sides were assessed using paired *t* test. The mean ROM for right shoulder flexion was 172.15±7.080 and 175.25±7.862 for the left. The mean ROM for right shoulder extension was 49.00±7.035 and 49.80±6.192 for the left. Mean ROM for right shoulder abduction was 173.90±7.268 and 177.15±7.291 for the left side. Mean ROM for right shoulder adduction was 95.10±9.898 and 96.25±8.539 for the left. Mean ROM for right shoulder internal rotation (IR) was 70.05±10.766 and 71.85±9.578 for the left. Mean ROM for right shoulder external (ER) rotation was 87.15±8.536 and 88.30±8.652 for the left side. It was found that there was a significant difference between right and left side flexion (0.001) and also for abduction (0.001). There was no significant difference for extension (0.155), adduction (0.77), internal rotation (0.55) and external rotation (0.70).

RESULTS AND DISCUSSION

It was found that there was difference between right and left side flexion (0.001) and also for abduction (0.001). There was no statistically significant difference for extension (0.155), adduction (0.77), internal rotation (0.55) and external rotation (0.70). But there was minimal clinical significance as far as the ROM measurement was concerned. Available studies have mostly concluded that some ROM differences exist between body sides and when they exist, they are minimal and not clinically significant [4,15].

In this study though the flexion and abduction ROM was different between sides, the difference was minimal (less than 10 %). Hence the results of this study support the practice of using opposite side of the body as an indicator of normal or pre-injury ROM.As the dominant arm is subjected to more constant stress as compared to the non-dominant arm, hand dominance is important for treatment recommendations because the dominant shoulder of an active individual provides a different therapeutic challenge than the non-dominant shoulder of a sedentary individual.

CONCLUSION

Hand dominance should be considered when shoulder flexion and abduction is evaluated in nonathlete young adult women. But in general, there is not much of a difference between the ROM of the other movements of shoulder between dominant and non-dominant sides. These results lead to the conclusion that, although there was a significant difference between sides for some motions, the differences between sides are small and therefore probably clinically insignificant.

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Table 1. Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	FlexionR	172.15	100	7.080	.708
	FlexionL	175.25	100	7.862	.786
Pair 2	ExtensionR	49.00	100	7.035	.704
	ExtensionL	49.80	100	6.192	.619
Pair 3	AbductionR	173.90	100	7.268	.727
	AbductionL	177.15	100	7.291	.729
Pair 4	AdductionR	95.10	100	9.898	.990
	AdductionL	96.25	100	8.539	.854
Pair 5	Internal RotationR	70.05	100	10.766	1.077
	Internal RotationL	71.85	100	9.578	.958
Pair 6	External RotationR	87.15	100	8.536	.854
	External RotationL	88.30	100	8.652	.865

Table. 2. Paired Samples Test

		Paired Differences					t	Df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	FlexionR – FlexionL	-3.100	6.620	0.662	-4.414	-1.786	-4.683	99	0.000
Pair 2	ExtensionR – ExtensionL	-.800	5.583	0.558	-1.908	.308	-1.433	99	0.155
Pair 3	AbductionR – AbductionL	-3.250	5.430	0.543	-4.327	-2.173	-5.986	99	0.000
Pair 4	AdductionR – AdductionL	-1.150	6.430	0.643	-2.426	.126	-1.789	99	0.077
Pair 5	InternalRotationR – InternalRotationL	-1.800	9.280	0.928	-3.641	.041	-1.940	99	0.055
Pair 6	ExternalRotationRExternalRotationL	-1.150	6.271	0.627	-2.394	.094	-1.834	99	0.070

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RESEARCH ARTICLE

Imidazole and Ag^+ Nano Material as Corrosion Inhibitor for Mild Steel in Hydrochloric acid Solutions

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ABSTRACT

The corrosion inhibition efficiency of Imidazole in controlling the corrosion of mild steel immersed in 0.1N HCl for 60 min in the presence and absence of Ag^+ has been studied by weight loss method. The formulation consisting of 240 ppm of Imidazole and 60 ppm Ag^+ offers 95% inhibition efficiency. The synergistic effect exists between Imidazole and Ag^+ system. Polarization study shows that the best formulation system controls anodic reaction predominantly. The FTIR spectra study reveals that the protective film consists of Fe^{2+} - C=O group and N-H stretch on metal surface. The mechanism of corrosion inhibition is proposed based on the results obtained from weight loss study and polarization study. Fourier transform infrared spectroscopy (FTIR) and scanning electron microscopy (SEM) were used to investigate the nature of protective film formed on the mild steel surface.

Keywords: Imidazole, corrosion inhibition, mild steel, FT-IR and SEM.

INTRODUCTION

The study of corrosion of steel and iron in acid media remains a global scientific problem which affects all kinds of industries. The economic cost of corrosion is enormous and has been estimated to be in the range of 2–4% of an industrialized country's gross national product. In the field of combating corrosion, both economic and scientific

considerations are involved [1-3]. Acids are widely used in industrial processes such as pickling, cleaning, decaling, and oil well acidizing. Because of the aggressively of acid, solutions inhibitors are used to reduce the rate of dissolution of metals. In general, an inhibitor retards corrosion reactions by(i)adsorption of ions/molecules on metal surface,(ii)altering the anodic and/or cathodic reaction, and(iii)decreasing the diffusion rate of reactants to the metal surface. Corrosion inhibition is reversible and a minimum concentration of the inhibiting compound is required to maintain the inhibiting surface film [4-6]. The effectiveness of inhibitor depends on solution corrosivity, concentration, and temperature. It is well known that the organic inhibitors having heteroatom –O, N, S are the best corrosion inhibitors in acid solution as they have higher basicity. These hetero atoms act as active centre for adsorption on metal surface. A corrosion inhibitor is a compound which can reduce the corrosion rate on the metal surface. The efficiency of corrosion inhibitors is usually related to the presence of polar functional groups with S, O or N atoms in the molecule, heterocyclic compounds, and π electrons. Polar functional groups are considered as the reaction canters for the establishment of the adsorption process between corrosion inhibitors and carbon steel surfaces. However, the corrosion inhibitor is expensive, volatile, toxic, and unstable at high temperatures. Therefore, the recent focus of research is to make environmentally friendly corrosion inhibitors, which have a low environmental risk [7-9]. The use of an organic compound is one of the best candidates as a raw material to make environmentally friendly corrosion inhibitors Lisac *et al.* Showed that 4-methyl imidazole plays a role as Lewis acid. When the steel was contacted by acid, the surface of the steel oxidized and released electrons. However, if they are released into water, they decompose and produce hydrofluoric (HF) and phosphoric acids (H_3PO_4) which are harmful to the environment. Consequently, the oxidizing agent, water, corrosive material, and oxygen can increase the corrosion rate in the system after the corrosion inhibitor left the steel surfaces. In this study, we developed new inhibitor with high hydrophobic properties. Polar functional groups are considered as the reaction centers for the establishment of the adsorption process between corrosion inhibitors and carbon steel surfaces. However, the corrosion inhibitor is expensive, volatile, toxic, and unstable at high temperatures. Therefore, the recent focus of research is to make environmentally friendly corrosion inhibitors, which have a low environmental risk. The use of an organic compound is one of the best candidates as a raw material to make environmentally friendly corrosion inhibitors. An organic compound-based corrosion inhibitor has several advantages, such as being environmentally friendly, relatively inexpensive, and having more effective inhibitor performance. Imidazole and its derivatives have potential as a corrosion inhibitor due to their nitrogen (N) atomic functional groups and free electrons in their N atom able to interact with carbon steel to protect from corrosion attacks.

MATERIALS AND METHODS

Weight-Loss Method

Determination of Surface Area of the Specimens

The length, breadth and the thickness of mild steel specimens and the radius of the holes were determined with the help of Vernier Calipers of high precision and the surface areas of the specimens were calculated.

Weighing the Specimens Before and After Corrosion

The weights of the specimens before and after immersion were determinedusing a balance, Shimadzu AY62 model.

Determination of Corrosion Rate (CR)

The weighed specimens, in triplicate were suspended by means of glass hooksin 100 mL beakers containing 100 mL of HCl and distilled water at interval of 15minutes, progressively for total of 60 minutes started from 30 minutes. After the specimens were taken out, washed inrunning water, dried and weighed. From the change in weights of the specimens, corrosion rates werecalculated using the following relationship.

$CR = \frac{86.7 \times W}{DAT}$mmpy

Where W = weight loss in mg

D = density of metal specimen, 7.87 g/cm^3
A = surface area of the specimen (dm^2) and
T = Period of immersion (hours)

Corrosion inhibition efficiency (IE) was then calculated using the equation **[3-7]**.

$$Inhibition\ Efficiency = 100\,[1 - \frac{W_2}{W_1}]$$

Where W_1 = corrosion rate in the absence of the inhibitor and
W_2 = corrosion rate in the presence of the inhibitor.

Potentio dynamic Polarization Study

Polarization study was carried out in Electrochemical impedance Analyzer model CHI 660A using a three electrode cell assembly. The working electrode was used as a rectangular specimen of mild steel with one face of the electrode of constant 1 cm^2 area exposed. A saturated calomel electrode (SCE) was used as reference electrode. A rectangular platinum foil was used as the counter electrode. A time interval of about 5 to 10 minutes was given for the system to attain a steady state open circuit potential.

AC Impedance Measurements

AC Impedance study was carried out in Electrochemical Impedance Analyzer model CHI 660A using a three electrode cell assembly. The working electrode was used as rectangular specimen of mild steel with one face of the electrode of constant1 cm^2 area exposed. A saturated calomel electrode (SCE) was used as reference electrode. A rectangular platinum foil was used as the counter electrode.AC impedance spectra were recorded. C_{dl} values were calculated using the following relationship.

$$C_{dl} = \frac{1}{2\pi \times R_{ct} \times F_{max}}$$

Surface Characterization Studies

The mild steel specimens were immersed in blank, as well as in inhibitor solutions for a period of one day. After one day, the specimens were taken out and dried. The nature of the film formed on the surface of the metal specimens was analyzed by various surface analysis techniques.

Surface Analysis by FTIR Spectra

After the immersion period of one day in various environments, the specimens were taken out of the test solutions and dried. The film formed on the surface was scratched carefully and it was thoroughly mixed so as to make it uniform throughout. FTIR spectrum of the powder (KBr pellet) was recorded using Perkin-Elmer1600 FTIR spectrophotometer with a resolving power of 4cm^{-1}.

Scanning Electron Microscopic Studies (SEM)

The mild steel specimen immersed in blank and in the inhibitor solution for a period of one day was removed, rinsed with double distilled water, dried and observed in a Scanning Electron Microscope to examine the surface morphology. The surface morphology measurements of the mild steel were examined using Hitachi S-3000 H computer controlled scanning electron microscope.

RESULTS AND DISCUSSION

Weight Loss Measurements

FT-IR Spectroscopy

The FT-IR spectrum of Imidazole extract demonstrated a broad band at 3359.85cm^{-1} due to hydroxyl group (OH) and another band exhibited at 1682 cm^{-1} for carbonyl group (C=O) as present. From FT-IR we can conclude that the main compounds of imidazole 1550 cm^{-1}. This observation concludes that 1500 cm^{-1} due to Amine group band at N-H bend. The C=O has shifted from 1569 cm^{-1} to suggest that imidazole has coordinated with Fe^{2+} on metal surface through oxygen atom of resulting in the formation of Fe^{2+}-imidazole complex on the anodic sites of the metal surface.

Electrochemical Measurements

Electrochemical Impedance Studies

Nyquist plots for mild steel immersed in control solution of 240 ppm of imidazole inhibitor solution of 0.1N HCl in the absence and presence of formulations are shown in Figure 2. The impedance parameters, charge transfer resistance (R_{ct}), Double layer capacitance (C_{dl}) from the Nyquist plot values are shown in Table2. When mild steel immersed in 0.1N HCl medium the Rct value is found to be 38(Ωcm^2).The C_{dl} value is 32 ($\mu F/cm^2$) When 240ppm of Imidazole are added to 0.1NHCl medium the R_{ct} value is formed to be 151 (Ωcm^2). The Cdl value is 1 ($\mu F/cm^2$). When 240ppm of Imidazolesolution are added to 0.1N HCl medium the Rct value has increased from 38 to151 (Ωcm^2) and the Cdl value decreased from 32 to 1 ($\mu F/cm^2$). The increase in Rct value and decreases in double layer capacitance values obtained from impedance studies justify the good performance of a compound as an inhibitor in 0.1N HCl medium. This behaviour means that the film obtained acts as a barrier to the corrosion process [10-11]

Potentiodynamic Polarization Studies

The potentiodynamic polarization studies were carried out to determine the kinetics of the cathodic and anodic reactions. Figure 4 shows the potentiodynamic polarization curves for mild steel electrodes in control solution of 0.1N HCl in the absence and presence of inhibitor combinations. Electrochemical kinetics parameters, i.e., the corrosion potential (E_{corr}) corrosion current density (I_{corr}), and anodic and catholic Tafel slopes (βa and βc), obtained from extrapolation of the polarization curves are listed in table. When mild steel is immersed in 0.1M HCl in acid medium, the corrosion potential (E_{corr}) is -0.476 mV/dec and the corrosion (I_{corr}) is 7.077 ($\mu A/Cm^{-2}$) . When 550ppm of inhibitor solution of Imidazole are added to 0.1NHCl in acid medium the corrosion potential is found to be(E_{corr}) is -0.482 mV/dec and corrosion current (I_{corr}) is 2.500($\mu A/Cm^{-2}$). The corrosion current decrease from 7.425 ($\mu A/Cm^{-2}$) to 2.500 ($\mu A/Cm^{-2}$) [12-13]. The shift in the E corr, through still less than 85mv was shifted more towards the anodic region. This shows that the formation of functions as an anodic inhibitor controlling both anodic and cathodic processes but more predominantly anodic process. This suggests, indicate that protective film is formed on the metal surface.

SEM analysis was performed to investigate the surface morphology of the mild steel in the absence (Fig.6a) and presence (Fig.6b) of 240ppm imidazole and 40 ppm of Ag^+ in 0.1NHCl solution. It is important to stress out that when the compound is present in the solution, the morphology of C-steel surfaces is quite different from the previous one, and the specimen surfaces were smoother. We noted the formation of a film which is distributed in a random way on the whole surface of the C-Steel. This may be interpreted as due to the adsorption of the Imidazole compound on the C-steel surface incorporating into the passive film in order to block the active site present on the C-steel surface [14-15]

CONCLUSION

The principle finding of the present work could be summarized as follows:

- The inhibition efficiency increases with increasing inhibitor concentrations to attain maximum value of 93% for inhibitor respectively.
- The formulation consisting of 0.1 N HCl medium, 240 ppm of imidazole with 40 ppm of Ag^+ offers 93%.

- The synergistic effect exists between 0.1N HCl-imidazole and Ag^{+} systems. The inhibitors show better inhibition efficiency than individual.
- The green inhibitor affects anodic Tafel slopes in HCl media and act as mixed inhibitor.
- AC impedance spectra prove the protective film formation on the mild steel.
- FTIR spectra reveals that the protective film consists of Fe^{2+} - C=O group and N-H stretch on metal surface.
- The SEM images offer a green inhibitor over metal surface thus preventing corrosion.

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Table 1. Inhibition efficiency (IE) of 0.1N HCl in various concentration of Imidazole and Ag^+ cation Inhibition system: Imidazole - Ag^+ Immersion period: 60 min

Imidazole (ppm)	Ag^+ (0 ppm)		Ag^+ (10 ppm)		Ag^+ (20 ppm)		Ag^+ (30 ppm)		Ag^+ (40 ppm)	
	IE %	CR (mmpy)	IE %	CR (mmpy)	IE %	CR (mmpy)	IE %	CR (mmpy)	IE %	CR (mmpy)
0	-	0.0080	5	0.00830	8	0.00800	10	0.00792	12	0.00790
20	5	0.00820	10	0.00810	15	0.00750	19	0.00732	18	0.00700
40	10	0.00800	16	0.00756	18	0.00688	26	0.00591	30	0.00550
60	14	0.00780	21	0.00740	26	0.00627	31	0.00531	51	0.00400
80	11	0.00761	26	0.00723	33	0.00593	39	0.00483	60	0.00313
100	15	0.00729	32	0.00706	38	0.00559	48	0.00452	70	0.00262
120	18	0.00710	37	0.00690	45	0.00506	59	0.00401	79	0.00159
140	24	0.00680	41	0.00635	49	0.00455	63	0.00307	86	0.00114
160	27	0.00670	44	0.00601	54	0.00409	69	0.00296	89	0.00101
180	29	0.00642	48	0.00556	59	0.00396	73	0.00185	92	0.00015
200	31	0.00630	56	0.00520	64	0.00304	77	0.00133	94	0.00011
220	33	0.00619	62	0.00500	70	0.00251	89	0.00113	95	0.00008
240	35	0.00619	62	0.00500	70	0.00251	89	0.00113	95	0.00008

Table 2.Impedance parameters of Mild steel immersed in 0.1N HCl in the absence and presence of inhibitors obtained by AC impedance spectra

Concentration of ppm	R_{ct} (Ωcm^{-2})	C_{dl} (μfcm^{-2})	I.E (%)
0.1NHCl	38	32	_
240ppm of Imidazole + 40 ppm of Ag^+	151	01	93.0

Table 3. Corrosion parameters of mild steel immersed in the absence and presence inhibitor obtained from potentiodynamic polarization studies

S.NO	Concentration	E_{corr} (mv/sce)	Icorr ($\mu A_{/cm^{-2}}$)	Ba (mv/dec^{-1})	Bc (mv/dec^{-1})	I.E (%)
1	0.1NHCl	-0.476	7.077×10^{-4}	110	221	_
2	240ppm of imidazole + 40 ppm of Ag^+	-0.487	2.500×10^{-4}	220	120	93

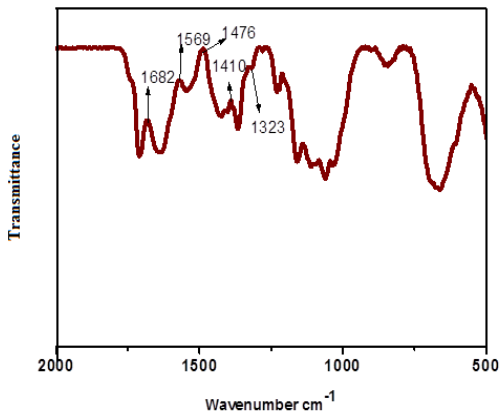


Figure 1.a FT-IR Spectrum of 0.1N HCl

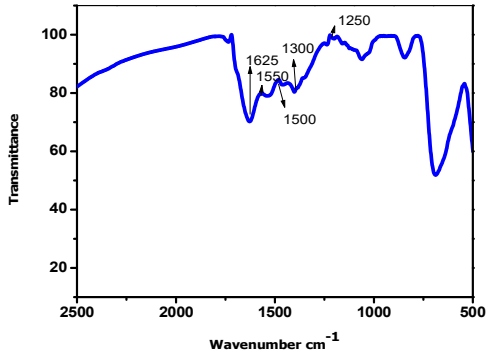


Figure 1.b FT-IR Spectrum of 0.1N HCl and b) 240 ppm of imidazole & 40 ppm Ag^+

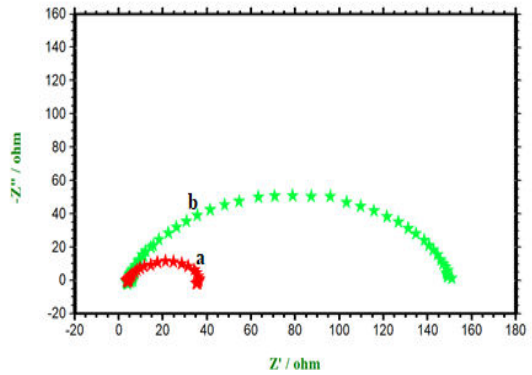


Figure 2.Impedance spectra curves of mild steel in various test solutions (a) 0.1 NHCl (b) 240 ppm of Imidazole& 40 ppm Ag^+

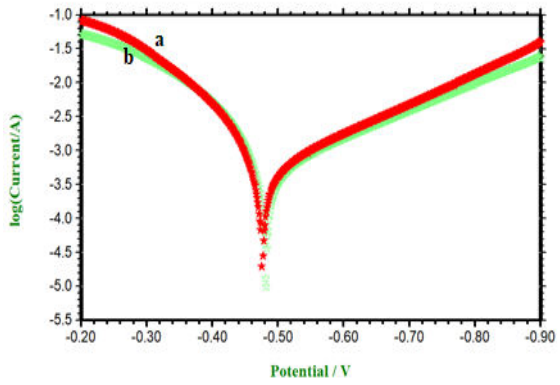
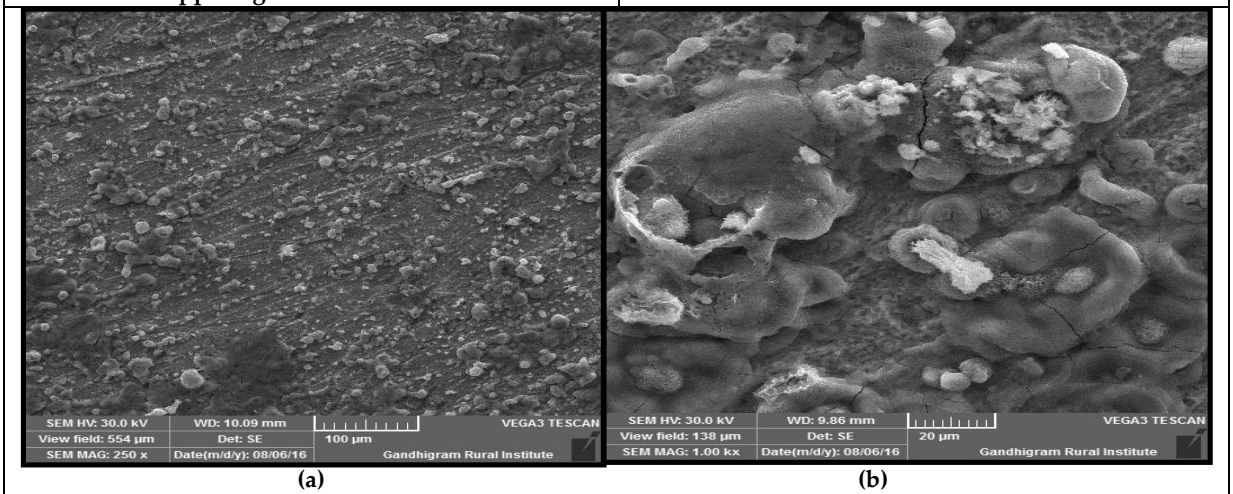


Figure 4. PolarizationSpectra a) 0.1 N HCl b) 240ppm of Imidazole& 40 ppm Ag^+



(a) **(b)**

Figure 6.Scanning Electron Microscopy (SEM) Studies fora) 0.1N HCl b)240 ppm imidazole+ 40 ppm of Ag^+

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RESEARCH ARTICLE

Phytochemical Screening, *In vitro* Antioxidant Activity and Chromatographic Profiling of Flavonoids from *Abrus precatorius* Linn. Leaf Extracts

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ABSTRACT

To evaluate phytochemical constituents and *in vitro* antioxidant activity by spectrophotometrically and bio autographic assays to highlight the importance of *Abrus precatorius* leaves as a potential source of bioactive determinants. Qualitative screening of secondary metabolites and quantitation of total alkaloids, flavonoids, and phenols were done in *A.precatorius* methanolic (APM), *A.precatorius* hydroalcoholic (APHA) and *A.precatorius* aqueous (APA) extracts of leaves by following standard methods. *In vitro* antioxidant activity evaluated through spectrophotometric methods(DPPH, HRS and FRAP) and TLC-DPPH bioautographic assay. Moreover, chromatographic profiling of flavonoids using optimized high performance thin layer chromatography(HPTLC) criteria at normal phase system was carried out.TLC plates were derivatized by anisaldehyde sulphuric acid (ANS) and natural product (NP)/polyethylene glycol (PEG) reagents, and functional group recognition was performed using fourier-transform infrared (FTIR) spectroscopy. Preliminary phytochemical screening confirmed the presence of alkaloids, flavonoids, carbohydrates, saponins, terpenoids, and glycosides. All the extracts exhibited substantial amount of flavonoid (27.96 ± 0.75 to 65.48 ±1.52mgQE/g) and phenol (50.94 ± 0.16 to 65.99 ± 0.46mgGAE/g) contents. APM showed maximum phenolic and flavonoid contents whereas, APHA demonstrated prominent antioxidant activity through spectrophotometric and TLC-DPPH assay. As per dissolution, each extract showed a specific chromatographic profile at 254nm and 366nm. The highest number of bands; 12 at 254nm and 9 at 366nm were found in APM extract. FTIR analysis confirmed the

existence of diverse biologically active functional group in each extract. From the pragmatic investigation, it can be concluded that APHA extract addresses potential scavenging activity with scientific provision through spectrophotometry as well as direct bioautographic techniques. These possessions might be allied with the existing high phenolic, flavonoid contents and their functional groups. Thus, it may find efficient implications in the treatment of diseases caused by nocuous free radicals.

Keywords: *Abrus precatorius* Linn., Phytoconstituents, Antioxidant activity, Flavonoid profiling, Bioautography, HPTLC, FTIR

INTRODUCTION

Treasure of traditional medicine has become puissant for the visionary therapeutics as Ayurveda, Chinese, Sidha, Unani, Korean, Kampo and Tribal practices are well admired [1]. These practices have not only been accepted in developing countries but are also popular in developed countries where contemporary medications dominate [2]. Moreover, people have faith in Ayurveda; one of the oldest holistic approaches to improve health via natural remedies derived from flora and fauna [3].

Herbs are the repository of abiotic constituents that are present in the form of phytochemicals such as phenols, flavonoids, alkaloids, steroids, glycosides, etc. and have been explored to the extreme for their medicinal properties [4]. Several studies illustrated that oxidative stress play role in degenerative disease [5]. Various pragmatic and epidemiological studies have shown that many phenolic ingredients like flavonoids are well known to act as natural antioxidants, may assert their ability by directly interacting with the free radicals and eventually creating a less reactive radical species or terminating the free radical chain reaction [6]. Additionally, the World Health Organization (WHO) also considers plants as an eventual source of plentiful drugs and promotes the continued use of these as pharmaceuticals for the betterment of life. Therefore, there is a convincing belief that daily intake of herbal products will reduce the risk of oxidative stress-mediated diseases [7]. However, numerous synthesized antioxidants are toxic and carcinogenic [8]. Hence, interest has been increased worldwide towards exploring new and safe plant constituents.

Moreover, it is challenging to quickly screen the antioxidants because of the diverse compositions of natural materials. A wide array of screening methods has been established to check probable antioxidants, including DPPH, FRAP, HRS, ABTS, and TLC bioautographic assays. Amongst, a simple, time saving, pocket-friendly TLC guided bioautography approach can easily detect and isolate the active components in a complex plant extract without sophisticated equipment [9]. Recently, High-Performance Thin Layer Chromatography (HPTLC) is being explored as an effective tool for the development of fingerprinting and considered as a primary reference for tracing bioactive constituents. It also provides an identical establishment to check the authenticity of drugs from herbal material [10]. HPTLC is a method of choice for testing plant extracts as we can deposit the whole extract even without pre-treatment, minimizing the experimental time and not losing compounds during sampling. In additament, multiple samples can be analyzed on the same plate allowing quick screening [11].

Currently, there has been an upsurge in the use of spectroscopy technique and has made striking advancements in the arena of clinical evaluation field. The Fourier-Transform Infrared (FTIR) spectroscopy is useful to recognize functional groups of chemical constituents by interpreting the infrared absorption spectrum in the biologically active components of plants [12]. In recent years, FTIR has been widely applied in quality control and identification of pharmaceutical drugs [13].

Globally, the phytoconstituents of abundant plants are used in relation to their ethnopharmacological attributes. One of those includes *Abrus precatorius*; belonging to the pea-family flowering plant, Fabaceae. The plant is native to India, found in all tropic and sub-tropic regions of the world [14]. This medicinal plant with woody vine, tamarind leaves,and striking red seeds (Figure: 1) is commonly known as Rosary pea, Gunja, Prayer bead, Crab's eye, and Jequirity bean. The leaves of *A.precatorius* have endowed with an inclusive array of phytochemicals viz. phenols, flavonoids, isoflavone, flavones, alkaloids, glycosides, terpenoids, steroids, etc. which makes this plant very significant for its medicinal properties. *A.preactorius* leaves are accredited for a broad range of therapeutics such as aphrodisiac, abortifacient, anti-diabetic, anti-oxidative, anti-cancer, anti-inflammatory, anti-microbial, anti-fertility [15,16]. However, scientific enlightenment on antioxidant properties and chromatographic flavonoid profile of *A. precatorius* leaves is in adequate thus the appraisal of phytochemicals by appropriate techniques is indeed required.

Keeping in view the above facts, the present study attempts to evaluate phytochemicals and *in vitro* antioxidant activity of various extracts of *A. precatorius* Linn. leaves. Moreover, to find out the flavonoids accountable for therapeutics, the study is engrossed in flavonoid profiling using HPTLC followed by its bioautography and functional group analysis.

MATERIALS AND METHODS

Chemicals

The DPPH (1,1-diphenyl-2-picrylhydrazyl), Folin-phenol were purchased from SRL, Mumbai, India. ANS (Anisaldehyde Slphuric acid), PEG-4000 (Polyethylene Glycol), Gallic acid, Quercetin, and Ascorbic acid were obtained from HiMedia, Mumbai, India. NP(Natural Product; 2-aminoethyl diphenylborinate) was purchased from TCI, Japan. The majority of the chemicals were of analytical grade and purchased from HiMedia, Mumbai, India and Sigma – Aldrich, USA.

Collection and Validation

The leaves of *A. precatorius* were collected from Ahmedabad district, Gujarat, India in September 2018 (latitude 23.08° N and longitude 72.52° E); instantly, its identification and pre-treatment were carried out. The plant material was identified by Department of Botany. The voucher specimen was deposited with reference identity GU/BOT/F/A2/2018.

Preparation of Extracts

The leaves were washed thoroughly thrice with distilled water (DW) to clean dust and soil particles. The leaves were shade dried for 60 days, pulverized with a mechanical grinder to obtain a fine powder, then stored at 4°C for further analysis. The leaf powder was subjected to methanolic extraction (APM) in a Soxhlet apparatus with 99% methanol. These fresh solid residues and solvent (solid-to-solvent ratio, 0.5:10.0g/ml) were placed in a 3.5cm × 14.0cm extraction thimble and extracted at 65°C with 300ml methanol for 14hrs with 2-3 cycles/hr. Moreover, 10% hydroalcoholic extract (APHA; DW: Methanol; 1:1v/v) and 10%aqueous extract (APA) were prepared by maceration in order to conquer the polar and nonpolar components. After extraction, each extract was filtered through a Whatman No.1 filter paper and collected in a petridish. The filtrates were dried in a hot air oven (Electroquip) for 18hrs at 40°C. The yield of each extract was stored in an amber bottle at 4°C to avoid deprivation by light and temperature. Lastly, the yield percentage of crude extracts was calculated according to the provided formula.

$$Y\ (\%) = \text{Final weight of extract obtained/Initial weight of raw material} \times 100$$

Qualitative screening of the phytochemicals

Qualitative phytochemical analysis of crude extract determines the presence of compounds like saponins, tannins, flavonoids, phenols, alkaloids, steroids, glycosides, etc. The preliminary phytochemical screening of crude extracts was carried out using the standard methods described in various literature [17,18,19,20].

Quantitative screening of the phytochemicals

Determination of total alkaloid contents (TAC)

Leaf powder (2g) was added into 200ml of 20% acetic acid in a beaker and covered to incubate for 4hrs at 25°C. After incubation, the mixture solution was filtered with Whatman No.1 filter paper and the filtrates were concentrated up to one quarter using a water bath. Concentrated ammonium hydroxide was applied drop by drop to this sample until the precipitation was achieved. The mixture was permitted to stabilize; the precipitate was collected by filtration and weighed [20]. The percentage of TAC was calculated as:

Percentage of total alkaloids (%) = Weight of residue/Weight of raw material taken × 100

Determination of total flavonoid contents (TFC)

TFC were estimated using the Aluminium chloride colorimetric method with some modification [21]. In this method, 0.5ml of extract (1mg/ml) followed by the addition of 100µl of 10% aluminum chloride, 100µl of 1M potassium acetate. Then, 4.3ml DW was added and incubated for 30min at 25°C. After incubation, absorbance was measured at 415nm using a spectrophotometer (Microprocessor UV-Vis double beam; Li-2800). TFC in various extracts were expressed by a standard curve with quercetin 10-60µg/ml and the final results were given as milligrams of quercetin equivalent (mg QE/g) dry extract.

Determination of total phenolic contents (TPC)

TPC of various leaf extracts were determined using Folin-Ciocalteu reagent as described by Siddhuraju and Becker with minor variations [22]. About 1ml of extract (1mg/ml) was mixed with 500µl of diluted Folin-phenol (optimized 1:4 with DW) and 2.5ml of 20% sodium carbonate. The solution was assorted well, incubated in dark (40min) for colour development, and measured spectrophotometrically at 725nm. A calibration curve of gallic acid was constructed and linearity was obtained in the range of 10-60µg/ml and the final results were given as milligram of gallic acid equivalents (mg GAE/g) dry extract.

In vitro antioxidant assays

1,1- diphenyl-2-picrylhydrazyl activity (DPPH)

The free radical scavenging activity of *A. precatorius* leaf extracts was assessed in terms of hydrogen donating capability using the stable DPPH radical by Blois method with minute modification [23]. In brief, 900µl (0.1mM) of methanolic DPPH solution was assorted with 100µl of various concentrations (50-300µg/ml) of dried extract. The mixture was shaken vigorously and allowed to stand in dark for 30min at 25°C. Control was prepared by following above but without the sample and methanol was used as a blank. The absorbance was measured at 517nm using a spectrophotometer. Results were compared with standard ascorbic acid. The ability of DPPH radical scavenging activity was calculated by using the below formula:

$$\% \text{ Inhibition} = A0 - A1 / A0 \times 100$$

Where, A0 = Absorbance of the control, A1 = Absorbance of the sample extract

Hydroxyl radical scavenging activity (HRS):

The hydroxyl radical inhibition efficacy of extracts was carried out according to the method of Smirnoff [24]. Briefly, the sample solution at different concentrations of extracts (50 to 300µg/ml) was mixed with 1ml of 9mM salicylic acid, 1ml of 9mM ferrous sulphate and 1ml of 9mM hydrogen peroxide. The reaction mixture was incubated at 37°C in an incubator for 60min. After incubation, the absorbance of the mixture was measured at 510nm using spectrophotometer. Quercetin was used as a standard and control was prepared without adding the sample. The HRS activity was calculated by,

$$\% \text{ Inhibition} = (A0 - A1) / A0 \times 100$$

Where, A0 = Absorbance of the control, A1 = Absorbance of the sample extract

Ferric reducing antioxidant power activity (FRAP)
The Fe^{+3} reducing ability of extracts was determined by using the method of Oyaizu with some modifications [25]. For this, 1ml of different concentrations of extracts (50-300µg/ml) was mixed with 2.5ml of 0.2M phosphate buffer (pH 6.6) and 2.5ml of 1% potassium ferricyanide, and then the mixture was incubated at 50°C for 30min. Afterward, 2.5ml of 10% trichloroacetic acid was added to the mixture, which was centrifuged at 3000rpm for 10min. After centrifugation, 2.5ml of the upper layer solution was mixed with 2.5ml of DW and freshly prepared 0.1ml of 0.1% iron chloride. The absorbance was measured at 700nm against a blank (phosphate buffer). Results were compared with standard ascorbic acid.

High Performance Thin Layer Chromatography (HPTLC) Profiling for Flavonoids
HPTLC (CAMAG System) criteria for plate layout, sample application, conditioning, development, and visualization were in accordance with the United States Pharmacopoeia (USP) General Chapter ⟨203⟩.

Preparation of Sample
For obtaining the maximum number of bands with sharp resolution, the concentration of extracts, mobile phase, saturation time, sample volume, were optimized. Each extract (20mg/ml) was prepared by adding in respective solvents and sonicated for 10min for complete dissolution.

Development of HPTLC Technique
HPTLC was performed on a 5×10cm aluminium packed TLC plate coated with 0.2mm layer of silica gel $60F_{254}$ (Merck, Germany) using semi automated CAMAG LinomatV applicator (S/N 180344). Sample (200µg/spot) of 8mm length was applied by the Hamilton microsyringe (Switzerland) with the nitrogen flow (150nl/s) at 25±2°C. The syringe was mounted on a LinomatV applicator and was programmed through VisionCATS software version 2.5. The plate was developed in an ascending manner in CAMAG twin through the chamber (10×10cm) previously saturated with the solvent [Chloroform: Methanol: DW (8:2:0.2)] for 30min. After development, the TLC plate was air-dried and scanning was performed using TLC Scanner 4 (S/N 180404) to develop chromatogram at 254 and 366nm. Densitograms and R_f values were documented using the software. The developed plate was then sprayed with universal derivatizers such as ANS and 1% methanolic NP followed by 5% ethanolic PEG reagent to visualize flavonoid compounds.

TLC-DPPH Bioautography
Using the TLC sprayer, a dry TLC plate was sprayed with 0.2% methanolic DPPH solution [26]. After spraying, keep the plate in dark for 30min then observation was carried out. Yellow spots on a purple background show the antioxidant activity of the separated fraction.

Fourier-Transform Infrared Spectroscopyanalysis (FTIR)
The extracts were grounded with KBr pellets with the help of KBr press Model M-15, Technosearch instruments, and analyzed in ranging frequency from 3500 to 500cm^{-1} for the functional group documentation. All the measurements were recorded in transmittance mode using Bruker Alpha, Lab India Instrument Private Limited, functioned by OPUS 7.5 software. The air spectrum was randomly measured and subtracted for the background.

RESULTS

Yield Value
The current research emphasizes the importance of yield to estimate the active constituents of raw material for therapeutics from *A. precatorius* leaves. The significant percentage yield was obtained from the APM extract, followed by the APHA and APA which is given in Table 1.

Qualitative screening of the phytochemicals

The outcome of phytochemical screening of various secondary metabolites such as alkaloids, flavonoids, carbohydrates, tannins, steroids, proteins, saponins, amino acids, terpenoids, and glycosides was given in Table 2. The results revealed that the plant is a virtuous source of phytochemicals and also indicates that the dissolution of phytochemicals is varied with the solvents used for the extraction. More number of phytochemicals were dissolved in APM compared to other extracts.

Quantitative screening of the phytochemicals

Determination of total alkaloid contents (TAC)

The gravimetric analysis of TAC is 30.75mg/100g for *A. precatorius* leaf powder.

Determination of total flavonoid contents (TFC)

TFC was the highest in APM extract (65.48mg QE/g extract) followed by APHA and APA extracts with 56.80 and 27.96mg QE/g extract respectively as shown in Table 3. In addition, the result clarified that flavonoids are more soluble in the alcoholic medium as compared to water. The equation from the calibrated curve is defined below.

$$Y = 0.0065x - 0.0073; R^2 = 0.9949$$

Determination of total phenolic contents (TPC)

From a pragmatic view, TPC was varying widely between 50.94 to 65.99mg GAE/g extract (Table: 3). APM extract demonstrated higher TPC (65.99mg GAE/g extracts) than other solvent extracts (APHA; 59.43 and APA; 50.94mg GAE/g). The equation from the calibrated curve is defined below.

$$Y = 0.0159x – 0.1079; R^2 = 0.9822$$

***In vitro* antioxidant assays**

1,1- diphenyl-2-picrylhydrazyl activity (DPPH)

DPPH assay is a rudimentary parameter to check the antiradical activity of natural compounds and its results can stipulate the presence of phenolic and flavonoid components [27]. The higher percentage of scavenging activity and lower IC 50 values usually imply greater antioxidant activity. Significant activities were found which was directly proportional to the concentration. Scavenging activity of ascorbic acid, APM, and APHA was found to be nearer to each other. The APM and APHA were able to scavenge the DPPH radicals with a %inhibition of 69.54 ± 0.83% and 64.85 ± 0.90% respectively (Figure: 2) at the highest concentration of 300µg/ml with the IC 50 values of 190.76 ± 0.23 and 201.48 ± 2.99µg/ml respectively (Table: 4). APA showed less %inhibition (56.59 ± 3.57%) compared to other extracts at the same concentration with the IC 50 value 245.48 ± 6.12µg/ml.

Hydroxyl radical scavenging activity (HRS)

During the HRS assay, all the extracts exhibited significant activity in a concentration dependent manner (Figure: 3) with maximal %inhibition of 56.53 ± 2.15% at 300µg/ml by APHA with the IC 50 value of 252.73 ± 4.09µg/ml. APHA was found to be a more powerful quencher of OH radical than ascorbic acid (55.71 ± 1.64%). APM extract (IC 50 =271.66 ± 7.13µg/ml) was able to inhibit 52.40 ± 1.20% at highest concentration. APA extract (34.62 ± 1.43%) was found to be a weak scavenger of OH with the IC 50 values 449.30 ± 17.25µg/ml.

Ferric Reducing Antioxidant Power Activity (FRAP)

The reducing power of different extracts was explored by perceiving the conversion of Fe+3 to Fe+2, whereby depending on the reducing power of the sample, the yellowish colour of the test solution changes to various shades of green and blue [28]. The reducing efficiency of the extract serves as a reflection of its antioxidant activity. This was scrutinized by measuring the formation of Perl's Prussian blue colour of Fe+2 at 700nm [29]. The absorbance value (0.344 ± 0.03) for APHA found to be higher than APM (0.203 ± 0.06) and APA (0.16 ± 0.03) extracts. This means the APHA has a considerable capacity to react to free radicals in order to terminate them into more stable non-reactive

species. All the extracts display some grades of electron-donating capacity in a concentration-dependent manner. The results were expressed as the mean ± SE (Figure:4).

TLC-DPPH Bioautography

In APHA extract (Figure:15) three different areas with the highest intensity of the clear yellow spot corresponding to the R_f values 0.37, 0.47, and 0.58 with respect to fractions 4, 5 and 6 depicted scavenging activity. APA extract possessed only one fraction (3) particular to the R_f value 0.425 indicating antioxidant activity.

FTIR Analysis

All the extracts were evaluated using FTIR spectrum to analyze functional groups and to identify peaks characteristic in the region of infrared radiation. Total twelve, ten, and six notable bands were detected between 1000 and 3500cm^{-1} in APM, APHA, and APA respectively; the transmission was converted into absorbance, and analysis was obtained. Table 7 illustrates the probable functional groups and the description of the peak value. APM spectra revealed a peak at 3370.22 and 3259.87cm^{-1} corresponding to bending vibrations of alcohol/phenol O-H stretch. Further peaks 2918.84cm^{-1} exhibiting strong N-H stretching verifying amine salt. A peak of 2849.93cm^{-1} (medium C-H stretching), 1603.78cm-^{1} (medium C-C stretching). A medium C-H bending was detected at both 1460.98 and 1383.48cm^{-1} vibration. Between the frequency range of 1000–1300cm^{-1}, five bands appeared amongst three peaks (1249.90cm^{-1}, 1176.86cm^{-1}, 1122.95cm^{-1}) indicating bands of C-H stretching and two peaks (1070.10cm^{-1}, 1010.37cm^{-1}) assigning bands of C-O stretching. APHA displayed bands at 3515.96 and 3250.45cm^{-1}(O-H stretching strong), 2831.60cm^{-1}(C-H stretching medium), 2337.22cm^{-1} (O=C=O stretching strong),1590.42cm^{-1}(C-C stretching medium), 1364.00cm^{-1}(C-Hbending medium), 1247.87 and 114.27cm^{-1}(C-H stretching strong). 1072.31cm^{-1}(C -O stretching strong). The spectra of APA disclosed bands at 3371.00cm^{-1}(water O-H stretching strong), 2919.93cm^{-1} (N-H stretching strong, broad), 2850.50cm^{-1}(C-H stretching medium), 1602.07cm^{-1} (C-C stretching strong), 1384.73cm^{-1} (C-H bending medium) and 1073.00cm^{-1}(C-H stretching, medium).

DISCUSSION

Phytoconstituents are well-known scavengers for noxious free radicals and are also reported to have plenty of therapeutic benefits [30,31]. Therefore, it is permissible to assess the phytoconstituents in the plants having ethnomedicinal properties. Subsequently, the leaf part of *A. precatorius* was selected and explored for its bioactive compounds via standard indices such as yield value, phytochemical assessment, antioxidant power, flavonoid profiling using TLC trailed with direct bioautography and FTIR spectroscopy. In the present study, the yield value of APM extract is highest and remarkable (Table:1) indicating more phytoconstituents are conquered in the methanolic solvent. The variation in yield value might be due to the extraction method, the solvent used, the degree of polarity, and the species nature of secondary metabolites (Venkatesan *et al.,* 2019) [32]. The outcomes of phytochemical screening revealed the presence of alkaloids, flavonoids, carbohydrates, glycosides, saponins, and terpenoids (Table: 2). These abiotic ingredients are frequently present and claimed for many biological activities as well a helping hand in euthenics [33]. The presence of these phytochemicals and their scientific validation enlighten the usage of *A. precatorius* leaves in folk medicine too. Each extract showed a significant quantity of phenolic and flavonoid components.TPC was found dramatically higher in APM extract (Table: 3) which was supported by the result obtained by Jain et al. [34] TFC was also higher in APM while other researchers found a high proportion of TFC in ethanolic extract [16,34]. The quantity of phytoconstituents are influenced by several environmental factors, including extraction method, temperature, time, and solvent types. Among them, the key factor is the selection of solvent for extraction [32].

As described by several researchers, estimation of antioxidant properties of a sample using a single assay will be inadequate to portray complete evolution because it is influenced by many circumstances [35]. Hence, the current research included a number of assays such as DPPH, FRAP, HRS and TLC-DPPH bioautography to explore the

antioxidant potential of *A. precatorius* leaf extracts. The DPPH is well described, stable, and model synthetic radical for the evaluation of antioxidant efficacy of any analyte. A comparative study of the antioxidant activity of extracts with standard antioxidant reference material viz. ascorbic acid was performed. The DPPH is reduced by accepting the hydrogen from the solution mixture which was confirmed by spectrophotometry and changes in colour of DPPH from purple to yellow in presence of extracts. Many researchers have found an optimistic correlation of antioxidant activity with phenolic and flavonoid contents [36,37,38]. In the present study, DPPH free radical was scavenged by the extracts in a dose-dependent manner and the result is in agreement with previous data [39,40]. Among all the tested extracts, APM exhibited higher (69.54 ± 0.83%) radical scavenging activity. This might be due to the presence of more phenolic and flavonoid contents which facilitate hydrogen atom transfer mechanism [41].

Further, hydroxyl radical is a highly reactive oxygen species and causes major impairment to biomolecule such as DNA, proteins, etc. Free hydroxyl radicals have been associated with the occurrence of several pathological conditions in the human body. Therefore, eradication of these radicals is not only essential but also the most effective defense mechanism of mankind against various diseases using herbs [42,43]. HRS activity was estimated by generating the hydroxyl radicals using hydrogen peroxide. As demonstrated in figure 3, a noteworthy reduction in the concentration of hydroxyl radical and significant %inhibition activity was observed due to the extracts. It is worth mentioning that APHA extract (56.53 ± 2.15%) had the highest quenching power compared to other extracts and standard reference ascorbic acid too, similar results were observed by Gul et al [16]. Hence, APHA extract can be employed to prevent free-radical-mediated diseases in the dietary or pharmaceutical fields. The lower IC50 values of the extracts reflect the significance of *A. precatorius* leaf extracts as an auspicious natural antioxidant.

The ferric reducing power of extracts served as a significant indicator of potent antioxidant property. In this study, APHA extract showed maximum reducing power (Figure: 4) whereas, an investigation by Jain et al [34] showed the highest reducing power in methanolic extract. The extracts might have a unique capacity to convert Fe3+ to Fe2+ by donating an electron [44]. A previous report suggested that the presence of an enormous amount of phenol and flavonoid contents served as potent reductants. The results are supported by the findings of several researchers [16,45].

HPTLC is a keystone tool in most of the pharmacopeia, in the field of plant taxonomy as well in identification, authentication, and documentation of raw materials as proved to be a linear, precise, reproducible, and accurate technique [46]. According to the literature, separation of flavonoids is generally achieved using ethyl acetate: acetic acid: formic acid: distilled water (100:11:11:26, v/v) as a mobile phase [26]. By having the goal of distinct flavonoid separation various mobile phases in different proportions such as toluene: ethyl acetate (5:2v/v), formic acid: acetic acid: distilled water (5:3:0.7:0.3:1v/v), petroleum ether: methanol: benzene (8:1:1.5v/v), and chloroform: ethyl acetate (8:2v/v) were practiced. However, chloroform: methanol: distilled water (8:2:0.2v/v) gave the best resolution which can be worked upon in further studies. Among all the extracts, the highest number of bands; 12 at 254 and 9 at 366nm with corresponding Rf values were found in the APM extract which is given in Table 6. Fractions 4, 5 and 6 were found in the same lane at 254nm in both APM and APHA extract (Figure: 8 and 9). However, fraction in APHA extract was more prominent than others and gives yellow colour immediately after derivatization with NP/PEG (TLC plate vii) and greenish colour by ANS (TLC plate v) reagent. APA extract showed only one similar band (band3) reference to Rf value 0.42 with band 4 in APHA extract (Table: 6) and also become intense after derivatization. This profile can also be used as a marker for the leaf of *A. precatorius* for the purpose of standardization, identification, and authentication of flavonoids.

TLC bioautography was approached for qualitative identification of antioxidative flavonoids in all the extracts of *A. precatorius* leaf. This approach offers accurate, reliable, and rapid detection with easy localization of the active fraction in a plant extract [26]. In spectrophotometric DPPH assay APM extract exhibited the highest antioxidant activity while in TLC-DPPH assay, antioxidative effects were elucidated by APHA extract which evident reactivity of fraction against DPPH radical.

Biological activity of any organic-biomolecule influence by its functional groups as they significantly contribute to partition coefficient, stereochemistry, crystal structure, inherent-base features, solubility, and so on. All these characteristics are intended to impact the absorption, distribution, metabolic extraction, and toxicity of bioactive molecule [47]. Therefore, identification and analysis of functional group helps to assess the structure-activity relationship and plays a crucial part in determining the complete physicochemical properties of the extract respectively. In the current study, FTIR spectroscopy of all the extracts demonstrated the existence of hydrogen-bonded OH group phytochemicals. It is well recognized that hydroxyl functionality is an integral element of most of the phenolic phytochemicals such as flavonoids. Recent studies show that numerous phytochemicals, including polyphenolic constituents (e.g., flavonoids) and various herbal extracts demonstrated antioxidant activity [48,49,50]. Moreover, our findings suggest that the leaf extracts of *A. precatorius* contain different biologically effective functional groups such as amines, amide, alcohols/phenols O-H stretch, carboxylic acids, aldehydes, etc (Table:7). Hence, we can confirm the plant possess considerable bioactive phytochemicals.

In sum, the research findings suggest that *A. precatorius* leaves are a potential source for phytoconstituents especially flavonoids having worthy antioxidant power by scavenging various free radicals. It is imperative to mention that APHA is a potent extract as it unveiled good scavenging activity amongst studied extracts. The present investigation delivers data for the identification and authentication of biologically active phytoconstituents. This basic and fundamental evidence will simplify in leading additional research on the discovery of therapeutic candidates, resolve their efficiency by *in silico, in vitro,* and *in vivo* studies. In line with promising findings, experiments are underway to stamp-out potential bioactive flavonoid entities using high-throughput techniques.

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Table 1: %Yield of various extracts of *A. precatorius* leaves

Extraction Method	Extraction Solvent	% Yield
Soxhlation	Methanol	29.73
Maceration	Hydro-alcohol	11.80
Maceration	DW	03.50

Table 2: Preliminary phytochemical screening of the different extracts of *A. precatorius* leaves

Phytocomponents	Test	Extracts		
		APM	APHA	APA
Alkaloids	[i] Hager's test	++	+	+
	[ii] Dragendorff's test	++	+	++
Flavonoids	[i] Alkaline test	+	+	+
	[ii] Aluminium chloride test	+	+	+
Carbohydrates	[i] Molicsh's test	+	+	+
	[ii] Fehling's test	++	+	+
	[ii] Benedict's test	+	+	+
Tannins	[i] Reaction of Stiasny	++	+	+
	[ii] Lead Acetate test	+	+	+
Steroids	[i] Liebermann Burchard test	-	-	-
	[ii] Salkowski's test	-	-	-
Proteins	[i] Biuret test	+	-	-
Saponins	[i] Frothing test	++	+	+
Amino acids	[i] Ninhydrin test	+	-	-
Terpenoids	[i] Terpenoid test	+	+	+
Glycosides	[i] Legal's test	+	++	++

Note: ++: high amount, +: low amount, -: absent

Table 3: Quantitative screening of the different extracts of *A. precatorius* leaves

Quantitative screening of phytochemicals		
Sample extracts	TFC (mg/g)	TPC (mg/g)
APM	65.48 ±1.52	65.99 ± 0.46
APHA	56.80 ±1.07	59.43 ± 0.19
APA	27.96 ± 0.75	50.94 ± 0.16

Note: Each value is expressed as a mean ± SE (n = 3).

Table 4: IC_{50} values obtained in the antioxidant activity assays

Sample Extracts	IC_{50} values (µg/ml)	
	DPPH	HRS
Ascorbic acid	245.48 ± 7.80	271.66 ± 07.44
APM	190.76 ± 0.23	313.76 ± 07.13
APHA	201.48 ± 2.99	252.73 ± 04.09
APA	251.04 ± 6.12	449.30 ± 17.25

Note: Each value is expressed as a mean ± SE (n = 3).

Table 5: Reducing power activity of various extracts

Sample extracts (µg/ml)	Ascorbic acid	APM	APHA	APA
50	0.143 ± 0.04	0.074 ± 0.05	0.057 ± 0.01	0.057 ± 0.02
100	0.222 ± 0.01	0.101 ± 0.01	0.078 ± 0.02	0.062± 0.02
150	0.311 ± 0.01	0.125 ± 0.01	0.097 ± 0.01	0.110± 0.01
200	0.320 ± 0.03	0.139 ± 0.03	0.105 ± 0.03	0.116 ± 0.02
250	0.33 ± 0.06	0.190 ± 0.04	0.171 ± 0.02	0.151 ± 0.02
300	0.416 ± 0.03	0.203 ± 0.06	0.344 ± 0.03	0.161 ± 0.03

Note: Each value is expressed as a mean ± SE (n = 3).

Table 6: Number of compounds with respective R_f value at 254 and 366nm

Peak No.	R_f values at 254nm			R_f values at 366nm		
	APM	APHA	APA	APM	APHA	APA
1	0.01	0.03	0.01	0.01	0.01	0.01
2	0.19	0.09	0.03	0.05	0.08	0.18
3	0.30	0.19	0.42	0.11	0.55	0.57
4	0.46	0.42	0.66	0.62	0.77	0.96
5	0.61	0.53	0.74	0.77	0.87	-
6	0.65	0.66	0.95	0.80	0.93	-
7	0.75	0.88	-	0.84	-	-
8	0.80	0.91	-	0.88	-	-
9	0.84	0.95	-	0.97	-	-
10	0.87	-	-	-	-	-
11	0.91	-	-	-		
12	0.95	-	-	-	-	-

Table 7: FTIR analysis revealed the presence of functional groups in the various extracts of *A. precatorius* leaves

Peak range cm^{-1}	Peak value			Appearance	Band interaction and Functional group	Possible compounds
	APA	APHA	APM			
3500-3100	3371	3515	3370	Strong, Broad	OH stretching	Alcohol
	-	3250	3259	Strong, Broad	OH stretching	Alcohol
3000-2800	2919	-	2918	Strong, Broad	N-H stretching	Amine salt
	2850	2831	2849	Medium	C-H stretching	Alkane
2400-2000	-	2337	-	Strong,	O=C=O stretching	Carbon dioxide
1650-1550	1602	1590	1603	Medium	C-C stretching	Conjugated alkene
1550-1300	-	-	1460	Medium	C-H bending	Alkane
	1384	1364	1383	Medium	C-H bending	Alkane
1300-1000	1073	-	-	Strong	C-H stretching	Primary alcohol
	-	1247	1249	Strong	C-H stretching	Alkyl aryl ether
	-	1114	1176	Strong	C-H stretching	Aliphatic ether
	-	-	1122	Strong	C-H stretching	Aliphatic ether
	-	1072	1070	Strong	C-O stretching	Primary alcohol

	-	1037	1010	Strong	C-O stretching	Primary alcohol
1000-650	868	835	867	Strong	C-Cl stretching	Halo compound
	-	703	745	Strong	C=C bending	Alkene
	-	656	670	Strong	C-Br stretching	Halo compounds
800-400			563	Out-of-plane ring bending	C-halogen	Halo compounds
			520			
			445			
			429			
			404			

Figure 1: ***Abrus precatorius;*** **(i)**Climber **(ii)**Leaves **(iii)**Seeds **(iv)**Flower

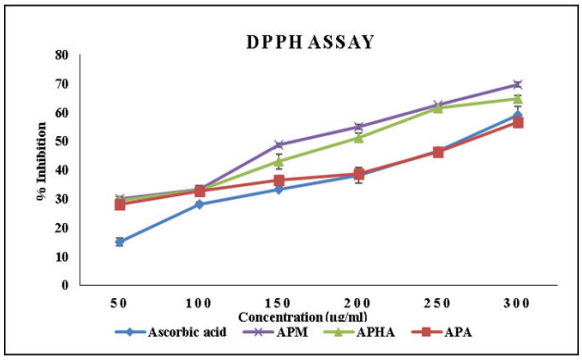

Figure 2: % Inhibition of DPPH radical scavenging activity of different extracts of A. precatorious leaves

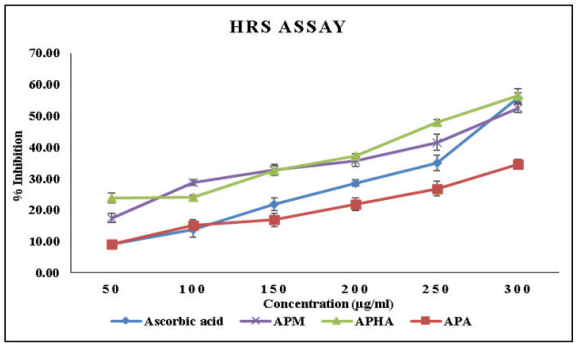

Figure 3: % Inhibition of HRS activity of different extracts of *A. precatorious* leaves

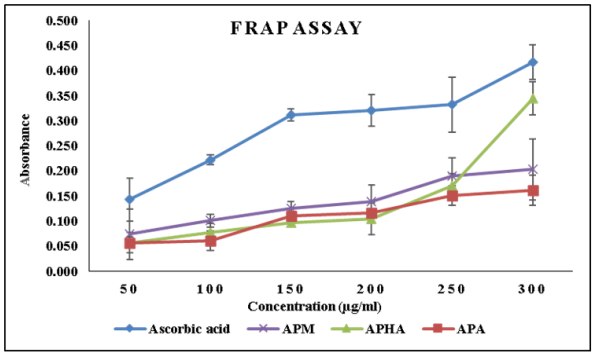

Figure 4: Absorbance of FRAP ASSAY

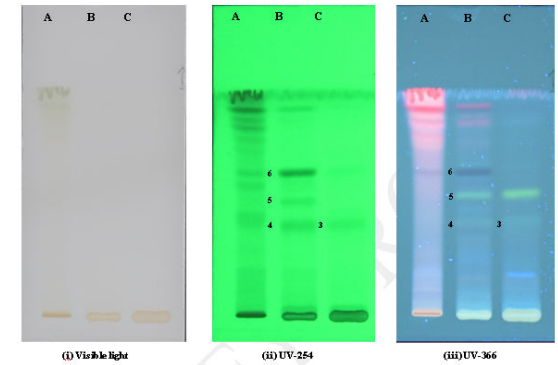

Figure 5: HPTLC fingerprinting profile for flavonoids in the various extracts of A. precatorius leaves Lane A: APM (200µg/spot); Lane B: APHA (200µg/spot); Lane C: APA (200µg/spot)

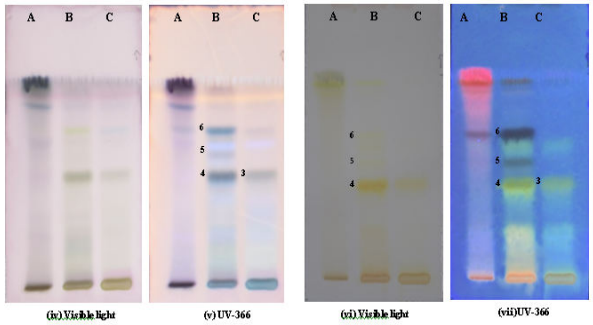

Figure 6: Detection of flavonoid: TLC chromatogram, detection using ANS reagent under (iv) visible light (v) UV-366 and detection using NP/PEG reagent under (vi) visible light (vii) UV-366
Lane A: APM (200µg/spot) ; Lane B: APHA (200µg/spot) ; Lane C: APA (200µg/spot)

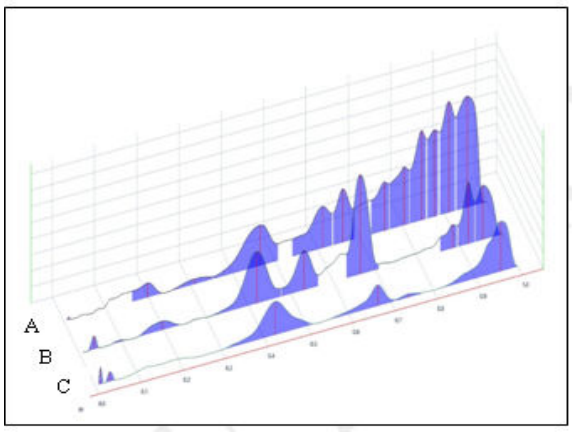

Figure 7: 3D diagram of various extracts (A: APM, B: APHA, C: APA) at 254nm

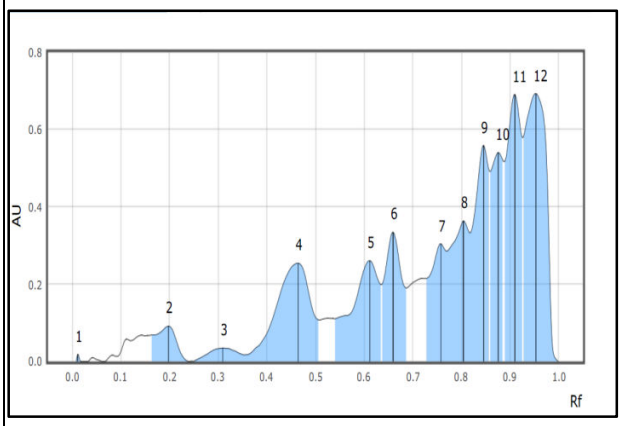

Figure 8: Chromatogram of flavonoids in APM extract at 254nm

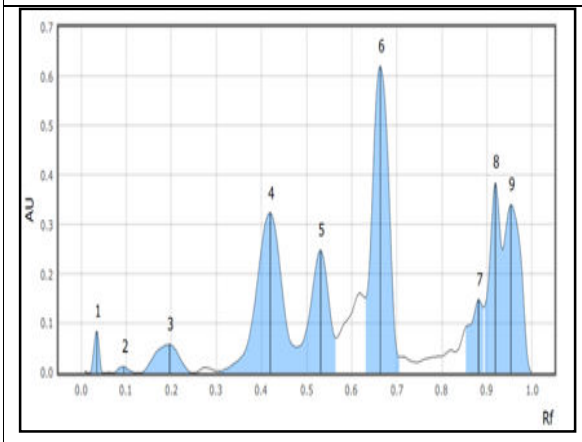

Figure 9: Chromatogram of flavonoids in APHA extract at 254nm

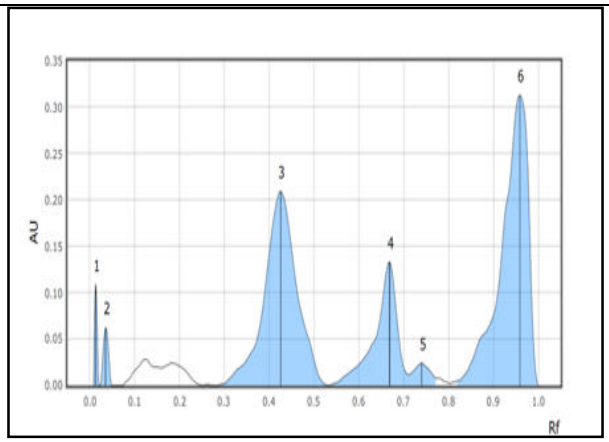

Figure 10: Chromatogram of flavonoids in APA extract at 254nm

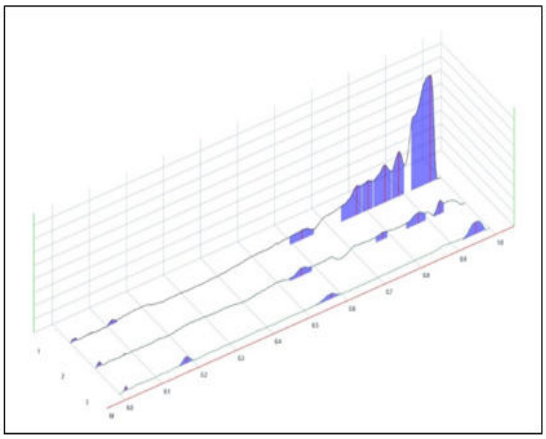

Figure 11: 3D diagram of various extracts (A: APM, B: APHA, C: APA) at 366nm

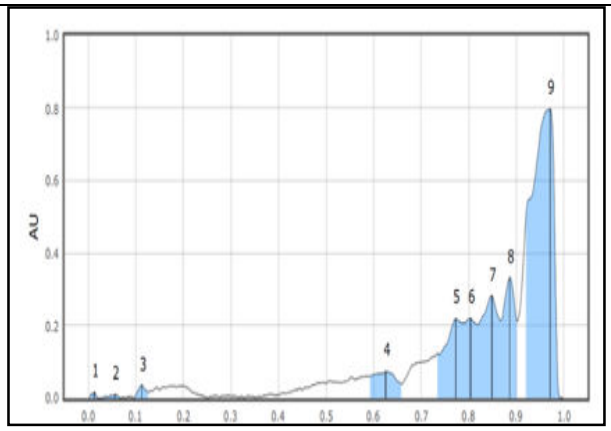

Figure 12: Chromatogram of flavonoids in APM extract at 366nm

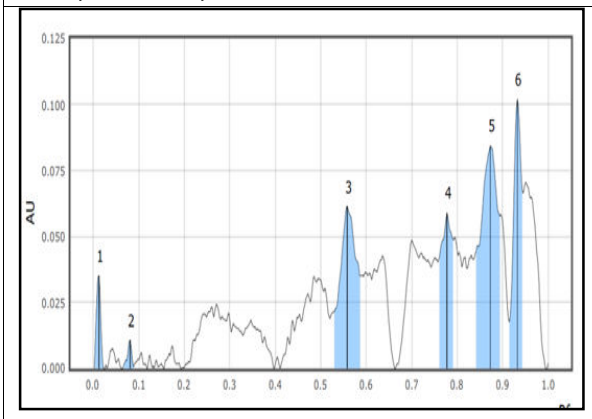

Figure 13: Chromatogram of flavonoids in APHA extract at 366nm

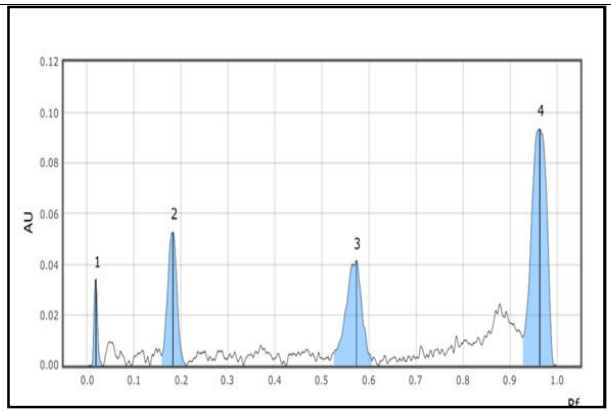

Figure 14: Chromatogram of flavonoids in APA extract at 366nm

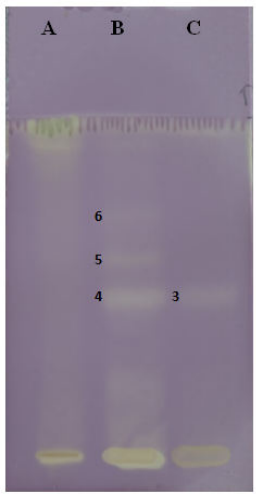

Figure15: (viii)TLC-DPPH bioautogram

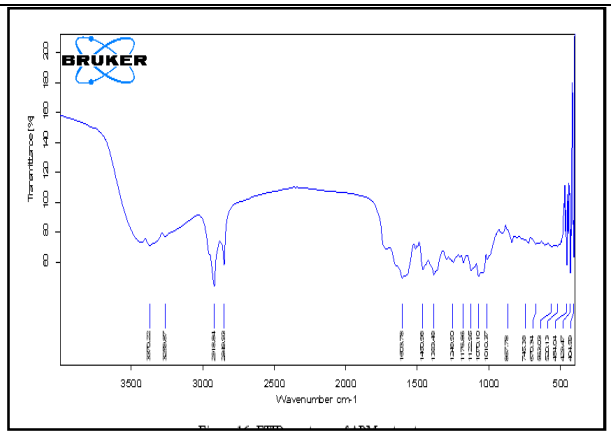

Figure 16: FTIR spectrum of APM extract

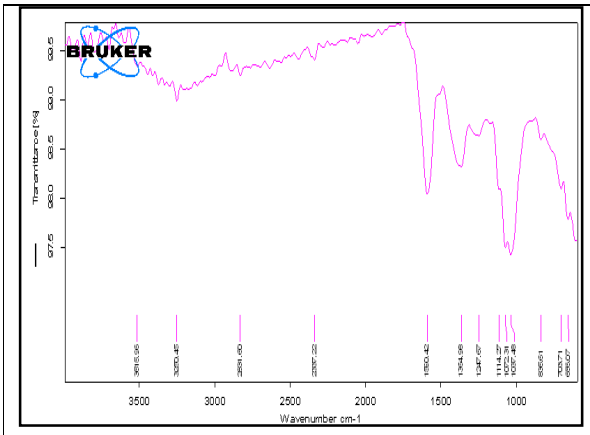

Figure 17: FTIR spectrum of APHA extract

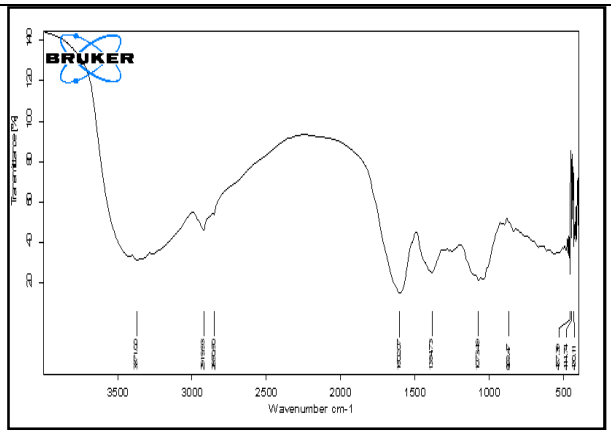

Figure 18: FTIR spectrum of APA extract

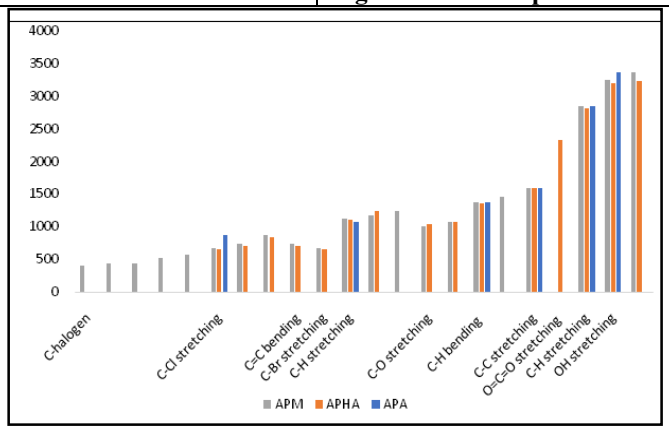

Figure 19: Comparative study of functional groups in various extracts of *A. precatorius* leaves

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REVIEW ARTICLE

Exosomes: Classification, Isolation, Characterization & Application in COVID-19

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ABSTRACT

Exosomes are defined as type of endogenous extravascular physical having particle diameter in nanometers. Exosomes of natural sources can be classified based upon their source widely into two main groups namely, plant, endogenous & animal. This was discovered in 1983, after microscopy was developed into advanced stage in 1970's. Brain-derived exosomes, NK cells derived exosomes, Macrophage derived exosomes are some of the endogenous exosomes from human. . The sources of natural exosomes from plant sources are Tomato, Ginger, carrots and grapefruits. Important animal sources for exosomes are bovine milk and dendritic cell of murine. Endosomal sorting complex required for transport (ESCRT) pathway is considered to be one of the most important pathways for synthesis of exosomes. Immuno affinity based purification, Ultracentrifugation, Microfluidic based isolation, are some of the isolation techniques employed for exosomes, but centrifugation is the most commonly employed method. Characterization of exosomes can be performed techniques like Dynamic Light Scattering and Resistive Pulse Sensing. Although, it is applied in Regenerative therapy and Cancer treatment, currently it is highly vital in treatment of covid-19 infection by acting as therapeutic agent, Nano-decoys & carrier for antiviral drugs. Covid-19 infection is actually a SARS-COV-2 infection caused by coronavirus. Current coronavirus and exosomes have a lot of similarity in terms of entry mechanism, morphology, targeting capacity and more, thus, creating a new hope and inspiration for scientists to employ exosomes in the treatment of covid-19 infection

Keywords: exosome, covid 19, cell, mesenchymal stem cells, natural killer cells

INTRODUCTION

Exosomes are defined as the type of endogenous extravascular physical having a particle diameter in nanometers[1,2]. Exosomes has present as one of the main populations of extravascular vesicles[3]. This type of vesicles is usually secreted by multiple cells in our human body. "Cellular trash bags" is another name of exosomes coined by scientists. This is due to the reason that it helps in the disposal of unnecessary cellular debris[4]. Exosomes help in delivering signals to recipient cells to perform the specific biological function[5]. This is widely applied in medical field due to the endogenous nature and beta distribution when compared to other extra vascular vesicles[6]. Currently, it is also widely applied in genetic transfer as well as treatment of covid-19 [7].

History of Exosomes

In the late 1970's, electron microscopy was developed into advanced stage after the developments of deep etch technique[8]. Applying this technique, the multi-vesicular endosomes was discovered, which was quite unique during those years. The genesis of exosomes by exocytosis of multi-vesicular endosomes was discovered by applying electron microscopy and biochemical purification [9-11]. This was done successfully by analyzing the immature sheep reticulocytes [11]. This led to a formation of new extra cellular membrane vesicles called exosomes in 1983. After this important discovery, there were several developments in this system[12,13].

Classification

Exosomes of natural sources can be classified based upon their source widely into two main groups namely, plant, endogenous & animal.

Sources of Exosomes

Endogenous Exosomes

The cells which produce exosomes are usually of immunological importance. For example, natural killer cell, dendritic cell, umbilical vein endothelial cell, mesenchymal cell, etc. [14,15]. There is also sufficient evidence for secretion of exosomes by macrophages[16]. In 2020, recent research specifies the isolation of exosomes from human brain. The type of exosomes which are usually isolated from nervous system is collectively called Brain derived exosomes (BDE)[17]. Let us discuss the various types of endogenous exosomes:

Brain-Derived Exosomes

This type of exosomes has better lipophilicity when compared to other types of extravascular vesicles. As a result, it can easily penetrate through the blood brain barrier (BBB)[18,19]. It should be noted that this kind of exosomes can act as biomarker for neuro-degeneration[20]. This is also widely employed as biomarkers for CSF. Application of exosomes is non-invasive nature and can be preferred over lumbar puncture. E. g:α-synuclein, Aβ-42, [21-23]. Astrocytes, neurons comprising the central nervous system, microglia are some of the sources for biogenesis of exosomes[24]. Brain-derived exosomes have been applied in exporting amyloidogenic proteins like Tau. This property of exosomes shows that it is not only responsible for disposal mechanism of unwanted proteins but also helps in transfer of essential proteins from one place to another[11, 25, 26].

Natural Killer Cells Derived Exosomes

The natural killer cells of our human body provide the first line of defense for our human body. NK cells are lymphocytes of huge size situated in blood. These cells comprise of 10 to 15% of total lymphocyte population[27]. Immuno-surveillance is one of the main functions of these cells [28]. CD-56 is considered to be one of the several widely used biomarkers used in direction of natural killer cells. The same biomarker is used in recognizing exosomes released by NK cells[29, 30]. Exosomes derived from dendritic cells have several medical applications. But, natural

killer cells derived exosomes are not used in medical field. Natural killer cells release secretory exosomes despite their active nature. Exosomes in both active and resting phases the study clearly suggests that NK cells derived exosomes have an essential role in in systemic control of immune response of the human body [30]. Exosomes derived from natural killer cells is widely used in the recognition of anti-neoplastic effectors. The anticancer activity of NK derived exosomes was enhanced in presence of fibrinogen and β-actin. Exosomes for less affected by extreme conditions like hypoxia due to high extravasation rate[31-33].

Macrophage Derived Exosomes

Macrophages are the class of cells which are released during self-healing conditions of a tissue and thereby providing innate immunity. This type of cells produces inflammatory response and helps in maintenance of homeostasis[34,35]. Based on the phenotype, the macrophages can be broadly classified into two sections namely, M-1 & M-2 [36-38]. Antigen presentation is usually M-1 type macrophages when compared to M2 [39]. Nanoparticles can be coated with exosomal coating for better anti-tumor efficacy. This antineoplastic efficacy can be achieved due to better tumor accumulation in presence of exosomal coating[40]. Storage of this type of exosomes is usually done around -20□ [65].

B-Cell Derived Exosomes

B-cell stands for bone marrow cell. This cell secretes exosomes, which is useful in carrying MHC class II loaded peptide [41]. α-4-intergrin is substance that is secreted by reticulocytes. In one research study it was found that it is also present in B-cell derived exosomes [42]. It is usually derived from patients with allergy, since only during the allergic reaction B-lymphocyte secrete this exosomes. In one experimental study, exosomes was derived from b lymphocytes in individuals with Birch pollen allergy. This experimental study mainly focuses on activation of T-lymphocytes using B-lymphocytes derived exosomes. This kind of approach can help in the treatment of cancer and other viral infections [41, 43]. There are still several sources of exosomes that can be derived from humans like cytotoxic t lymphocytes, platelets, mast cells, osteocytes, etc. [44-49]. It also exists in biological fluids like urine and saliva [48-51].

Plant-Derived Exosomes

Exosomes are usually endogenous nanoparticles secreted by cells of viviparous animals [48]. Exosomes can be obtained in the form of edible nanoparticles in a eco-friendly manner. The sources of natural exosomes from plant sources are Tomato, Ginger, carrots and grapefruits[49]. Nano-vesicles have been obtained from sources like grapefruit and lemon [50, 51]. Some studies suggest that these are actually not complete exosomes but exosome like nano-vesicles. The particle diameter of these vesicles ranges around 40 to 150 nm [17, 52]. After isolation of exosomes from plants it is subjected to ligand and drug to form modified plant exosome like nanovesicles[10, 12]. Such nano-vesicles can be applied in the form of targeted Drug delivery system (TDDS). The cell are organ specific targeting is based upon the plant source of the exosomes [53]. Generally ultracentrifugation is considered as the prime method for isolation of plant based exosomes from the raw material. Where is the probability of viewing physicals of Nano level using scanning probe microscopy in high resolution [55]. Apoplast of leaf is considered to be a good source for exosomes [60].

Animal Based Exosomes

Exosomes usually play a crucial role in maternal health. This is present in specific quantities in breast milk, thereby providing a boost to perinatal nutrition [61,62]. Breast milk derived exosomes from mammalian cells play a vital role in inflammation and immunological responses[63,64]. Animal based exosomes are usually less table under fluctuation of pressure, climate and temperature. But it into have better stability in lower temperatures upto -20°C[65-67]. Some studies suggest that mammalian exosomes can be used as nutraceutical compound delivery system. For example, fetal calf serum exosome, murine exosome [13, 68, 69]. Other important animal sources for exosomes are bovine milk and buffalo's milk, dendritic cell of murine, etc. [13, 70, 71].

Biogenesis of Exosomes

Endosomal sorting complex required for transport (ESCRT) pathway is considered to be one of the most important pathways for synthesis of exosomes, which involves for different complexes of protein[72]. It should be noted that ESCRT must be needed for formation of intra-luminal vesicles (ILV). When this pathway is applied, intra-luminal vesicles are generated endogenously by invagination of endosomal membranes[73-75]. These intra-luminal vesicles are called exosomes. When these are released into extracellular space, they tend to fuse with plasma membrane of the cell [76,77]. However, it should be noted that ESCRT is not the only pathway for production of exosomes. There are other sources of secretion of exosomes like STAM-1 TSG-101 (tumor susceptibility gene-101). CD-63 plays an important role in supporting of intra-luminal vesicle with pre-melanosome, which is not dependent of ESCRT [78,79].

Isolation of Exosomes

Immuno Affinity Based Purification

It involves direction of antibody against surface proteins which are specific for exosomes. For example cd9, CD 81, etc.[80]. This process is also called immuno-affinity chromatography, which is based upon the antigen antibody reaction performed in year specific and reversible manner [81]. Although there are some drawbacks like expensive cost and chances of lesser purity in finished product, there are also several advantages like intact vesicular recovery, higher degree of purification when compared to other methods [82,83]. In one research study employing to b8 has an epitope antibody, immunoaffinity chromatography is suitable for ELISA and Western blot[84]. Before the procedure takes place, antibodies required for the immunoaffinity technique must be purified after obtaining from the specific animal and stored under cold temperature for preservation purpose [85].

Ultracentrifugation

This technique is widely used for isolation of memory and cell derived exosomes. This method however has its drawbacks like higher batch variation, poor practical yield, etc. Sucrose based ultracentrifugation can be employed for isolation of mesenchymal stem cells based exosomes[86, 87]. it should be noted that ultracentrifugation technique should be employed just after centrifugation at a lower speed for a period of 10 minutes especially for isolating exosomes from mesenchymal stem cells, which were already cultured in serum free media. The exosomes are confirmed using biomarkers searches HLA-I and CD-90 using flow cytometry[87-89]. The only difference between ultracentrifugation with sucrose from the conventional method is that 4 ml of 30% sucrose is first added followed by conditioned media. Although, ultracentrifugation is one of the widely employed methods, it should be noted that differential centrifugation is the most commonly employed method for isolation of exosomes. Using sucrose ultracentrifugation, Cup shaped exosomes from 30-120 nm was obtained. But in absence of sucrose the particle diameter is 175 nm[87-90].

Microfluidic Based Isolation

It is considered to be one of the fastest isolation techniques of exosomes. The variables during this process are fluid velocity and acoustic power. Using the nano-deterministic lateral displacement arrays, quantification of exosomes can be effected [91, 92]. This can be used for reducing the maximum level of impurity present in the isolated exosomes. However since it produces maximum purity with quicker processing time, this technique is expensive in terms of cost [93].

Size Exclusion Chromatography

The usual time taken for performing this operation is around 1 to 2 hours. This method usually kills heterogeneous population of exosomes when compared to other methods like affinity based isolation, etc. It employs gel filtration to exclude vesicles based on their size. Fractionation is the main concept by using columns like sepharose 2B. The exosomes which are obtained after this process are considered to be highly pure. This method is not used alone and is used in combination with techniques like ultracentrifugation to achieve more homogeneity and purity of isolated exosomes [94-97]. One of the main drawbacks of this technique is that exosomes are separated from larger molecules

but not from the molecules, which are smaller than exosomes like micro-vesicles[98].It should be noted that there 2015 survey concluded that ultracentrifugation is the most widely used technique for exosome isolation. But, the application of size exclusion chromatography has been doubled from 2015 onwards. This may be due to the minimum degree of contamination leading to a better level of homogeneity during the process [99-101].

Characterization of Exosomes

Dynamic Light Scattering

This evaluation procedure can be defined as the technique in which the particle size can be determined under laser light applying the principle of Brownian motion and the Tyndall effect. Both of these phenomena are present in colloidal particles. The particle detection angle is usually kept at right angle. Based upon the nature of particle to be detected the detection angle can vary. For example, sucrose particles can be detected with high sensitivity in the angle of 173 degrees with backscatter [102]. Proper signal-to-noise ratio must be observed during the process. This can be ensured by maintaining the scattering intensity between solvent and sample at 1:10. Apertures must be used in front of detector to evaluate the randomness in signaling during the process [103]. This technique can be widely used for analyzing the homogeneity in particle size of the prepared exosomes[104]. When this technique is combined with the NMR spectroscopy, the permeability of lipid bi-layer can be observed with high accuracy [105,106].

Microscopic Techniques

There are several types of microscopic methods for evaluation of particle size of finished exosomes. The most widely used microscopic techniques for exosomes are listed below:

Scanning Electron Microscopy

This technique is used to focus on the intracellular organelles and provide sharp images [107]. There are various types of scanning electron microscopic techniques like environmental, hydrated (wet), cryo, etc. this process may require dehydration of the biological specimen performed by thin film evaporation[108]. This can be performed to increase electrical conductivity on the surface of the specimen [109]. Topography of the biological specimen can be obtained by employing backscatter detector. Sample preparation methods are usually less tedious when compared to other forms of microscopy. Quick analysis time and good imaging resolution are considered to be some of the essential merits of this technique [110].

Transmission Electron Microscopy

This microscopic technique and its types are similar to that of SEM. Cryo-TEM is usually considered to be essential for macromolecular specimens including exosomes [108, 111]. Staining agents like urinal acetate can be employed for negative staining, if embedding by plastic is not possible[112]. Electrons can be enhanced by employing an electron gun. This also provides high resolution images similar to SEM [113,114].

Atomic Force Microscopy

This microscope is applied based on the principle of force sensation between the surface of sample and probe. Focusing on the intracellular morphology of the biological specimen under live conditions is considered to be one of the main advantages of this technique[115-118]. Considering all these merits, it is easy to understand the structure of exosomes in vesicular level[119].

Nanoparticle Tracking Analysis

This characterization technique works on the principle which is similar to that of dynamic light scattering (DLS). The exosomes isolated on the basis of particle size by applying the phenomenon of diffusion coefficient. For this technique of characterization, proper validation must be performed to avoid deflection from accuracy [120]. This technique has been considered for almost several drug delivery systems including nano-particles. It usually consists

of a sample chamber and a laser along with elastomer ring[121]. Detection of modulation in secretion levels of exosomes can be performed with constant monitoring using this technique. All exosomes are not uniform in nature and can tend to be polymorphic. At this situations, usage of several biomarkers are required this process [122].

Resistive Pulse Sensing

This process of evaluation employs the principle of coulter for effective counting of particles along with statistical data based on size. There are several types of this technique like microfluidic, tunable and nano-fluidic. The main principle of this characterization is that each particle passing through the equipment or operators will emit a Pulsar of resistance against the circuit of amplification. The magnitude of pulse limited by the particle is directly proportional to the ratio of volume of particle crossing the sensor gate. There are novel ways which focus on usage of solutions with less conduction in order to diminish the sensing channel volume. For example, hexadecane[123, 124]. Tunable resistive pulse sensing (TRPS) has entered the medical Science as a characterization technique for nano-materials recently. Membrane size, pore size and conducting electrolyte solution are considered to be the variables of this technique [125]. This is a multi-dimensional characterization technique which is helpful in determination of particle charge, size and also concentration [126-128].

Flow Cytometry

It can produce good reproducibility along with the detection and characterization of exosomes in an indirect manner [129]. This technique is mainly used for detection of surface proteins of exosomes followed by classification of the total volume of the substance based on shape and size. Proper labeling with device accepting fluorescence is necessary [130, 131]. Modern flow cytometers are providing better resolution of particle when compared to the earlier versions [132].

Applications of Exosomes

Cancer Therapy

Exosomes have a vital application in alleviation of various classes of cancer [132]. Research studies clearly suggest that it can be used the form of biomarkers for various types of cancers including glioblastoma and Melanoma [133]. It should be noted that this micro-vesicles can also be secreted by neoplastic cells. It can be released by colon cancer cells and even prostate cancer cells upon high exposure to radiation [134-136]. The latter type can be deadly and increase the mortality rate. In overall aspect, neoplasm therapy can be performed by applying any one of the given two different approaches:

i. Secretion, isolation and application of exosomes derived from either plant or human source like dendritic cell, etc. [138]
ii. Inactivating the exosomes secreted by the cancer cells responsible for tumor formation and growth

Exosomes derived from cells of immunological importance can help in effective cancer treatment like natural killer cells (NK) and T-Lymphocytes [138-141]. Cancer secreted exosomes usually responsible for several unwanted effects like resistance to drug and immune cells. By initiating blockade of this kind of exosomes secreted by metastatic neoplastic cells, deadly form of cancers like Melanoma can be effectively treated [142-144]. The role of exosomes in Cancer therapy is multidimensional, since it can act as gene carrier, biomarker, and diagnosis and also in direct treatment. Exosomes can also help in diagnosis and learning pathophysiology of neoplasm of different types. This can help in formulation of the novel drug delivery system for cancer by the scientists in upcoming years [135, 138, 142, 145, 146].

Treatment of Alzheimer Disease

Alzheimer's disease is the most prevalent form of dementia even today around the globe. Elderly population is highly susceptible to this disease. This is usually caused due to lack of β-amyloid and tau proteins [147-150]. Recent research shows that exosome can be secreted by proteins present in cerebrospinal fluid (CSF) and microglia [149, 150]. Dendritic cell derived exosomes, which are modified by rabies virus glycoprotein can be utilized as an effective

carrier for Bace-1 targeting siRNA. This acts as a targeted delivery carrier in the formulation [13]. Exosomes isolated from immunological cells like macrophages acts as a perfect transporter of anti-Alzheimer drugs, since it can easily penetrate through blood brain barrier (BBB) [151]. These extracellular vesicles are very useful for protection of nervous system, because these help in completion of the signal processing and communication between neurons. Astrocyte-derived exosomes are widely used for this application. They also play a crucial role in treatment of Alzheimer's disease, since it helps in transportation of amyloid beta [152, 153].

Drug Delivery

This can be utilized as drug delivery agents due to its nanoscale size [154]. Shape and size transformation is possible due to high flexibility of the extracellular vesicles. This is considered to be an important property since this can be helpful in loading drugs which can be both small and large in size [155]. Exosomes are very important second degree targeting agents [151]. Batrakova et.al infers that exosomes have drug loading efficiency per particle. There are also several merits including biocompatibility, poor toxicity and lesser chances of accumulation. Due to the above features, this class of extracellular vesicles has lesser chances of promoting chronic side effects are long-term adverse reactions by it [156-158]. The delivery function properties can be enhanced by using exosomes with liposomes. The process of fusion is performed by freeze-thaw cycles. This concept helps in improving the biological half-life of exosomes in human body and increase the quick elimination [159].

Gene Therapy

Exosomal transfer of peptides for transfection has overtaken the conventional methods, which utilized cationic lipids- our constituent of DNA cationic liposomal complexes [160]. It is employed in the form of genetic carrier in the treatment of neoplasm, especially in case of miRNA. Because, exosome possesses better targeting action when compared with liposomes and other gene carrier molecules[1, 161, 162]. These extra vascular vesicles are helpful in gene transcription and gene translations [7]. These are highly helpful in delivery offer all types of genetic quotes including non-coding RNA, which may help in permanent cure of cancer and arthritis [163]. However, exosomes should not be used blindly and proper method must be followed depending upon the nature of gene to be inserted [164].

Retardation of Aging Process

Despite all the advantages in presence of exosomes, there are certain detrimental activities regulated by these vesicles. An essential characteristic of aging process is considered to be inflammaging. This is long-term condition of inflammation. Urbanelli et.al infers that exosomes are responsible for transmission of signals of senescence [165-167]. These vesicles crossing point between inflammation and virome[168].

Bone Health

Osteocyte-derived exosomes plays an essential role in bone health and wellness. It helps in resorption of bone and root, thereby casting groundbreaking application in dentistry, orthodontics and orthopedics [111]. Fibrous dysplasia can be treated by employing osteoblast derived exosomes carrying RANK ligand by accelerating the process of osteoclastogenesis. Consequently, osteopenia, which is characterized by low bone density, can also be treated by using osteoblast derived exosomes, which help in signaling of bone growth [169].

Regenerative Therapy

These are widely involved in tissue and bone regeneration techniques. Extracellular vesicles derived from mesenchymal stem cells helps in promotion of pluripotent stem cells, thereby creating a brighter future for stem cell therapy. Immunity can be further enhanced or decreased by application of exosomes derived from my amniotic fluid stem cells [170, 171]. It is also helpful in accelerating sealing process of wound, nerve and even cardiac tissue with impetus. This can also be called designer exosome since, the structure and shape along with the function is engineered by scientists [172-175].

Miscellaneous

An exosome has its own applications in cardiology. It helps in maintenance of homeostasis by applying myocardium derived ones in performing localization and immunological functions. In case of hypoxia, exosomes are released by cells of cardiac muscles with up-regulation of circHIPK3. This process helps in relaxation of heart by acting against dysfunction induced by oxidative stress [176, 177]. Besides, these vesicles are applied in the field of diagnostics in the form of biomarkers. It proves to be effective diagnostic agent in identification of a cardiovascular diseases renal diseases and disorders [17, 178, 179]. Antigen presentation of MHC class-II was started the year 1996 by using exosomes [163]. Cancer can be diagnosed by quantitative estimation of tumor secreted exosomes. The amount of tumor secreted exosomes directly proportional to the severity of Cancer of the specific region[145, 180]. It helps mainly in the cellular mechanism like phagocytosis and differentiation. It plays a crucial role in immunology and also shows anti-inflammatory properties [181-183].

Exosomes: Eye-Opener for Covid-19 Therapy

Covid-19 infection is actually a SARS-COV-2 infection caused by coronavirus. It was named covid-19 since the pandemic started in the year 2019 by coronavirus disease. The epicenter of this pandemic is considered to be Wuhan of China. It can be understood that this disease can be indeterminate off any symptoms at sometimes. The main reason of mortality due to covid-19 is generally acute respiratory distress syndrome (ARDS), which is often characterized by cytokine storm. Cytokines storm is deadly condition in which pro-inflammatory cytokines like IL-12, IL-33 and chemokines like CXCL8, CCL 5 are secreted in high quantities and released into bloodstream. The reproductive number is defined as the term by which the viability and violence of the microbial strain and the infected capacity of affected patient. In case of covid-19, this number ranges from 3.8-8.9 in value [184-187]. The current coronavirus and exosomes have a lot of similarity in terms of entry mechanism, morphology, targeting capacity and more, thus, creating a new hope and inspiration for the scientists to employ exosomes in the treatment of covid-19 infection. Exosomes derived from stem cells are considered to be the therapeutic agent of choice in the covid-19 vaccine manufacturing. Since, coronavirus infection damages the lungs and respiratory tract, language derived exosomes considered in the treatment of this deadly infection. The exosomes can involve in the treatment of diseases & disorders in three following dimensions:

It can act as a carrier for antiviral drugs that can help in the treatment of covid-19 infection.

It can play a crucial role in the form of nano-decoys, which is composed with the receptor like ACE-2 receptor. This exosome-bound receptor binds with virus. But this only helps in the retardation of infection, and never involve in complete inhibition of the viral infection. Due to this technique, severity of the symptoms can be lessened for a longer period of time.

Exosome derived from Natural sources can help in actual treatment of coronavirus infection as a therapeutic agent by inducing competitive binding [191-196]. Mesenchymal stem cells derived exosomes are highly essential in treating covid-19 infection of severe form effectively with no adverse drug reactions (ADR).

It should be noted that ACE-2+ excess Om helps in blocking the pseudo type of SARS COV-2 infections. Cytokines storm, which is the deadly symptom in severe covid-19 patients, can be weakened are prevented by employing this novel delivery. This is an important step in treating this deadly infection since this symptom increases the mortality rate, thereby declaring covid-19 infection to be lethal [196-199]. Thus, it helps in vaccine development of not only covid-19 but also several diseases and disorders including Melanoma [200, 201].

CONCLUSION

There are several emerging diseases and pandemics, which can be treated quickly only upon proper understanding of pathophysiology of that specific ailment. Since, Exosomes are messengers of human body and several cellular mechanisms, they can help scientist to learn about the pathophysiology behind each disease in less period of time. This helps in treating, curing and prevention of diseases by improving the formulation required for these processes. Exosome is also helpful in treating coronavirus infections by playing a crucial role in vaccine development and

opening new approaches in treatment of this pandemic in symptomatic manner. Targeting specificity can be boosted by employing this nano-carriers deriving from a specific region like Mesenchymal stem cells, Lung and even astrocytes. Nevertheless, the sources for derivation of exosomes are almost infinite. One class of exosomes help in therapeutic approach meanwhile, other set of exosomes is hand-in-glove in harmful processes like tumorigenesis and aging. But, the latter class helps in understanding pathophysiology thereby inspiring scientists and biotechnologists to develop formulations that block these harmful and unwanted mechanisms. This can be concluded by stating that exercise is a Nano physical which enlightens the inspiration the scientist for inventing breakthrough technologies in the field of biotechnology, microbiology, oncology and other medical sciences alarm with treatment development for pandemics like covid-19 (SARS COV-2) or coronavirus infection.

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Table.1 :The stages in covid-19 infection can be classified into three main divisions as follows [188-190]:

STAGE	SYMPTOM	TEST FOR VIRUS (COVID-19)	SIGNIFICANCE
1	Asymptomatic	+/-	Incubation
2	Mild to moderate	+	Confirmation of COVID-19
3	Severe	+	ARDS, Cytokine Storm

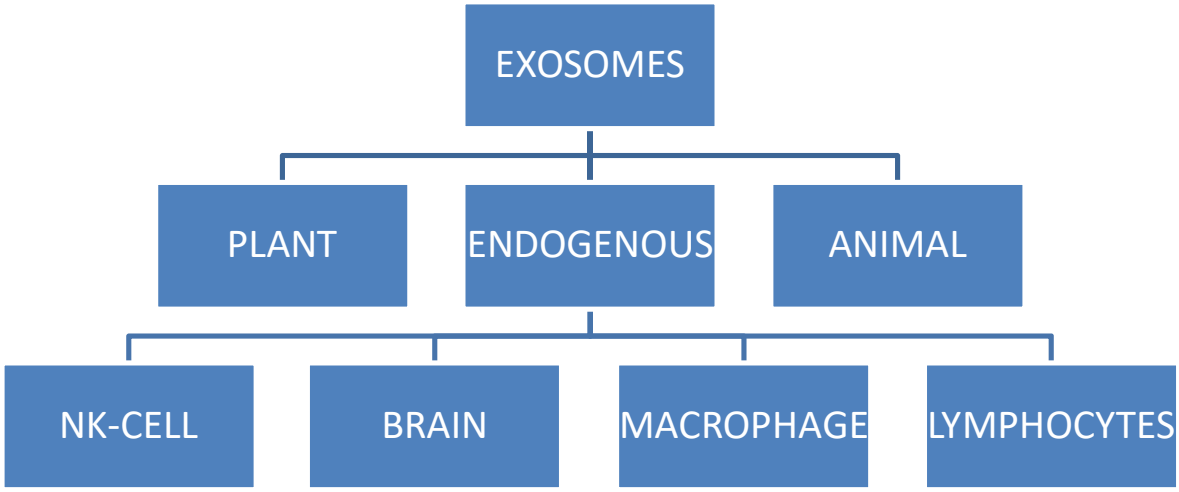

Fig.1 Sources of Exosomes

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RESEARCH ARTICLE

Development and Validation of a Nutritional Screening Tool for Adolescents (NSTA)

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ABSTRACT

Adolescence is a period of transition between childhood and adulthood that occupies a crucial position in the life of human beings. This period is an important physiological phase of life characterized by an exceptionally rapid rate of growth and development both physical and psychological. The present study was conducted to develop and validate a nutritional screening tool for Adolescents. This observational study was done over a period of six months (July 2018 – November 2018) involving a sample size of 240 participants, 24 in each gender of age group 10-19 years. Two tools were used in this study (NSTA-Developed Tool and PNST). The results of Developed tool (NSTA) were compared with PNST. It was observed that 6.6 % boys were mild to moderately malnourished and 13.3 % of girls were mild to moderately malnourished. The Developed Tool identified 10% of patients at risk and PNST identified 9.1%. It was observed that the developed tool identified the patients as similarly as PNST. There was no significance difference found (p – 0.87). The Developed Screening Tool for Adolescents was easy to use, and did not consume time. It can be used in hospitals to assess the nutritional status of adolescent population.

Keywords: Nutrition Screening; Adolescent; NSTA PNST

INTRODUCTION

World Health Organization (WHO) defines adolescence as the segment of life between the age group of 10-19 years. Adolescence is a transition phase through which a child becomes an adult. Specific nutritional needs and considerations are required for efficient growth and development [1].

There is a change in the nutritional status of adolescents because of the urbanization and the global economic development. The deficiency of calories and other micro-nutrients causes growth problems in adolescents. Therefore, good nutrition is essential for proper growth and development of adolescents.

The rate of growth and development with psychosocial changes has an increasing need for independence and a desire to make lifestyle choices that differ from those of the family, places adolescents at risk of poor nutritional status. Because biological, psychosocial growth and development are dynamic through adolescence, therefore it is important that adolescents should be screened for dietary intake and nutritional status each year. The Guidelines for Adolescent Preventive Services (GAPS) recommends that nutrition screening be done as a routine part of annual health guidance.

The nutrition screening tool should include overweight, underweight, eating disorders and excessive intake of foods and beverages that have high fat or sugar contents. Adolescents who are found to be at risk during nutrition screening can benefit from full nutrition assessment to determine dietary change recommendations [10]. The need for the study is to develop a screening tool to assess the nutritional risk in adolescents and there is not much literature for adolescents screening tool. Therefore, it was developed.

MATERIALS AND METHODS

An observational study was conducted and simple random sampling was used in this study. The period of study was for six months from July to December 2018. The Inclusion criteria were the children between the age group 10 to 19 years of age and both the genders were recruited. The subjects with acute illness were considered in this study. The participants who are willing to participate were included in this study. The exclusion criteria were children below 10 years or above 19 years are not considered. And those who are not willing to participate are excluded in this study.

Subjects were selected based on inclusion criteria and their willingness to participate during the study period. The sample size was determined as 240 by a statistician, using the prevalence of malnourished adolescents. Ethical Approval was obtained from Institutional Ethical Committee on 02/05/2018. CSF/18/APR/69/145. The study protocol was explained to all the subjects at the beginning of the study and permission was obtained from their parents and the participants by providing a copy of protocol and the assent form. The study was carried out in Multi-Speciality Hospital, Chennai. The demographic data such as age, gender, medical history, details such as diagnosis, etc were obtained from the patient and from their respective medical records.

This tool (NSTA) was developed by reviewing various literatures and 4 components - Basic anthropometry, weight loss, reduced food intake and will the child's nutritional status will be affected by recent admission/ condition during the next week. Unintentional loss of body weight is a characteristic of under-nutrition, which is caused by decreased food intake from lack of appetite or increased losses as well as requirements. Weight loss less 10% of usual body weight is an indicative of under-nutrition and it is related to higher morbidity and mortality [4].

Reduced Food intake is a well- established etiologic criteria for malnutrition that has strong validity. Some of the causes are poor oral health, side effects of medications, depression, dysphagia, gastro-intestinal problems, anorexia and inadequate nutrition support [6]. Some patients are at risk of becoming undernourished during the hospital admission or after their discharge, because of the effect of the medical condition on their nutritional status. This can be due to decreased intake, increased gut losses and increased energy requirements [3].

Each component was scored and total was summed up, and with that total score obtained, the patients were categorized. The Paediatric Nutrition Screening Tool (PNST)was developed by Children's Health Queensland. The

aim of the tool is to identify hospital inpatients at nutritional risk. The tool consists of four simple questions which can be done by nurses, parents or nutrition assistants, to help in the clinical diagnosis of patients. The Paediatric Nutrition Screening Tool is designed for all paediatric in-patients on admission. It contains questions which are easy to understand and takes little time to complete. PNST can used for paediatric patients in tertiary and regional hospitals. It is validated against the paediatric Subjective Global Nutritional Assessment and anthropometry [7].

This tool is used in this study to validate against the developed nutrition screening tool for adolescents. The subjects were also assessed using this tool. The Developed Nutritional Screening Tool for Adolescents interprets the nutritional status as follows. This tool was checked for content validation by expertise – Chief Dietitian of Madras Medical Mission and Paediatric Consultant of Sri Ramachandra Institute of Higher Education and Research. The Statistical Analysis was done using SPSS Software and the chi- square test was used. The data collected were subjected to statistical tools such as mean, standard deviation to obtain the results.

RESULTS

Table 2 shows the anthropometric measurements such as height, weight and body mass index of the subjects. It was observed that among boys the measured height was found to be greater than the expected value in the age group 10 to 13 years and same observation was seen in girls in the age group 10 to 12 years. It was also observed that among boys, the measured height was found to be lesser than the expected height in the age group 14 to 19 years and the same observation was seen in girls in the age group 13 to 19 years. It was observed that among boys, the measurable weight was found to be greater than the expected value in the age group of 10 to 14 years and same observation was found in girls in the age group 10 to 12 years. It was also observed among boys that the measurable weight was found to be lesser than the expected value in the age group 15 to 19 years and the same observation was seen in girls in the age group 13 to 19 years. The mean Body Mass Index was compared with WHO standards and it was observed that girls were normal. In boys, Overweight was seen in the age group 10 and 17 years, whereas other age groups were normal.

In Table 3 it is observed that 8.3% of boys in the age group 12, 13 and 14 years were found to be severely malnourished, 29.1 % of boys in the age group 14, 16 and 17 years were found to be moderately malnourished. It was also found that 8.3% of boys in the age group 11, 13, 15 and 16 years had weight loss. In a study, Weight loss during hospitalization occurred in 65% of the children and was >2% of admission weight in 45% of patients [2]. It is also seen that 8.3% of boys in the age group 11,13,15,16 years had a reduced food intake. It is also observed that 8.3 % of boys in the age group in the age group 14 and 18 will be affected in the next week.

Table 4 shows the developed tool assessed for girls. It is observed that 8.3% of girls were severely malnourished in the age group 12, 13 and 14 years. In a study, with the use of SGNA, 85 children (49%) were found to be well-nourished, 64 children (36%) were moderately malnourished and 26 children (15%) were severely malnourished. It is also found that 20.8 % of girls in the age group 17 year had weight loss due to reduced intake of food and acute illness. It is also seen that 20.8 % of girls in the age group 13, had a reduced food intake due to acute illness (loss of appetite, vomiting, nausea).In a study, 71% of patients who reported recent reduced intake were identified as being at nutritional risk using the PNST. [11]. It is observed that 12.5 % of girls in the age group 13 and 16 years will be affected by recent admission/ condition during the next week

Figure 1 shows the nutritional status using developed score based on age and gender. It is observed that 8.3% of boys in the age group 13, 14 and 15 were mild to moderately malnourished and 20.8 % of girls in the age group 17 were mild to moderately malnourished. In a study, Nutritional assessment identified 64 patients (25.6 %) as under-risk, 40 of whom were malnourished (16%) [7]. In a study, 24.9% subjects were found to be mild malnourished and 1.8% subjects belonged to severe under-nutrition [5]. P => 0.05 (Not Significant) The above table 5 represents the

comparison between Developed Tool and PNST. It is observed that the developed tool identifies the patients as similarly as PNST. The P value shows that it is not significant (p – 0.87) In a study, The PNST identified 37.6% of patients at nutrition risk, whereas the pediatric SGNA identified 34.2% at risk[11].

Figure 3 represents the Correlation between Developed Score and PNST. It clearly shows that both the tools identify patients at risk similarly. In a study, PNST identified 37.6 % of patients at risk, whereas the pediatric SGNA identified 34.2 % of patients at risk. Therefore, it provides a sensitive valid, and simpler alternative nutrition screening tools such as Screening Tool for the Assessment of Malnutrition in Paediatrics (STAMP), Screening Tool Risk on Nutritional Status and Growth (STRONG kids), and Paediatric Yorkhill Malnutrition Score (PYMS) to ensure the early detection of hospitalized children at nutrition risk [11].

CONCLUSION

The Developed Screening Tool for Adolescents is validated and it can be used in hospitals to assess the nutritional status of adolescent population.

Limitation

The limitation of this tool is that cannot be applied for adolescents with chronic illness. Disease condition, biochemical parameters are not included in this tool. Another limitation of the study results is that, the data was based on South Asian Populations

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Table 1: Interpretation of the Developed Nutritional Screening Tool for Adolescents

Interpretation	Scores
Well - Nourished	0 – 2
Mild to Moderately Malnourished	3 – 5
Severely Malnourished	6 -7

TABLE 2 – Anthropometric Measurements of the Subjects

AGE (IN YEARS)	HEIGHT (cm)				WEIGHT (kg)				BODY MASS INDEX (kg/m2)			
	BOYS		GIRLS		BOYS		GIRLS		BOYS		GIRLS	
	MEAN ± SD	WHO (2010)	MEAN ± SD	WHO (2010)	MEAN ± SD	WHO (2010)	MEAN ± SD	WHO (2010)	MEAN ± SD	INTERPREATATION	MEAN ± SD	INTERPRETATION
10	152.1 ± 4.3	137.5	156.4 ± 4.5	138.3	43.1 ± 5.8	31.4	41.5 ± 3.0	32.7	19.0 ± 3.9	Overweight	16.0 ± 0.8	Normal
11	153.6 ± 5.9	143.5	155.4 ± 4.5	144.8	44.0 ± 6.0	35.3	46.2 ± 4.9	36.9	18.5 ± 1.7	Normal	19.0 ± 1.1	
12	156.8 ± 3.8	149.7	151.4 ± 3.2	151.1	47.2 ± 7.1	39.7	44.3 ± 9.5	41.5	19.1 ± 2.0		19.2 ± 3.7	
13	157.1 ± 4.6	156.5	153.2 ± 3.8	157.1	48.4 ± 10.1	44.9	43.0 ± 8.6	46.2	19.4 ± 3.4		18.5 ± 2.8	
14	157.6 ± 5.3	163.1	153.6 ± 6.1	160.4	54.1 ± 8.2	50.7	51.4 ± 11.0	52.1	21.7 ± 3.2		21.6 ± 3.8	
15	158.5 ± 4.7	169	154.2 ± 3.3	161.8	55.0 ± 9.8	56.7	52.6 ± 7.7	53.6	21.8 ± 4.2		22.1 ± 3.1	
16	158.6 ± 4.9	173.5	156.5 ± 3.6	162.7	53.1 ± 7.6	62.1	53.9 ± 9.1	54.1	21.0 ± 2.7		21.9 ± 3.6	
17	161.2 ± 4.9	176.2	157.0 ± 6.3	163.4	64.3 ± 8.9	66.3	53.0 ± 8.6	56.6	24.7 ± 2.7	Overweight	21.6 ± 4.2	
18	166.0 ± 7.6	176.8	157.4 ± 3.7	163.7	65.2 ± 12.4	68.8	53.6 ± 9.0	56.8	23.6 ± 4.1	Normal	21.5 ± 4.2	
19	159.6 ± 7.1	176.9	156.1 ± 2.9	163.8	58.1 ± 9.9	70.0	53.3 ± 7.1	57.0	22.6 ± 2.5		21.8 ± 2.1	

Table 3 – The Developed Tool (NSTA) For Boys

COMPONENTS	AGE (IN YEARS)									
	10	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**
1. ANTHROPOMETRY	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
NORMAL	9 (37.5)	7 (29.)	9 (37.5)	6 (25)	3 (12.5)	6 (25)	4 (16.6)	4 (16.6)	4 (16.6)	9 (33.3)
MODERATE	2 (8.3)	5 (20.8)	2 (8.3)	4 (16.6)	7 (29.1)	5 (20.8)	7 (29.1)	7 (29.1)	6 (25)	3 (12.5)
SEVERE	1 (4.16)	-	2 (8.3)	2 (8.3)	2 (8.3)	1 (4.16)	1 (4.16)	1 (4.16)	1 (4.16)	-
2. WEIGHT LOSS										
PRESENCE	-	2 (8.3)	1 (4.16)	2 (8.3)	1 (4.16)	2 (8.3)	2 (8.3)	1 (4.16)	1 (4.16)	-
ABSENSE	12 (50)	10 (41.6)	11 (45.8)	10 (41.6)	11 (45.8)	10 (41.6)	10 (41.6)	11 (45.8)	11 (45.8)	12 (50)

3. FOOD INTAKE										
REDUCED	-	2 (8.3)	1 (4.16)	2 (8.3)	1 (4.16)	2 (8.3)	2 (8.3)	1 (4.16)	1 (4.16)	-
NORMAL	12 (50)	10 (41.6)	11 (45.8)	10 (41.6)	11 (45.8)	10(41.6)	10 (41.6)	11 (45.8)	11 (45.8)	12 (50)
4. CHILD'S NUTRITIONAL STATUS										
ALMOST NIL	-	-	-	-	-	-	-	-	-	-
REDUCED	-	1 (4.16)	-	1 (4.16)	2 (8.3)	1 (4.16)	-	-	2 (8.3)	-
NORMAL	12 (50)	11 (45.8)	12 (50)	11(45.8)	10 (41.6)	11(45.8)	12 (50)	12 (50)	10 (41.6)	12 (50)

Table 4 – The Developed Tool (NSTA) For Girls

COMPONENTS	**AGE (IN YEARS)**									
	10	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**
1. ANTHROPOMETRY	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
NORMAL	12 (50)	9 (37.5)	8 (33.3)	7 (29.1)	6 (25)	6 (25)	6 (25)	4 (16.6)	6 (25)	8 (33.3)
MODERATE	-	3 (12.5)	2 (8.3)	3 (12.5)	4 (16.6)	5 (20.8)	5 (20.8)	7 (29.1)	5 (20.8)	4 (16.6)
SEVERE	-	-	2 (8.3)	2 (8.3)	2 (8.3)	1 (4.16)	1 (4.16)	1 (4.16)	1 (4.16)	-
2. WEIGHT LOSS										
PRESENCE	-	-	2 (8.3)	4 (16.6)	2 (8.3)	1 (4.16)	2 (8.3)	5 (20.8)	1 (4.16)	1 (4.16)
ABSENSE	12 (50)	12 (50)	10 (41.6)	8 (33.3)	10 (41.6)	11 (45.8)	10 (41.6)	7 (29.1)	11 (45.8)	11 (45.8)
3. FOOD INTAKE										
REDUCED	-	-	2 (8.3)	5 (20.8)	1 (4.16)	1 (4.16)	1 (4.16)	4 (16.6)	3 (12.5)	2 (8.3)
NORMAL	12 (50)	12 (50)	10 (41.6)	7 (29.1)	11 (45.8)	11 (45.8)	11 (45.8)	8 (33.3)	9 (37.5)	10 (41.6)
4. CHILD'S NUTRITIONAL STATUS										
ALMOST NIL	-	-	-	-	-	-	-	-	-	-
REDUCED	-	-	1 (4.16)	3 (12.5)	1 (4.16)	-	3 (12.5)	1 (4.16)	2 (8.3)	-
NORMAL	12 (50)	12 (50)	11 (45.8)	9 (37.5)	11 (45.8)	12 (50)	9 (37.5)	11 (45.8)	10 (41.6)	12 (50)

Table 5: Comparison between Developed Score and PNST

TOOL	AT RISK	NOT AT RISK	P value
Developed Tool(NSTA)	24	216	0.87
PNST	22	218	(Not Significant)

P => 0.05 (Not Significant)

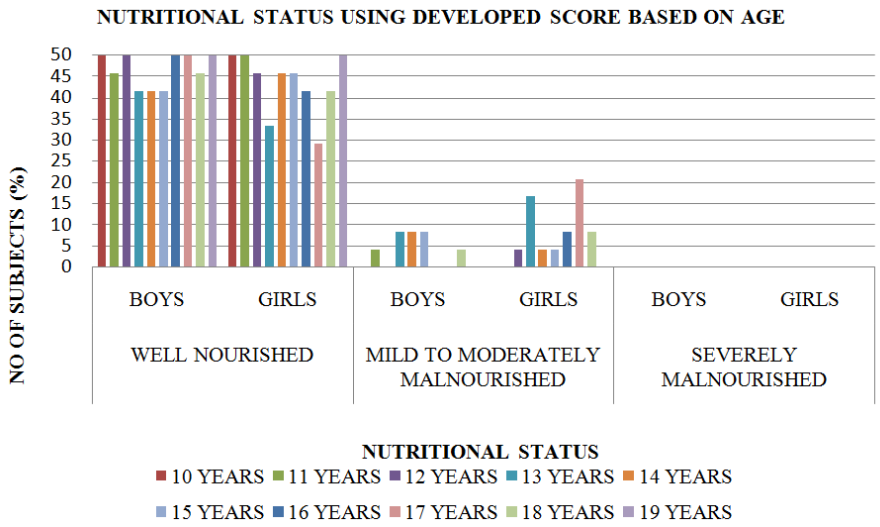

FIGURE 1: Nutritional Status Using Developed Score Based On Age

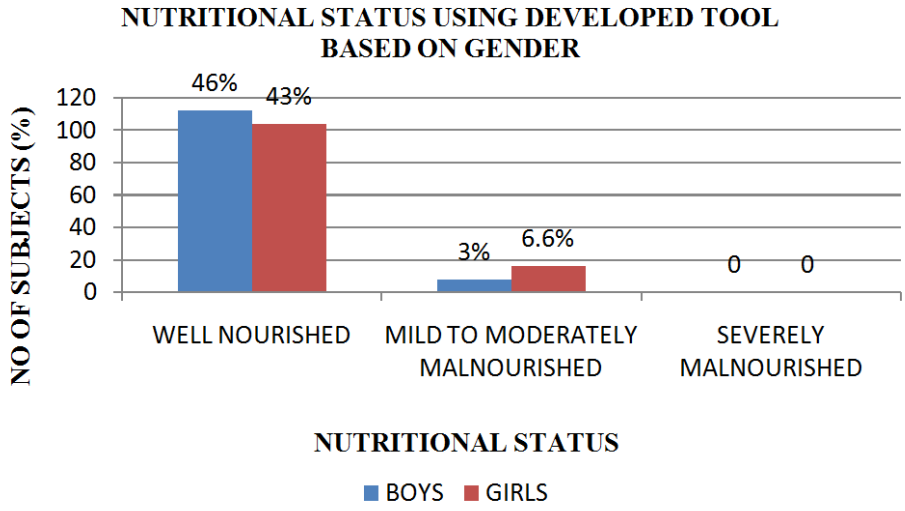

Figure 2: Nutritional Status Using Developed Score On Gender

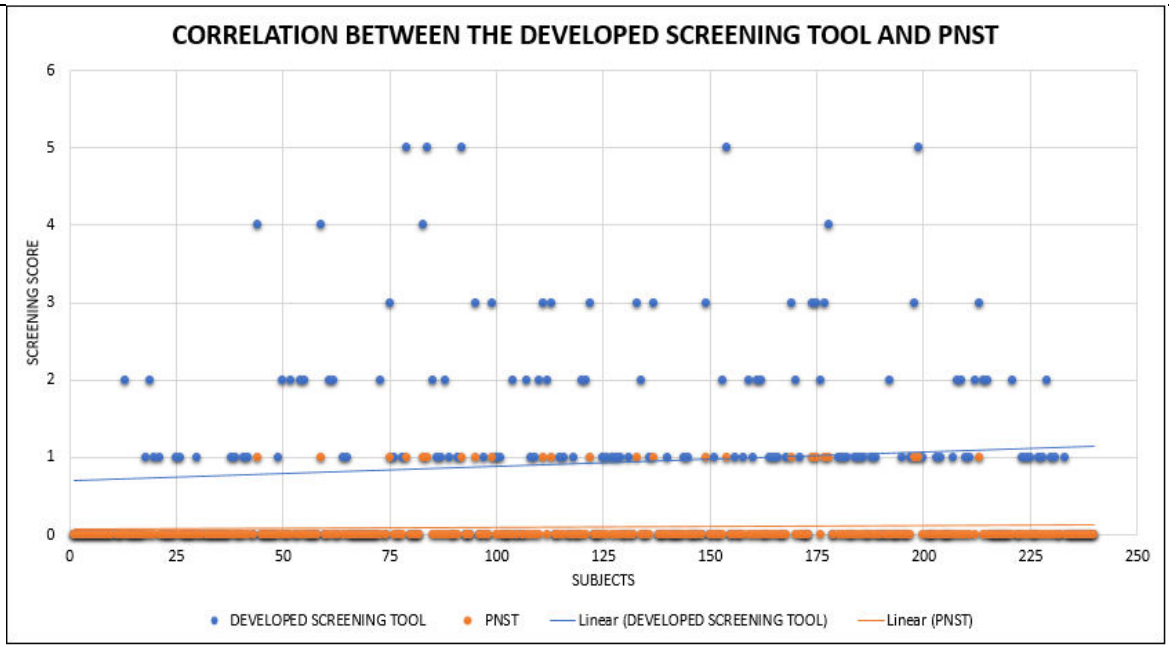

Figure 3: Correlation Between Developed Tool And PNST

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RESEARCH ARTICLE

Development of a Cost-effective Antibacterial Analysis Model using Milk Fermentation by *Lactobacillus* through Monitoring pH Change in Fermenting Milk

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ABSTRACT

There has been a keen interest in research and development of new antimicrobial agents from different sources against the increasing pathogenic microbes. The initial screening of the compounds is very significant in any antibacterial drug discovery programs. Development of a cost effective and simple antibacterial screening test will boost the screening programs that can be initiated even by a layman without any microbiological skills. Fermentation of milk by *Lactobacillus* is the process used here. The bacteria multiplies in 12 hours and converts Lactose sugar to Lactic acid followed by pH drop. This conversion can be evaluated using different plant extracts. Aqueous extracts of 15 plants were investigated for its antibacterial property using this method. More the pH of the treated milk close to the pH of the sterile milk, higher will be the antibacterial property. This system can be tested with antibiotics with proven antibacterial properties. The results revealed that aqueous extract of *Cinnamomum zeylanicum* has the highest antibacterial activity followed by *Azadirachta indica* and *Aegle marmelos* and has IC 50 values 14.05, 306.34 and 322.47 respectively. It can be concluded that milk fermentation by *Lactobacillus* can be effectively used as a model organism to conduct preliminary screening for antibacterial property.

Keywords: Antibacterial, *Lactobacillus,* Fermentation, Lactose sugar, Lactic acid, Antibiotics.

INTRODUCTION

Plants are the inevitable source of antimicrobial agents in different countries. About 60 to 90% of the population in the developing countries use plant-derived medicine. Traditionally, crude plant extracts are used as herbal medicine for the treatment of various human infectious diseases. They are rich in a variety of phytochemicals including

tannins, terpenoids, alkaloids and flavonoids which have been found *in vitro* that have antimicrobial properties. Although the mechanism of action and efficacy of these herbal extracts in most cases is still needed to be validated scientifically, these preparations mediate important host responses. Khan UA *et al*[1].

The global prevalence of infectious diseases caused by bacteria is a major public health problem. The bacterial agents including *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Escherichia coli*, *Proteus vulgaris* etc cause human infections. The recent emergence of antibiotic resistance and related toxicity issues limit the use of antimicrobial agents and is prompting a revival in the research of the antimicrobial role of plants against strains due to comparable safety and efficacy.

During the last few decades, the global interest in the study of various medicinal plants has increased rapidly due to their antibacterial and antioxidant activities, low toxicity and the potential to be a cheaper alternative to costly synthetic drugs. The determination of antibacterial activities of different medicinal plants is of special interest these days due to the current global issue of increasing antibiotic resistance of microorganisms. It is assumed that the drug resistance in pathogenic microorganisms is developing due to the indiscriminate use of commercial antimicrobial drugs. Antimicrobial resistance threatens the prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi. Therefore it is highly imperative to determine compounds which can be used to develop novel medicines with higher antimicrobial properties.

Nowadays there are different methods to test and find out the antimicrobial properties of plants. The currently available methods for antibacterial screening use sophisticated microbiology culture facilities and bacterial culture facilities and bacterial culture medium to test the compounds. We aim at developing a cost-effective antibacterial analysis model using milk fermentation by *Lactobacillus* through monitoring the pH change in milk.

MATERIALS AND METHODS

Standardization

The experiment was standardized by using four antibiotics which can be used as a positive control against *Lactobacillus acidophilus*. The Selected antibiotics were Ampicillin, Azithromycin, Amoxicillin and Doxycycline. 500mg of Ampicillin injection, 1.2g of Amoxicillin injection, 500mg of Azithromycin, 200mg of Doxycycline were taken and 5ml, 12ml, 5ml, 2ml of distilled water added respectively. All the test tubes were shaken well for uniform concentration.

Well sterilized containers were taken in 3 replicas of 4 concentrations (25, 50, 75, 100 microliters) of each antibiotic for precision and control is kept for comparison. Then added 25 ml of milk to each container followed by 500 ul of inoculum (curd). Well prepared stock of antibiotics added in 25, 50, 75, 100 ul in respective glasses. In order to make an equal volume 75, 50, 25, 0 ul of water added respectively and shaken well for uniform concentration. Finally it was kept for 12 hours for measuring the pH.

Testing the System with Plants

Collection and Extraction

Plants were collected in the evening from its area of abundance. The leaves of the collected plants were shade dried for 24 hours in an open space. Next day in the evening, the leaf extract was prepared. 5g of the leaves weighed out in an electronic weighing balance. Weighed out leaves were crushed using a mortar and pestle for 15 minutes using distilled water. Then filtered using a cotton cloth into a beaker and labelled accordingly.

The following plants were collected for analysis (Figure 1 -3).

1. *Aegle marmelos* (L.) Correa

2. *Azadirachta indica* A.Juss
3. *Cinnamomum zeylanicum* Blume
4. *Crotalaria pallida* Aiton
5. *Curcuma longa* L.
6. *Justicia gendarussa* Burm.f
7. *Lantana camara* L.
8. *Leucas aspera* (Wild.) Link
9. *Moringa oleifera* Lam.
10. *Murraya koenigii* (L.) Spreng.
11. *Ocimum sanctum* L.
12. *Phyllanthus emblica* L.
13. *Polyalthia longifolia* (Sonn.) Thwaites
14. *Psidium guajava* L.
15. *Vitex peduncularis* Wall. ex schauer

Treatment
The plant extracts were added in different concentrations as depicted in the table to the inoculated milk. It was then incubated for 12 hours under room temperature followed by measurement of the pH using both pH meter and pH paper.

pH Reading:
After 12 hours the pH of each container was measured using a pH meter and values were noted. Simultaneously the pH were measured by using pH paper also. The variability of the color in pH paper gives the result.

Statistical analysis:
The pH values obtained were subjected to statistical analysis by calculating the Mean and standard deviation and the variance within and between groups were calculated by One way anova by using the statistical package SPSS. Values were considered significant when the *p* value is ≤ 0.05.
Percentage of Inhibition and IC50 Value:
The percentage of inhibition each tested compound exhibited was calculated using the formula.

$$(\boldsymbol{pH\ of\ Inoculated} - (\boldsymbol{pH\ of\ Inoculated} + \boldsymbol{Test\ Treated}))/((\boldsymbol{pH\ Uninoculated} - \boldsymbol{pH\ of\ Inoculated})) \times \mathbf{100}$$

The Percentage inhibition and IC 50 values were used to draw graphs for an easy depiction of the data. The percentage inhibition of each dose in a Linear scale is used to calculate IC 50 value by Linear regression using GraphPad Prism Ver 4.

Organoleptic Identification:
The changes in milk after varying levels of fermentation was further monitored by means of visual clues on the nature of fermented milk. The changes in texture and nature of fermented milk was monitored.

RESULTS AND DISCUSSION

The plant selection was based on the availability and reported activity in the previous studies. The weight of the leaves of plants taken for the study and the volume of distilled water used for homogenization was used to calculate the final effective concentration of the plant part. It is depicted in table 1. These values were further used in depicting the percentage inhibition and further calculation of the IC 50 value on test elements having linear dose dependency.

pH Reading with pH Meter

The pH readings has been used to do statistical analysis using anova and tukey post hoc analysis to determine significance of the test in comparison with the control. The results of post hoc analysis is depicted after each table where $p \leq 0.05$ were considered as significant.

Standardization Using Antibiotics

The percentage inhibition of the 4 antibiotics tested were given graphically in Figure 4 graph 1. From the graph it is evident that all the antibiotics have a very high inhibition percentage ranging from 65 - 85% as expected from the standard antibiotics. It is curious that even strong antibiotics are not able to induce a 100% inhibition on the growth of *Lactobacillus.* The various levels of inhibition by antibiotics is a clear indication that the system works as expected. Weight of leaves used in the study and effective concentration of the plant has been given in table 1.

Testing using Plant Extracts

The different plant extracts have shown various levels of inhibition of bacterial growth. A graphical representation of the percentage growth inhibition by different plant extracts are shown in figure 3 Graph 2 and figure 4 Graph 3 and 4. From the Graphs it is evident that the plants *Cinnamomum zeylanicum*, *Aegle marmelos*, *Murraya koenigii*, *Azadirachta indica,* and *Leucas aspera* has shown comparatively higher inhibition percentage above 50. There are many other plants that still have moderate inhibitory activity and have shown excellent dose responses like *Crotalaria pallida, Psidium guajava, Polyalthia longifolia, Justicia gendarussa* etc. Many plants tested have shown feeble activity of bacterial growth inhibition like *Vitex peduncularis, Phyllanthus emblica* etc. Curiously the Turmeric powder (*Curcuma longa*) has shown moderate to feeble activity against *Lactobacillus*.

IC 50: The IC 50 was calculated for the plants that have shown clear dose response. The IC50 values of the plants were given in table 2 below

The lowest IC50 *i.e.* highest antimicrobial activity was for *Cinnamomum zeylanicum* and *Azadirachta indica* followed by *Aegle marmelos* and *Lantana camara*. The highest IC50 was shown by *Phyllanthus emblica* and *Justicia gendarussa* showing moderate or lower antimicrobial activity.

pH reading Using pH paper

The pH paper was used as an alternative method to read the pH values to ensure layman practicability. The pH values are as similar as that of the readings from the pH meter but the color developed is transient after a few minutes it faded to the base color of the paper. The issue may be the problem of the pH paper brand or the method in general.

Organoleptic Identification

During the course of experiments, we have noted that the changes in pH is evident in texture and nature of the fermented milk. The more acidic the pH is, the more coagulated and condensed the curd will be. At times we could directly assume the pH of the medium and hence could understand the activity of the compound tested. This is a huge advantage as it doesn't need any equipment to understand the pH change and hence the antimicrobial activity of the test compound.

Perdigon G *et al* [2] investigated the effect of feeding fermented milk containing *Lactobacillus casei, Lactobacillus acidophilus* and mixture of both on the specific and non-specific host mechanisms in Swiss mice. Results indicate that both are associated with intestinal mucosae and can influence the level of activation of the immune system. Rossland E *et al*[4] co-cultured 5 strains of *Lactobacillus* or 2 strains of *Bacillus* cereus and observed organic acids and other potentially antimicrobial metabolites are produced. Study of Rani JMJ et al [3] on *Lantana camara* L showed high antibacterial activity against *Lactobacillus* sp., *Streptococcus mitis, Candida albicans* and *Aspergillus niger.* Our study showed only a moderate result for *Lantana camara*. Philip JM *et al* [5] in their experiment using *Azadirachta indica, Melia azedarach* and *Spilanthes acmella* proved Antimicrobial effect on common denture plaque bacteria. Comparative

analysis of phytochemical antibacterial and antioxidant activity of different extracts of *Azadirachta indica* leaves was evaluated by Sharma G *et al* [7] and showed antibacterial property on the plant. Current study on *Azadirachta indica* showed a similar result against *Lactobacillus*. The studies led by Rakesh N *et al* [6] with *Aegle marmelos* leaves extract against *Staphylococcus aureus, Escherichia coli, Protease vulgaris* and *Lactobacillus* showed a positive result. Current study also showed a similar result. Antimicrobial and cytotoxic activity of *Cinnamomum zeylanicum*, Calcium hydroxide and triple antibiotic paste as root canal dressing materials was carried out by Abbaszadegan A *et al* [8] and the antifungal and antibacterial activity and analysis of bioactive phytochemical compounds of *Cinnamomum zeylanicum* using gas chromatography by Hameed IH *et al* [9] showed a positive result. Current study on the same plant showed a similar positive result.

Islam MZ *et al* [10] studied antioxidant and antibacterial activities of *Crotalaria pallida* and showed an antibacterial property to the plant for different strains of bacteria. Current study with this plant against *Lactobacillus* showed a moderate result. Antibacterial activity of *Curcuma longa* varieties against different strains of bacteria was carried out by Naz S *et al* [11] and Gunes H *et al* [12] evaluated the antibacterial effect of curcumin with the minimum inhibitory concentration method in standard bacterial strains. Also Singh N *et al* [13] carried out the comparative anti microbial study of ethanolic extract of leaf and rhizome of *Curcuma longa* Linn. These three experiments had positive results, showing the antibacterial property to the plant. Current study on the same plant against *Lactobacillus* showed a negative result. Sugumaran P *et al* [14] evaluated biomass production and antibacterial activity of *Justicia gendarussa* against various human pathogens and showed the antibacterial property. Current study also showed a positive result for the same plant. Naz R *et al* [15] carried out the antimicrobial, antioxidant and phytochemical screening for Methanolic, ethanolic and aqueous extract of leaves of *Lantana camara* against different bacterial strains. The result was positive but Current study showed only a moderate activity. Chew AL *et al* [16] evaluated antimicrobial activity *Leucas aspera* and it showed notable antimicrobial activity against test organisms. *Leucas aspera* showed a comparatively higher antibacterial activity against *Lactobacillus* in Current studies.

The antibacterial activity of leaf extracts of *Moringa oleifera* was investigated by Abdallah EM *et al* [17]. Their study has a positive result but it was negative in Current study. The studies led by Elumalai K *et al* [18] evaluated leaf extract of *Murraya koenigii* and its antimicrobial properties and showed antibacterial property. Same plant showed a positive result on current study. The studies led by Saranya CV *et al* [19] carried out an experiment on the antibacterial activity of *Ocimum sanctum* against human pathogens and tested positive. Current study showed least antibacterial activity against *Lactobacillus.* Dhale DA and Mogle UP [20] evaluated the phytochemical screening and antibacterial activity of *Phyllanthus emblica* and Kanthimathi M and Soranam R [21] investigated the antibacterial effects of *Emblica officinalis* and *Phyllanthus niruri* crude extracts against bacterial pathogens. Both had a positive result on the antibacterial property. Current study showed a negative result. Antibacterial potentiality and phytochemical analysis of mature leaves of *Polyalthia longifolia* carried out by Ghosh A *et al* [22] against different bacteria showed a positive result where our result on this plant was negative. The studies led by Soudawat P *et al*[23] investigated the phytochemical and antibacterial activity of *Psidium guajava* against some clinical pathogens and showed a positive result. Current study showed a negative antibacterial effect on this plant against *Lactobacillus*. The current experiment has shown the potential of Milk fermentation in conducting preliminary screening for antimicrobial activity. It is 1st that we are reporting the use of milk fermentation as a method for antibacterial analysis.

CONCLUSIONS

The milk fermentation by *Lactobacillus* can be effectively used as a model organism to conduct preliminary screening for antibacterial activity. The initial standardization using common antibiotics has proved that the growth inhibition by antibiotics can be tracked through monitoring pH of the inoculated milk. Consecutive testing with different plants has shown the efficacy of this method in depicting the antibacterial effect.

Out of the 15 plants tested, *Cinnamomum zeylanicum* has shown the highest antibacterial activity. Despite the well known previous reports as an antimicrobial agent, *Curcuma longa* has performed poorly in inhibiting the growth of *Lactobacillus*. The use of pH paper as an alternative method to read pH was found to be a crude but effective method. Likewise, organoleptic identification of the pH by monitoring texture and nature of the fermented milk is an effective alternative crude method for screening antibacterial activity.

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Conflict of Interest

The authors declare no conflicts of interest

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Table 1. Weight of leaves used in the study and effective concentration of the plant.

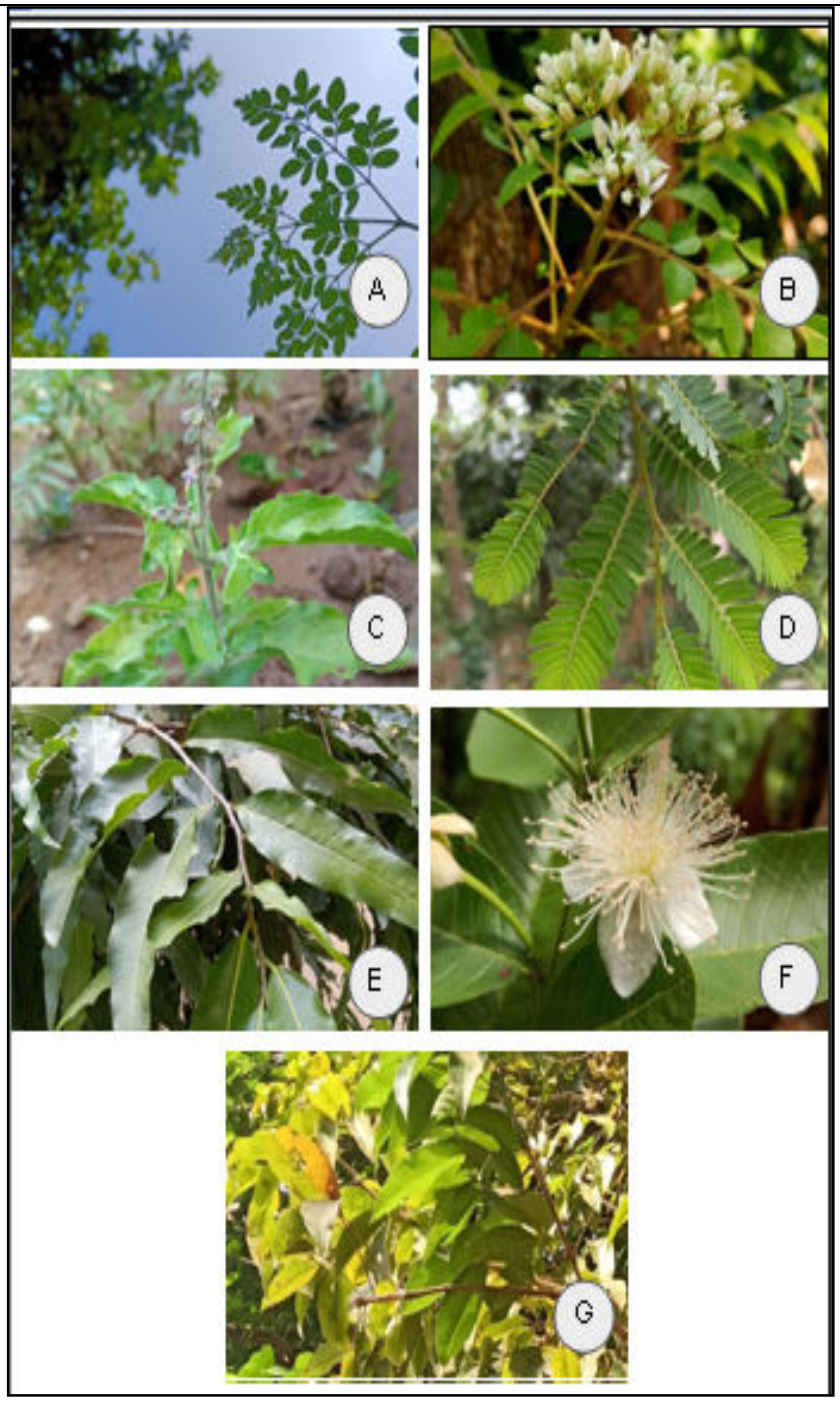
Sl No	Plant	Weight in mg	Volume of DW in ul	Dosage	Effective Dosage in mg plant tissue
1	*Aegle marmelos*	5012.7	15000	500	167.1
		5012.7	15000	1000	334.2
		5012.7	15000	1500	501.3
		5012.7	15000	2000	668.4
2	*Azadirachta indica*	5008	25000	500	100.16
		5008	25000	1000	200.32
		5008	25000	1500	300.48
		5008	25000	2000	400.64
3	*Cinnamomum zeylanicum*	5005	20000	500	125.01
		5005	20000	1000	250.03
		5005	20000	1500	375.05
		5005	20000	2000	500.07
4	*Crotalaria pallida*	5016.3	30000	500	83.605
		5016.3	30000	1000	167.21
		5016.3	30000	1500	250.815
		5016.3	30000	2000	334.42
5	*Curcuma longa*	5008.4	25000	500	100.168
		5008.4	25000	1000	200.336
		5008.4	25000	1500	300.504
		5008.4	25000	2000	400.672
6	*Justicia gendarussa*	5003.5	25000	500	100.07
		5003.5	25000	1000	200.14
		5003.5	25000	1500	300.21
		5003.5	25000	2000	400.28
7	*Lantana camara*	5014.3	30000	500	83.58

		5014.3	30000	1000	167.14
		5014.3	30000	1500	250.72
		5014.3	30000	2000	334.29
8	*Leucas aspera*	5002	15000	500	166.73
		5002	15000	1000	333.47
		5002	15000	1500	500.2
		5002	15000	2000	666.93
9	*Moringa oleifera*	5003.5	25000	500	100.07
		5003.5	25000	1000	200.14
		5003.5	25000	1500	300.21
		5003.5	25000	2000	400.28
10	*Murraya koenigii*	5007	15000	500	166.9
		5007	15000	1000	333.8
		5007	15000	1500	500.7
		5007	15000	2000	667.6
11	*Ocimum sanctum*	5006.7	25000	500	100.134
		5006.7	25000	1000	200.268
		5006.7	25000	1500	300.402
		5006.7	25000	2000	400.536
12	*Phyllanthus emblica*	5000	25000	500	100
		5000	25000	1000	200
		5000	25000	1500	300
		5000	25000	2000	400
13	*Polyalthia longifolia*	5001.4	25000	500	100.028
		5001.4	25000	1000	200.056
		5001.4	25000	1500	300.084
		5001.4	25000	2000	400.112
14	*Psidium guajava*	5031	25000	500	100.62
		5031	25000	1000	201.24
		5031	25000	1500	301.86
		5031	25000	2000	402.48
15	*Vitex peduncularis*	5004	25000	500	100.08
		5004	25000	1000	200.16
		5004	25000	1500	300.24
		5004	25000	2000	400.32

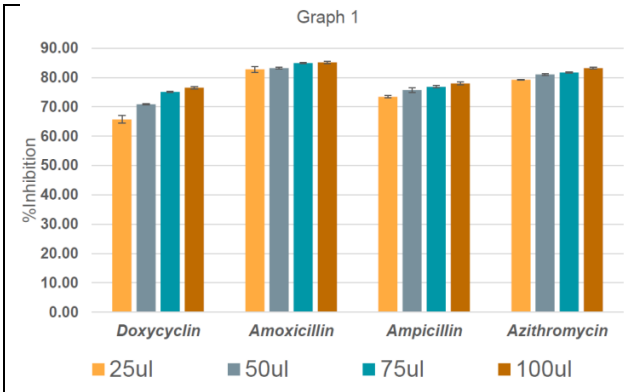
Table 2: IC50 Values of the plants showing dose response.

Plant	IC50 in mg Plant Tissue
Cinnamomum zeylanicum	14.05
Azadirachta indica	306.34
Aegle marmelos	322.47
Lantana camara	385.14
Crotalaria pallida	426.54
Phyllanthus emblica	1039.18
Justicia gendarussa	1941.47

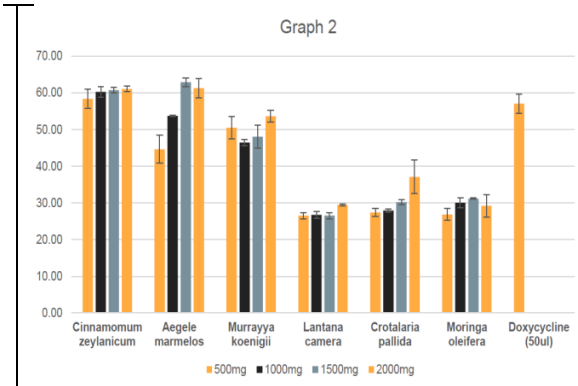
A: ***Aegle marmelos*** **L.; B:** ***Azadirachta indica*** **A. Juss.; C:** ***Cinnamomum zeylanicum;*** **D:** ***Crotalaria pallida*** **Aiton; E:** ***Curcuma longa*** **L.; F:** ***Justicia gendarussa*** **Burm. f.; G:** ***Lantana camara*** **(L.).;H :** ***Leucas aspera*** **(willd.) Link**



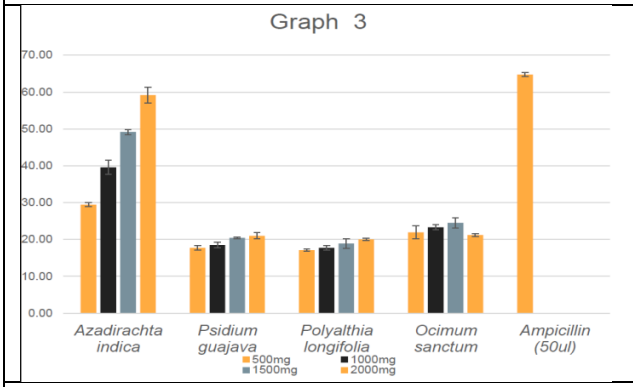
A: ***Moringa oleifera*** **Lam.; B:** ***Murraya koenigii*** **(L.). ; C:** ***Ocimum sanctum*** **L. ; D:** ***Phyllanthus emblica*** **(L.).; E:** ***Polyalthia longifolia*** **(Sonn.) Thwaites.; F:** ***Psidium guajava*****; G:** ***Vitex peduncularis*** **wall. ex schauer**

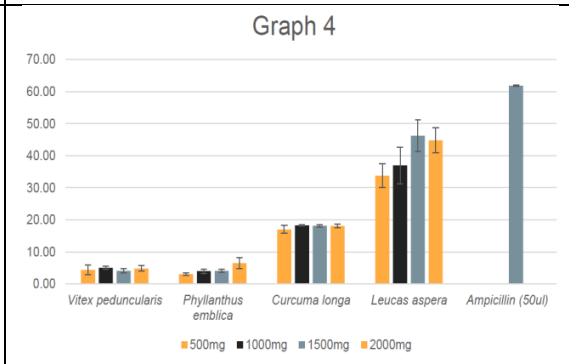


Graph 1: Percentage inhibition as shown in different antibiotics that has been used to standardize the method.



Graph 2: Percentage inhibition of the Different plants tested along with positive control Doxycyclin. Values are mean ± Standard deviation.n=3.





Graph 3 & 4: Percentage inhibition of the Different plants tested along with positive control Ampicillin. Values are mean ± Standard deviation.n=3.

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RESEARCH ARTICLE

In silico Analysis of Annexin A3 and Annexin A4 and Their Molecular Evolution in Vertebrates

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ABSTRACT

In the present study, two annexin proteins annexin A3 and annexin A4 were studied for their in silico analysis of protein sequences and structure, localization in the cell, presence in evolutionary tree, level of conservation by comparing them with histone H4 and cytochrome – C. Annexin are calcium and phospholipid binding proteins. They are forming an evolutionary conserved multigene family. All the members of the family being expressed throughout animal and plant kingdoms. Structurally, annexin are characterized by a highly α-helical and tightly packed protein core domain considered representing a calcium regulated membrane binding module. Annexin have also been found outside the cell within the extracellular space. They are evolutionarily conserved in different species ranging from amphibians to humans by comparing them with histone H4(a highly conserved protein) and cytochrome–C(a semi-conserved protein). Syntenial analysis of annexinA3 and annexin A4 provides conservation of homologous genes between the genomes of different species. Through their apparent ability to arrange or integrate into membranes with which they interact, annexin may therefore have roles as effectors, regulators, and mediators of Ca^{2+} signals. They have been linked to fibrinolysis, coagulation, inflammation and apoptosis. However, we still have a long way to go to understand the precise functions of individual annexin.

Keywords: Annexin, calcium, proteins, effectors, regulators, membranes

INTRODUCTION

Annexin were first identified from bovine adrenal glands which comes from the Greek word "synexis" meaning "meeting" [1]. It is a calcium dependent protein that was responsible for aggregation of granules amongst one another and also the plasma membrane. The protein family of annexin has continued to grow since their association with intracellular membranes was first reported in the year of 1977 [2]. The recognition is that, these proteins were members of a broad family first came from protein sequence comparisons and their cross-reactivity with antibodies [3].One of these workers (Geisow) coined the name 'Annexin' shortly after [4]. Quite a 100 annexin are identified in many various species [2]. Twelve proteins are identified in humans; these were conventionally mentioned to as annexin A1-13 (the ANX-A12 gene is unassigned) [2]. The descriptor 'A' denotes their presence in vertebrates; 'B' denotes their presence in invertebrates; 'C' denotes their presence in fungi and a few groups of unicellular eukaryotes; 'D' denotes their presence in plants; and 'E' their presence in protists [5,6].The 12 human annexin genes range in size from 15 kb (*ANXA9*) to 96 kb (*ANXA10*) and are spread throughout the genome on chromosomes 1, 2, 4, 5, 8, 9, 10, and 15[5]. Other vertebral annexin genes may vary slightly in size and chromosomal linkage, but orthologues are similar in their sequence and splicing patterns [2]. Annexin gene expression levels within human organs have a broad range, from universal (for example, annexin A1, A2, A4, A5, A6, A7, and A11 to selective, like annexin A3 in neutrophils, annexin A8 within the placenta and skin, annexin A9 within the tongue, annexin A10 within the stomach and annexin A13 in the small intestine[5]. Annexin A11 has the highest gene expression in macrophages, neutrophils and T-cells suggests that it may have a significant role in immune system function and possibly in autoimmune diseases[7,8].An annexin core comprises four segments [9]. Each annexin consists of two principal domains, one is the divergent NH2-terminal "head" and the other one is a conserved COOH-terminal protein core[5].It forms a highly α-helical and tightly packed disk with a slight curvature and two principal sides [6]. The more convex side contains novel kinds of calcium-binding sites, the so-called type II sites, and faces the membrane when an annexin is associated peripherally with phospholipids [10].The three-dimensional structure of annexin A3 has recently been solved. The conserved core consists of four domains with five α-helices each [5]. The N-terminal part of the protein is three amino acids long [11]. Annexin A3, also named lipocortin III or placental anticoagulant protein III (PAP III), has an apparent molecular mass of 33 kDa (Kilo Dalton) with 322 amino acids [5].Annexin A3 is expressed almost exclusively in differentiated cells of the myeloid cell lineage. Moreover, it's expression increases during the differentiation of these cells into neutrophils or macrophages, and promotes neutrophil granules aggregation in a calcium-dependent manner [12]. Annexin A4 (Anxa4) could also be a cytosolic calcium-binding protein with four repeat domains, each containing one calcium-binding site (CBS) and interacts with lipid membranes in a calcium-dependent manner. Annexin A4 is localized to the cytoplasm in a variety of cells, including epithelial and secretory cells of the liver, brain, pancreas, intestine, adrenal medulla, and kidneys [13].Calcium-dependent and calcium-independent interactions between annexin and phospholipid membranes is necessary for the regulation of ion channels. In the former case, such interactions depend largely on the conserved annexin core and the calcium-binding sites and in both cases a degree of reversibility is a characteristic of membrane binding for most members of the annexin family [10]. Phylogenetic reconstruction of the annexin gene can also provide informative evidence for positive or negative selection and the dates, rates and patterns of divergence or conservation[14].As yet, no human diseases are described during which a mutation in an annexin gene could be a primary cause. However, there is evidence that through changes in expression, properties, or localization, annexin may contribute to the pathophysiology of disease phenotypes. The most striking examples of these secondary effects are termed as "annexinopathies" and are characterized by dysregulation of what could be the normal antithrombotic properties of extracellular annexin [6].

Annexin A3 (Anxa3) exhibits important roles in tumor development, metastasis and drug resistance. Anxa3 might specifically functionalize either as a tumor suppressor or as a tumor promoter depending on the types of tumor cells and tissues [14]. Annexin A4 modulates membrane permeability and membrane trafficking, participates in cellular growth and apoptosis, enhances tumor invasion and promotes anti-tumor drug resistance. The

overexpression of ANXA4 has been identified in various clinical epithelial tumors including: lungs, gastric, colorectal, pancreatic, gallbladder, breast, renal, ovarian, laryngeal, and prostate cancers [15].

In the present study, it was identified that annexin A3 and annexin A4 both are evolved during the Devonian era, when amphibians started evolving from fishes. Mostly the in silico analysis of these proteins that is the protein sequence and its structure, its localization in cells, its level of conservation, its presence in evolutionary phylogenetic tree and its interaction with other functional genes. We were collected all the aminoacid sequences, their protein Id and length to align the protein sequences for construction of phylogenetic tree. Syntenial analysis of annexin A3 and annexin A4 was done to identify conservation of homologous gene and gene order between genomes of different species [16]. The present study demonstrates that annexin A3 and annexin A4 are evolutionary conserved proteins.

MATERIALS AND METHODS

Sequence Retrieval of Protein

The Annexin protein Id, length and the amino acid sequences(in Fasta format) were retrived from uniprot which was created in 1986 by Amos Bairoch during his Phd and developed by the Swiss Institute of Bioinformatics .This is freely accessible and a functional information data base of protein sequence.

Alignment of Proteins

The sequential alignment of annexin proteins is done by using the software MEGA(Molecular Evolutionary Genetics Analysis) version7.0(2016).This is a computer software which promotes molecular evolutionary research for conducting conservation of proteins and it is also used for constructing phylogenetic tree. It is an integrated tool for conducting automatic and manual sequence alignment, inferring phylogenetic trees, mining web-based databases, estimating rates of molecular evolution, and testing evolutionary hypotheses.This program was used to align amino acid sequences of all the domains of annexin by downloading them from different databases of uniprot.

Construction of Phylogenetic Tree

A phylogenetic tree or evolutionary tree coined by Charles Darwain in 1859, is a braching diagram or tree showing the evolutionary relationships among various biological species or other entities – their phylogeny –based upon similarity and differences in their physical or genetic characteristics. In a phylogenetic tree, each node with descendants represents the most recent common ancestor of the descendants, and the edge lengths in some trees correspond to time estimates. Each node is called a taxonomic unit. Taxonomy is the classification of organisms according to similarity. The complete amino acid sequences of all annexins from different vertebrate species were retrived from NCBI (National Centre for Biotechnology Information) database and their accuracy were confirmed from Uniprot database. Protein alignment program i.e. MEGA 7 was used to align the amino acid sequences of all annexin for the purpose of phylogenetic analysis. The phylogenetic tree was constructed by Maximum likelihood method based on JTT matrix – based model.

Calculation of Evolutionary Time Scale by Million year Plotting

In order to explore the molecular evolution of annexin in the term of Million year, the amino acid sequences among different classes of vertebrates were compared and changes in number of amino acids per hundred amino acids was calculated by comparing mammals vs other primates, birds vs amphibians, fishes vs amphibians with different available annexin sequences. Human annexin sequence of all annexin families has been taken as the recent one in the history of evolution. Therefore, the evolutionary time reference of human annexin sequences is considered as Zero Million year. The average sequences were calculated and radiations of mammalian annexin were plotted against Million years.

For the analysis, we used histone–H4 as an example of highly conserved protein and cytochrome–C as a semi - conserved protein. Human annexin sequence of all annexin families has been taken as the recent one in the history of evolution. Therefore, the evolutionary time reference of human annexin sequences is considered as Zero Million year. The average sequences were calculated and radiations of mammalian annexin were plotted against Million years. While calculating radiation of primate mammals, annexin sequences from Northern white cheeked Gibbon, Chimpanzee, Olive Baboon were compared with human annexinA3 and A4. For calculating non – primates, Dog, Cat, Mouse sequences were compared with annexinA3 and annexinA4.In these cases the average value representing the amino acid change /100 amino acid were considered. We compared two amino acid with one another, the similarity of both of them was noted and then the percentage of changes between them was calculated in an excel sheet. Average of each group was taken and then by comparing the same with the averages of histone H4 and cytochrome – C graph was plotted in Origin pro software which is named as Million year plotting.

Statistical Analysis

Using the saved alignment files in MEGA7, distance matrices were generated for different aligned data sets. Using this method, pair wise distances of any two different amino acid sequences within a group can be measured. Bootstrap methodology was used to estimate variance. In case of data gaps or data missing, pair-wise deletion method was used. For each data set, there would be one matrix which informs about the pair wise distances of all sequences in a group. In the matrix window distances between each sequence with another is calculated along with overall mean distance of all sequences. Then the pair wise distance values (generated within the distance matrix) were imported in "R" software for statistical analysis and graphical representation. Using 'R' statistical software, box-plots were generated to represent the evolutionary relationships of different protein sequences. The Kruskal – Wallis analysis of variance test is done for each set of data to check the reliability and significance of the data points [17].

Syntenial Analysis of All Annexin

Synteny analysis is regularly performed on assembled sequences that are fragmented, neglecting the fact that most methods are developed using complete genomes. We utilised Pubmed Genome Data Viewer was provided all the genes present adjacent to annexin A3 and annexin A4 for building synteny of all annexin gene loci from selected vertebrate genomes.

RESULTS

Protein Id and Length of Annexin Proteins

We explored that annexin protein was present in all classes of vertebrates including mammals, birds, amphibians, reptiles and fishes. There we found out annexin A3 and annexin A4 were particularly present in which species. Then we arranged all the species serially according to their scientific names in an excel sheet. Then we searched the protein Id and the length of protein by using Uniprot. Next, they were downloaded in Fasta format for further analysis and the entry of the protein Id and length was done into the same excel sheet made earlier. Table -1 and Table -2showing the data of annexin A3 and annexin A4 protein that we obtained from Uniprot website.

Multiple Sequence Alignment of Annexin Proteins

A multiple sequence alignment was a sequence alignment of three or more biological sequences. It was a way of arranging the primary sequences (here as protein) to identify regions of similarity that may be a consequence of functional, structural, or evolutionary relationships between the sequences. During the alignment, gaps were inserted between the residues so that residues with identical or similar characters were aligned in successive columns. If two sequences in an alignment shared a common ancestor, mismatches can be interpreted as point mutations and gaps can be interpreted as indels (insertion or deletion mutations) introduced in one or both lineages in the time since they diverged from one another. We arranged all the domains of annexin A3 and annexin A4 in a

notepad in Fasta format one after the other sequentially. In order to analyse the degree of conservation of the different domains present in annexin A3 and annexin A4, their various structural regions and domains were analysed separately. In addition, conservation of specific functional regions such as region involved in interaction between two different protein sequences and their assembly were also explored by using the website Emboss Needle. The details of these regions were summarised separately. Somewhere the human sequences were used as the template and other species sequences were also used as template. Specific domain sequences described for other species were used as query in order to find the corresponding regions present in the human annexin also in the annexin protein sequences of different species.

Construction of Phylogenetic Tree

Phylogenetics is the study of evolutionary relatedness among various groups of organisms (*e.g.*, species, populations).We explored how annexin protein has evolved during molecular evolution, for that purpose we have retrieved full length or partial sequences of annexinA3 and annexinA4 from different available data bank. Full length protein sequences were used Maximum likelihood method based on JTT matrix – based model of annexinA3and annexinA4, which depicted that there is a single copy of annexin A3 and annexinA4 gene conserved across different lineageof vertebrates with statistical support. This also suggest that annexin protein originated at point between 390 to 400 MYA of vertebrates, mostly during the Devonian era. Furthermore, we calculated the evolutionary age and pattern of annexin A3(Fig:1) and annexin A4(Fig:2). We compared the conservation of full length annexin in different species ranging from amphibians to human. The bootstrap consensus tree inferred from 500 replicates is taken to represent the evolutionary history of the taxa analysed. Initial tree for the heuristic search were obtained automatically by applying Neighbour – Join and BioNJ algorithms to a matrix of pair - wise distances estimated during a JTT model and then selecting the topology with superior log likelihood value.

Conservation Analysis of Annexin Protein

We compared the conservation of annexinA3 and annexinA4 in different species ranging from amphibians to humans with histone H4 and cyt – C by using histone – H4 as an example of highly conserved protein and cytochrome – C as a semi-conserved protein. This analysis indicates that annexinA3 and annexinA4 had evolved during the Devonian era (approximately 400MYA),when amphibians started evolving from fishes. In the first 50 million years (since its origin to till middle of the Cretaceous era), many changes were seen in the plotting. But in the first 100 million years (since its origin to till middle of the Permian era), annexinA4 had not required any changes. Since late half of the cretaceous era, itacquired many changes rapidly indicating that these changes probably coincide with the development of amphibians from fishes. During the tertiary era, annexinA3 incorporated only a very few changes supporting that annexin structure – function relationship is fairly stabilized during the primate evolution.Fig-3(A) and (B) was shown the conservation analysis of annexin A3 and annexin A4.

Distributional Analysis of Conservation of Different Domains of Annexina3 and Annexin A4

Boxplots were created to provide a succinct distributional summary that could easily be created by hand, and supported comparison across groups. As computers have become more prevalent and more powerful, it has become easier to produce compact summaries that display more data. This has led to an explosion of box plot variations that stay true to the original goals to various extents, while supporting much richer display of the underlying distributions. By using 'R' statistical, box plots were generated to represent the evolutionary relationship of different protein sequences. The pair wise distance values were imported in R software for statistical analysis and graphical representation. For each data set there will be one matrix which informs about the pair wise distances of all sequences in a group. As we have measured the pair wise evolutionary distances of protein sequences, the graphical representation reflects values on the Y–axis, which is inversely proportional to the conservation. Therefore, the conserved sequences showed lower values and divergent sequences showed higher values in the Y–axis. Along with this calculation, the median values of each data set were calculated and also represented along with conservation. Here we compared all the annexinA3 and annexinA4 sequences with histone because histone is highly conserved in nature. We represented all the data in the Fig:4(A) and (B).

Synteny Analysis

The syntenial analysis of the protein annexin A3 and annexin A4 provides a frame work in which conservation of homologous adjacent genes and their order were identified. There were 9 genes present adjacent to annexin A3 and 7 genes present adjacent to annexin A4. We represented the data in Table: 1 and Table: 2. and the Fig:5 and Fig:6 was showing the syntenial analysis of annexin A3 and annexin A4 respectively.

DISCUSSION

During this work, we explored that Annexin function as a whole most likely resides in their unique mode of membrane interaction, which in turn can influence a number of membrane-related events, e.g., membrane traffic, the organization of compartment membranes and the plasma membrane [10]. Many of the annexin cores are crystallized and their molecular structures reveal interesting features that have the architecture of the annexin-type Ca^{2+} binding sites and a central hydrophilic pore proposed to function as a calcium channel. In this work we explored the molecular structure, functional and evolutionary status of annexin family protein, annexin A3 and annexin A4. Basically, we have focused on the evolution and divergence in amino acid sequence in most of the vertebrate organisms. Our analysis indicates that annexin A3 and annexin A4 has evolved from 400 Mya during the Silurian age. Furthermore, we demonstrated that different domains of annexin A3 and annexin A4 remained not that conserved and showed divergence more than that of Histone and Cytochrome -C. Also, we got to know about the essential genes which coevolved with the annexin A3 and A4 during the Vertebrate Evolution. So, we conclude that annexin A3 and A4 are evolutionary conserved protein altogether.

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Table.1 : Annexin A3 Present In Vertebretes

SL.No.	ORGANISMS	SCIENTIFIC NAME	PROTEIN ID	LENGTH
	MAMMALS			
1	Human	*Homo sapiens*	P12429	323
2	Mouse	*Mus musculus*	O35639	323
3	Rat	*Rattus norvegicus*	P14669	324
4	Bovine	*Bos taurus*	F1MWQ2	323
5	Dog	*Canis familiaris*	E2R0N3	323
6	Chimpanzee	*Pan troglodytes*	H2QPR8	323
7	Rhesus monkey	*Macaca mulatta*	G7MSZ8	323
8	Cat	*Felis catus*	M3WET7	323
9	American chameleon	*Anolis carolinensis*	G1KFA2	326
10	Gray short-tailed opossum	*Monodelphis domestica*	F6S7A7	323
11	Horse	*Equus caballus*	F6ZAK1	323
12	Northern white-cheeked gibbon	*Nomascusleucogenys*	G1RAG3	323
13	Guinea pig	*Cavia porcellus*	H0VMD9	323
14	Chinese softshell turtle	*Pelodiscus sinensis*	K7FVZ9	323
15	European domestic ferret	*Mustela putorius furo*	M3Y5V5	323
16	Thirteen-lined ground squirrel	*Ictidomystridecemlineatus*	I3NAE7	323
17	Sheep	*Ovis aries*	W5QBI9	323
18	Crab-eating macaque	*Macaca fascicularis*	G7P536	323
19	Green monkey	*Chlorocebussabaeus*	A0A0D9QWV0	323
20	Little brown bat	*Myotis lucifugus*	G1PL69	324
21	Giant panda	*Ailuropoda melanoleuca*	G1LFR9	324
22	Olive baboon	*Papioanubis*	A0A096N9E8	323
23	Pygmy chimpanzee	*Pan paniscus*	A0A2R9AXV0	323
24	White-tufted-ear marmoset	*Callithrix jacchus*	F7H4N2	323

25	African elephant	*Loxodonta africana*	G3T860	323
26	Bolivian squirrel monkey	*Saimiri boliviensisboliviensis*	A0A2K6V239	323
27	Black snub-nosed monkey	*Rhinopithecus bieti*	A0A2K6JU47	323
28	Naked mole rat	*Heterocephalus glaber*	A0A0P6IY75	323
29	Pig-tailed macaque	*Macaca nemestrina*	A0A2K6BHX3	323
30	Peters' Angolan colobus	*Colobus angolensispalliatus*	A0A2K5HNM8	323
31	Sooty mangabey	*Cercocebusatys*	A0A2K5NWX6	323
32	Philippine tarsier	*Tarsius syrichta*	A0A1U7T420	323
33	Ma's night monkey	*Aotusnan cymaae*	A0A2K5D2H8	323
34	Western European hedgehog	*Erinaceus europaeus*	A0A1S3W8B9	323
35	Ord's kangaroo rat	*Dipodomy sordii*	A0A1S3FG48	324
36	bottle-nosed dolphin	*Tursiops truncatus*	A0A2U4B589	323
37	Golden hamster	*Mesocricetus auratus*	A0A1U7Q8Y5	323
38	Sperm whale	*Physeter catodon*	A0A2Y9ERB5	323
39	Beluga whale	*Delphinapterus leucas*	A0A2Y9QBZ8	323
40	Yangtze river dolphin	*Lipotes vexillifer*	A0A340X647	323
41	Hawaiian monk sea	*Neomonachus schauinslandi*	A0A2Y9I902	323
42	Yangtze finless porpoise	*Neophocaena asiaeorientalis asiaeorientalis*	A0A341C649	323
43	Beaver	*Castor canadensis*	A0A250YFJ4	323
44	Polar bear	*Ursus maritimus*	A0A384C9H2	323
45	North Pacific minke whale	*Balaenoptera acutorostratascammoni*	A0A383YSD1	323
	FISHES			
1	West Indian ocean coelacanth	*Latimeria chalumnae*	H2ZUH7	323
2	Japanese pufferfish	*Takifugurubripes*	H2RWC0	323
3	Northern pike	*Esox lucius*	C1BZS7	324
4	Asian bonytongue	*Scleropagesformosus*	A0A1W4YKY7	325
5	Pacific walrus	*Odobenus rosmarusdivergens*	A0A2U3WF72	323
6	Channel catfish	*Ictalurus punctatus*	E3TG24	321
7	Turquoise killifish	*Nothobranchius furzeri*	A0A1A8V7E5	343
8		*Nothobranchiuskadleci*	A0A1A8E0A6	343
9		*Nothobranchiuspienaari*	A0A1A8L5I8	343
10		*Iconisemion striatum*	A0A1A7Y0P1	343
11	Beira killifish	*Nothobranchiuskuhntae*	A0A1A8IYH5	343
12	Bluefin notho	*Nothobranchiusrachovii*	A0A1A8RM66	312
	AMPHIBIANS			
1	African clawed frog	*Xenopus laevis*	A0A1L8HMI8	323
2	American bullfrog	*Lithobatescatesbeiana*	C1C3Z2	323
	REPTILES			
1	American alligator	*Alligator mississippiensis*	A0A151MPW6	323
2	Chinese alligator	*Alligator sinensis*	A0A1U7RTS0	323

Table 2: Annexin A4 Present in Vertebrates

SL.No.	ORGANISMS	SCIENTIFIC NAME	PROTEIN ID	LENGTH
	MAMMALS			
1	Human	*Homo sapiens*	P09525	319
2	Bovine	*Bos taurus*	P13214	319
3	Pig	*Sus scrofa*	P08132	319
4	Mouse	*Mus musculus*	P97429	319
5	Dog	*Canis lupus familiaris*	P50994	319
6	Rat	*Rattus norvegicus*	P55260	319
7	Rhesus macaque	*Macaca mulatta*	A0A1D5R5Q6	321
8	Horse	*Equus caballus*	F6S9R7	321
9	Gray short-tailed opossum	*Monodelphis domestica*	F7GDF3	318
10	Sumatran orangutan	*Pongo abelii*	H2P5Y6	321
11	Rabbit	*Oryctolagus cuniculus*	G1TA83	319
12	Northern white-cheeked gibbon	*Nomascus leucogenys*	G1RGJ9	319
13	Olive baboon	*Papio anubis*	A0A096NDM9	321
14	Crab-eating macaque	*Macaca fascicularis*	G7PME1	321
15	Green monkey	*Chlorocebus sabaeus*	A0A0D9RRC2	321
16	Giant panda	*Ailuropoda melanoleuca*	G1MCK4	323
17	Little brown bat	*Myotis lucifugus*	G1PD28	321
18	Guinea pig	*Cavia porcellus*	A0A286XL58	321
19	Pygmy chimpanzee	*Pan paniscus*	A0A2R9A478	321
20	Sheep	*Ovis aries*	W5QEU6	320
21	African elephant	*Loxodonta africana*	G3SQQ3	319
22	Black snub-nosed monkey	*Rhinopithecus bieti*	A0A2K6N0I0	321
23	Golden snub-nosed monkey	*Rhinopithecus roxellana*	A0A2K6QP81	321
24		*Cebus capucinus imitator*	A0A2K5Q8P9	321
25	Peters' Angolan colobus	*Colobus angolensis palliatus*	A0A2K5J500	321
26	Sooty mangabey	*Cercocebus atys*	A0A2K5P404	321
27	Drill	*Mandrillus leucophaeus*	A0A2K5YKS2	321
28	Pig-tailed macaque	*Macaca nemestrina*	A0A2K6B2T1	321
29	White-tufted-ear marmoset	*Callithrix jacchus*	A0A2R8N3F1	321
30	Ma's night monkey	*Aotus nancymaae*	A0A2K5CXL2	321
31	Cat	*Felis catus*	M3WIJ2	319
32	Yangtze river dolphin	*Lipotes vexillifer*	A0A340XUG5	320
33	Chimpanzee	*Pan troglodytes*	A0A2I3TUK6	320
34	Thirteen-lined ground squirrel	*Ictidomys tridecemlineatus*	A0A287DDQ6	215

35	Weddell seal	*Leptonychotes weddellii*	A0A2U3YWH3	319
36	Western European hedgehog	*Erinaceus europaeus*	A0A1S2ZLR3	319
37	Ord's kangaroo rat	*Dipodomys ordii*	A0A1S3FNS1	321
38	Atlantic bottle-nosed dolphin	*Tursiops truncatus*	A0A2U4BYX2	319
39	Philippine tarsier	*Tarsius syrichta*	A0A1U7TSB2	321
40	Naked mole rat	*Heterocephalus glaber*	A0A0P6JGA5	321
41	Golden hamster	*Mesocricetus auratus*	A0A1U8C197	319
42	Yangtze river dolphin	*Lipotes vexillifer*	A0A340X2V5	319
43	Beluga whale	*Delphinapterus leucas*	A0A2Y9M4G8	319
44	Beaver	*Castor canadensis*	A0A250YFC4	319
	BIRDS			
1	Mallard	*Anas platyrhynchos*	U3ID99	303
2	Rock dove	*Columba livia*	A0A2I0LN02	314
3		*Patagioenas fasciata monilis*	A0A1V4KR22	315
4	Bengalese finch	*Lonchura striata domestica*	A0A218UCL0	315
5	Chicken	*Gallus gallus*	A0A1D5PTL7	315
	FISHES			
1	Atlantic salmon	*Salmo salar*	B5XEI6	319
2	Nile tilapia	*Oreochromis niloticus*	I3J673	320
3	Zebrafish	*Danio rerio*	Q804G7	321
4	Channel catfish	*Ictalurus punctatus*	C1K7M3	321
5		*Iconisemion striatum*	A0A1A7XCV4	322
6	West Indian ocean coelacanth	*Latimeria chalumnae*	H3BFB1	323
7	Japanese pufferfish	*Takifugu rubripes*	A0A3B5K819	320
8	White-tufted-ear marmoset	*Callithrix jacchus*	U3DQF6	321
9	Turquoise killifish	*Nothobranchius furzeri*	A0A1A8V9E0	322
10	Northern pike	*Esox lucius*	C1BZR8	319
11		*Austrofundulus limnaeus*	A0A2I4AUS2	320
12	Yangtze finless porpoise	*Neophocaena asiaeorientalis asiaeorientalis*	A0A341CC87	319
13	Blackstripe livebearer	*Poeciliopsis prolifica*	A0A0S7HGP3	319
14		*Nothobranchius korthausae*	A0A1A8HJW9	321
15		*Nothobranchius kadleci*	A0A1A8EFV1	322
16	Beira killifish	*Nothobranchius kuhntae*	A0A1A8IU60	322
17		*Nothobranchius pienaari*	A0A1A8NXN6	322
18	Bluefin notho	*Nothobranchius rachovii*	A0A1A8PL10	322
19		*Paramormyrops kingsleyae*	A0A3B3S0Y9	322
20	Mediterranean greater amberjack	*Seriola dumerili*	A0A3B4V111	320
21		*Periophthalmus magnuspinnatus*	A0A3B4AKJ2	320
22	Bicolor damselfish	*Stegastes partitus*	A0A3B4Z6Z7	320
23		*Pundamilia nyererei*	A0A3B4FSE2	320
24		*Seriola lalandi dorsalis*	A0A3B4XXG4	320

	AMPHIBIANS			
1	African clawed frog	*Xenopus laevis*	Q90X16	321
2	American bullfrog	*Lithobates catesbeiana*	A5LHA6	321

Table 3 : Description of genes adjacent to Annexin A3.

Sl.no.	NAME OF GENES	SITE OF EXPRESSION	FUNCTIONS
1	**FRAS1**	found in basement membranes	provides instructions for making a protein that is part of a group of proteins called the FRAS/FREM complex, also involved in the proper development of certain other organs and tissues, including the kidneys, although the mechanism is unclear.
2	**MRPL1**	highest expression level in multi-cellular organism	helps in protein synthesis within the mitochondrion. This gene encodes a 39S subunit protein that belongs to the L1 ribosomal protein family.
3	**CNOT6L**	Has 3'-5' poly(A) exoribonuclease activity for synthetic poly(A) RNA substrate	linked to various cellular processes including bulk mRNA degradation, miRNA - mediated repression, translational repression during translational initiation and general transcription regulation. Additional complex functions may be a consequence of its influence on mRNA expression, Mediates cell proliferation and cell survival and prevents cellular senescence.
4	**CXCL13**	strongly expressed in the follicles of the spleen, lymph nodes, and Peyer's patches	promotes the migration of B lymphocytes (compared to T cells and macrophages), apparently by stimulating calcium influx into, and chemotaxis of, cells expressing Burkitt's lymphoma receptor 1 (BLR-1). It may therefore function in the homing of B lymphocytes to follicles
5	**BMP2K**	gene is the human homolog of mouse BMP-2-inducible kinase	Play a key role in skeletal development and patterning
6	**PAQR3**	encodes a seven transmembrane protein localized in the golgi apparatus in mammalian cells	Functions as a tumor suppressor by inhibiting the Raf/MEK/ERK signaling cascade. Alternative splicing results in multiple transcript variants.
7	**NAA11**	a Protein Coding gene	Include transferase activity, transferring acyl groups other than amino-acyl groups and peptide alpha-N-acetyl transferase activity.
8	**CMPK1**	include kinase activity and nucleobase-containing compound kinase activity.	encodes one of the enzymes required for cellular nucleic acid biosynthesis. This enzyme catalyzes the transfer of a phosphate group from ATP to CMP, UMP, or dCMP, to form the corresponding diphosphate nucleotide. Alternate splicing results in both coding and non-coding transcript variants.

9	**CNOT6L**	a Protein Coding gene, Has 3'-5' poly(A) exoribonuclease activity for synthetic poly(A) RNA substrate	linked to various cellular processes including bulk mRNA degradation, miRNA-mediated repression, translational repression during translational initiation and general transcription regulation. Additional complex functions may be a consequence of its influence on mRNA expression, Mediates cell proliferation and cell survival and prevents cellular senescence

Table-4 : Description of genes adjacent to AnnexinA4.

Sl no.	NAME OF GENES	SITE OF EXPRESSION	FUNCTIONS
1	**GMCL1**	Protein Coding gene	Encodes a nuclear envelope protein that appears to be involved in spermatogenesis, either directly or by influencing genes that play a more direct role in the process.
2	**MXD1**	member of the MYC/MAX/MAD network of basic helix-loop-helix leucine zipper transcription factors	mediate cellular proliferation, differentiation and apoptosis, mutations in this gene may play a role in acute leukemia, and the encoded protein is a potential tumor suppressor
3	**TGFA**	act as either a transmembrane - bound ligand or a soluble ligand	encodes a growth factor that is a ligand for the epidermal growth factor receptor, which activates a signaling pathway for cell proliferation , differentiation and development.
4	**ADD2**	Membrane-cytoskeleton-associated protein	heteromeric proteins composed of different subunits referred to as adducin alpha, beta and gamma,binds to the erythrocyte membrane receptor SLC2A1/GLUT1 and may therefore provide a link between the spectrin cytoskeleton to the plasma membrane. Binds to calmodulin. Calmodulin binds preferentially to the beta subunit.
5	**AAK1**	Adaptor-related protein complex 2 (AP-2 complexes)	functions during receptor-mediated endocytosis to trigger clathrin assembly, interact with membrane-bound receptors, and recruit encodytic accessory factors, alternatively spliced transcript variants have been described, but their biological validity has not been determined.
6	**NFU1**	encodes a protein that is localized to mitochondria	plays a critical role in iron-sulfur cluster biogenesis
7	**GFPT1**	encodes the first and rate-limiting enzyme of the hexosamine pathway and controls the flux of glucose into the hexosamine pathway	product of this gene catalyzes the formation of glucosamine 6-phosphate , regulates the circadian expression of clock genes

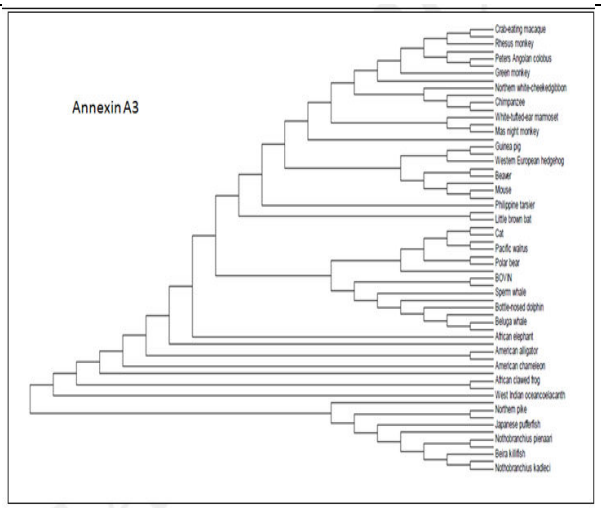

Fig.1:Phylogenetic tree depicting the evolution of Annexin A3 across different species.

The figure depicts the order of Annexin A3 evolution across various species. Starting from the Fishes , Amphibians , Reptiles , Birds to the modern Mammals, Annexin A3 has shown a diverse plethora of functionality.

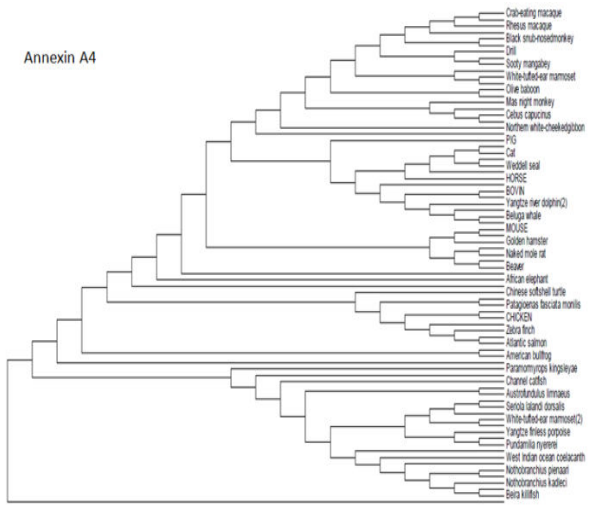

Fig.2:Phylogenetic tree depicting the evolution of Annexin A4 across different species.

The figure depicts the order of Annexin A4 evolution across various species. Starting from the Fishes, Amphibians, Reptiles, Birds to the modern Mammals, Annexin A4 has shown a diverse plethora of functionality.

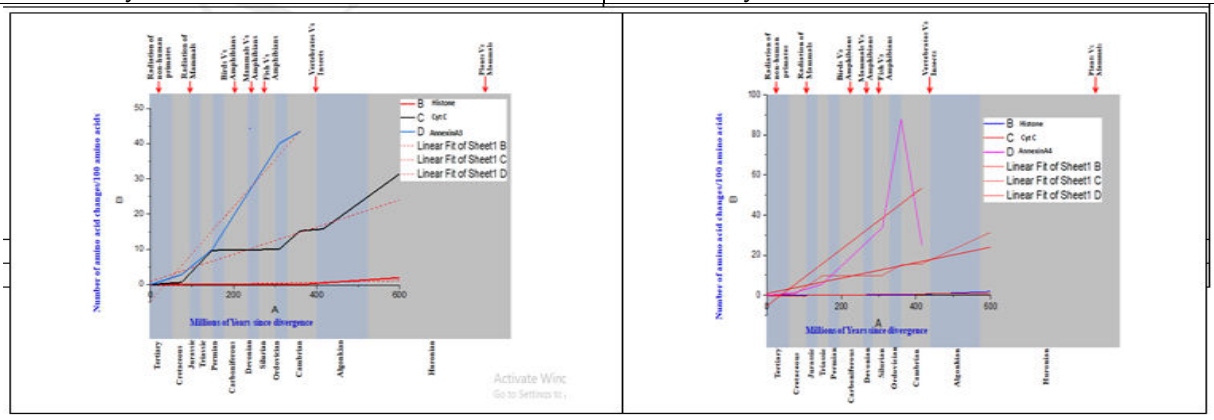

Fig.3:(A)Conservation analysis of annexinA3 in comparision to HistoneH4(highly conserved) and cytochromeC(semi-conserved). This analysis indicates that annexinA3 has evolved during permian era which means it is highly conserved.(B) Conservation analysis of annexinA4 in comparision to histoneH4(highly conserved) and cytochromeC(semi-conserved).This analysis indicates that AnnexinA4 has evolved during permian era which means it is not conserved.

Kruskal–Wallis test: chi–square = 8493.4, df=185, P < 0.0001, n=186

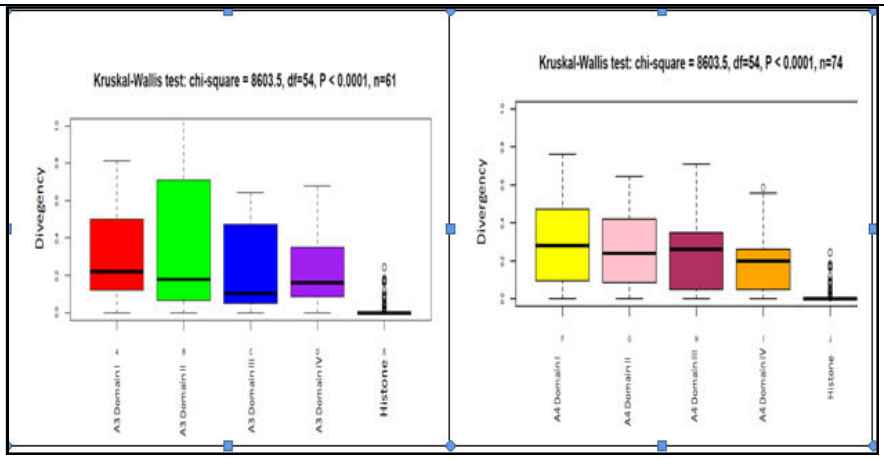

Fig.4: Analysis of conservation of different domains of Annexin A3(A) and Annexin A4(B) in comparision with histone protein.

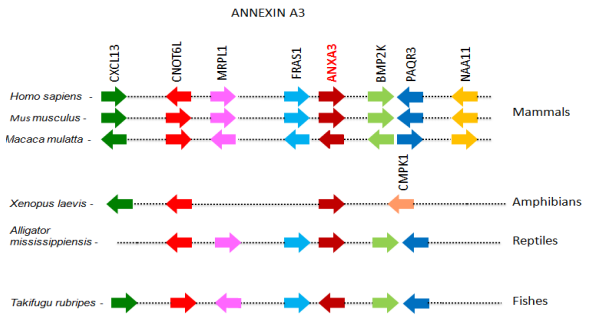

Fig.5:Analysis of genes adjacent of Annexin A3.

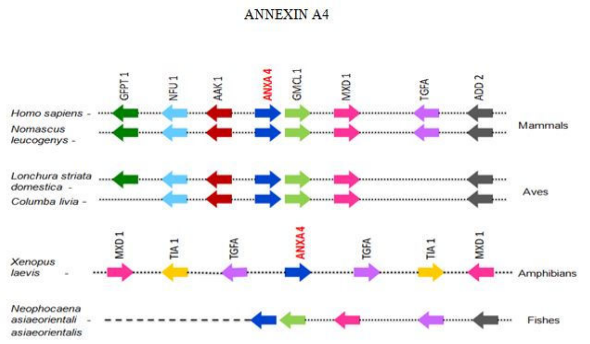

Fig.6: Analysis of genes adjacent of Annexin A4

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REVIEW ARTICLE

Nanoparticles: An Overview

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ABSTRACT

The study of nanoparticles drug delivery systems allows the development of Novel platforms for the efficient transport and controlled release of drug molecules in the harsh microenvironment of diseased tissues of living systems, thus offering a wide range of functional nanoplatforms for smart application in biotechnology and nanomedicine. This article highlights recent advances of organic (including polymeric micelles and vesicles, liposomes, dendrimers, and hydrogels) and inorganic (including quantum models), gold and mesoporous silica nanoparticles) materials. Despite the remarkable developments of recent synthetic methodologies, most of all efficient use in biotechnology and nanomedicine applications. This highlights some critical issues in the design and engineering of nanocarrier systems for biotechnology applications, arising from the complex environment and multiform interactions established within the specific biological media.

Keywords: Nanoparticles, Methods, Drug Delivery, Drug Release, Nanospheres

INTRODUCTION [1,2,4,5,15,26,28,29,38]

The term "nano" has found that over the past decade the application of education to various fields has continued to grow. Nanoscience and nanotechnology, nanomaterials or Nano chemistry is one of the most recent discoveries in the nanoscale which are commonly used in scientific reports, popular books and magazines and have become very popular, even outsourced. This is the department. The prefix comes from the ancient Greek Latin nanus, which literally means dwarf, so it is much smaller. It is used in conjunction with the International Organization for Standardization (SI) standards to indicate a time-saving key. Therefore, a nano meter-sized planet is measured in nano meters (1 nm) and includes structures whose size is larger than the particle extent and more than the

macroscopic size usually> 1 nm and <100 nm. Nanotechnology is a small science, a small science. This is the use of fraud and petty things. At this size, atoms and molecules work differently, providing interesting and interesting things. Research in nanotechnology and nanoscience has grown rapidly in different product areas in recent years. This allows for medical applications where traditional technology can reach its limits. Nanotechnology should not be used as a technology that will only affect certain regions. Often mentioned to as "basic science," nanotechnology does more than just mean small objects and products. Nanoscale abilities are frequently housed in more and larger compartments. Nanotechnology represents the design, manufacture, and application of materials in the measurement of atoms, molecules, and macromolecules to yield original nano-symmetrical materials. Pharmaceutical nanoparticles are defined as high-density and low-density (less than 100 nm in diameter) nanoparticles that may not be harmful. The term nanoparticle is a combination of nanospheres and nanocapsules. The nanosphere is a matrix system in which the drugs are completely dispersed, and the nanowires are the systems in which the drug surrounds a special polymer membrane. This process overview focuses on nanoparticle classification, process preparation, operation, and application.

Need For Study [6,7,8,10,24,28,38]

The main goal in cell design as a message delivery system is to control cell size, space properties, and the release of pharmacological agents to achieve special treatment of the appropriate cells. Polymer nanoparticles offer several specific advantages over liposomes. For example, they help increase metabolism / protein and have liberating properties. benefits: Some of the benefits of using organic materials as a medication delivery system are:

- ❖ Ease of manipulation of particle size and surface properties of nanoparticles to achieve effective and active drug targets after parenteral administration.
- ❖ Modify the surface nanoparticles to change the bio-distribution of the drug and then clean the drug to achieve the maximum therapeutic effect while minimizing the drug effect.
- ❖ The switch and controlled air particles are easy to extract by selecting the matrix connector.
- ❖ You can access certain web pages by connecting a link to the top of the cell or using a magnet.
- ❖ There are different types of management, including oral, nasal, parental, and uterine.
- ❖ The weight of the medicine is very high and it can be injected into the system without chemical effects. This is an important factor in maintaining medication administration.
- ❖ Liposomes and polymer nanoparticles are usually corrosive and do not accumulate in the body, so they are not at risk.
- ❖ Nanoparticles can penetrate into micro-organisms and thus effectively accumulate drugs in the desired location

Advantages [5,12,23,24,28,34,38]

- ✓ Nanoparticles can cross the blood vessel barrier and are very useful as a means of administering drugs directly to the brain.
- ✓ On the other hand, the nanoparticles used to transport drugs can be toxic to the brain, which is also a major drawback.
- ✓ Material changes cause particles to accumulate and are small in size, making it difficult to process nanoparticles in water and in dry form.
- ✓ Small particle size is larger than the surface, and this property makes nanoparticles very responsive in the cellular environment.
- ✓ Due to the small size of the cell, the payload is limited and explosives are emitted.
- ✓ These useful issues need to be resolved before the organism can be used clinically or commercially.

Application of Nanoparticles: [3,9,13,14,19,20,22,28,33,35,37,38]

Nanoparticles can be divided into several types according to size, morphology, physical and chemical properties. Some of them are carbon dioxide, ceramic nanoparticles, metal nanoparticles, semiconductor nanoparticles, polymer nanoparticles and lipid-based nanoparticles.

- **Carbon Based Nanoparticles:** Carbon compounds contain two main components. Carbon nanotubes (CNTs) and fullerenes. CNT is nothing more than a sheet wrapped around a tube. These materials are 100 times stronger than steel and are typically used to strengthen systems. CNTs can be subdivided into single-stranded carbon nanotubes (SWCNTs). CNTs are special because they are very fast throughout the tube and do not flow through the tube. Carbon dioxide of this structure is organized into pentagons and hexagons. Due to its controlled nature, structure, strength and their connection to electronics, it is a commercial application.
- **Ceramic Nanoparticles:** Ceramic nanoparticles are volatile organic compounds including oxides, carbides, carbonates, and phosphates. These materials have high heat resistance and low chemical resistance. They are used in photography, painting, delivering medicines and photography. By controlling certain ceramic nanoparticles properties such as size, surface, porosity, surface area / size value, they act as carriers.
- **Metal Nanoparticles**: Metal nanoparticles are made from stainless steel. These molecules can be synthesized by chemical, electrical, or photographic methods. In chemical processes, nanoparticles are obtained by reducing the expression of ions in solution with a chemical reducing agent. For example, this gold material is used to clean the sample before it is analyzed by SEM. This is usually done to increase energy flow and help obtain high quality SEM images.
- **Semiconductor Nanoparticles**: Semiconductor nanoparticles have metallic and non-metallic properties. They are in the periodic table groups II-VI, III-V or IV-VI. These particles have a wide band space and exhibit different properties when activated. These are used in portrait photography applications, electronics, portrait photography and water sharing. Some examples of low density devices are group III-V GaN, GaP, InP, InAs, ZnO, ZnS, CdS, CdSe, CdTe are semiconductor II-VIs and silicon and germanium are group IVs.
- **Polymer Nanoparticles Molecules**: Polymer nanoparticles are nanoparticles-based. Although it depends on the preparation method, it has a structure similar to nano capsules and nanospheres. Nanosphere has a matrix-like structure, whereas nano separated cells have a morphological structure. In the end, the joints are closed and surrounded by a polymer shell. Some of the benefits of high molecular weight nanoparticles are treated, protected from bacteria, and can be combined with care and photography, special guidance, and more. They have been applied in drug delivery and research. Supply solutions containing polymer nanoparticles are highly corrosive and can corrode.
- **Nanoparticle Basic Lipid**: Lipid particles generally have a characteristic shape with a diameter of 10 to 100 nm. It consists of a solid center made of lipids and a matrix containing soluble lipophilic molecules. The external sources of these organisms are regulated by the delivery and release of receptors and RNA in the treatment of cancer. Therefore, the field of nanotechnology is incomplete and, as statistics say, is at the limits of the developing environment. Originally, it was at the same level as the communication technology of the 1960s and the technology of the 1980s. Therefore, it is easy to predict that this area will show the same magnitude as the other two technical areas above.
- **Delivery of Polymeric Nanoparticle Drug**: the use of polymeric nanoparticles (NP) to further deliver drug nanoparticles to side health targets NP polymers in cancer. It demonstrates the importance of therapeutic potential as it can be used to manage tumor recurrence for tumor cells by reducing efficacy and cytotoxicity. .Cleaners are used in fast-moving objects as delivery trucks because of their quality, supply, quality, comfort, and lack of harmful substances. Various nanoparticle systems, general synthesis and encapsulation process, release control.
- **Drug Delivery of Iron Oxide Nanoparticles**: Super paramagnetic iron oxide nanoparticles (SPION) are the most studied inorganic nano-carrier system for drug delivery. This nano transporter is non-toxic, highly perishable, non-synthesized, and can be completely removed from the human body through the process of iron processing. In addition to the images, it could target external magnetic fields. SPION can be used to cause indoor heating in additional areas.

- **PLGA Nanoparticles**: Poly (lactic acid-co-glycolic acid) (PLGA) is one of the most effective antioxidants (NPs). The US FDA has approved its use in drug delivery systems due to its sustainability, toxicity, organic and biological properties. Strategies for directing PLGA NP to the site are general and practically recommended. In addition, treatments have been introduced to improve NP growth and quality of treatment.
- **Provide Drug Nanoparticles:** Nanoparticles of alginate, known as anionic polysaccharides, are distributed on the cell walls of brown algae and are one of the most naturally occurring compounds, producing viscous properties when treated with water. Most often used in drug delivery, it refers to set of management methods. Its use includes the synthesis of neurotransmitters that allow for the chemical modification of together web structures, as well as their diversity and genetic profile, and mucosal integration.

DISCUSSION AND CONCLUSION

Nanoparticles provide a beautiful and attractive platform for a wide variety of applications. The terrain and status of these systems can be considered for individual multi-model applications, with mechanical engineering, satisfying delivery, biology and biology. The above shows that the nanoparticle system is very capable of transforming living things that are difficult to digest, delivery system designed to enhance pharmacology and traditional medicine. The advent of nanotechnology can have a profound impact on the affecting almost All aspects of management,from oral to injection.Current drug combinations are often associated with malnutrition, which resultin high costs to patients,effective treatment, and moreimportantly, an increased risk of accidents and death. Nanotech nology focuses on the small things and is ideal for creating systems that can deliver drugs to smaller areas of the body.

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RESEARCH ARTICLE

Effect of Organic Manure on the Growth and Yield of *Amaranthus blitum* L.

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ABSTRACT

The present study is aimed to evaluate the effect of organic manure on the growth and yield of *Amaranthus blitum* L. was conducted. Organic manure is defined as the product resulting from the biological decomposition of organic matter and can be prepared from the yard trimmings, bio solids (sewage sludge), wood by-products, animal manures, crop residues, biodegradable packing, and food scraps. The effect of organic manure was accessed using physical parameters such as plant height, stem length, and stem breadth, number of leaves and length and breadth of leaves. Further the leaves were subjected to analysis of macro nutrients (carbohydrate and protein) and mineral content (nitrogen, phosphorus and iron). The results revealed that the plants treated with onion waste showed increased physical parameters such as plant height, stemlength, stem breadth, number of leaves and length and breadth of leaves. The increased amount of nutrient content (macronutrient and mineral content) was observed when compared to manure untreated plants (normal). The plant treated with onion waste, tea powder and ash showed moderate amount of nutrient content. To conclude the data, results revealed that the onion waste based organic manure increased the growth and yield of the *Amaranthus blitum* L. Plant.

Keywords: *Amaranthus blitum* L. Nitrogen, Phosphorus, Iron, Plant height, Stem length

INTRODUCTION

Organic manure is defined as the product resulting from the biological decomposition of organic matter. Manure can be prepared from the yard trimmings, bio solids (sewage sludge), wood by-products, animal manures, crop residues, biodegradable packing, and food scraps. Organic matter is the key constituent of cultivated soils. Compounds

containing ring structure (phenol, tannins, hydrocarbon), miscellaneous substances like antibiotics, auxins, vitamins, enzymes and pigments through biological oxidation organic matter is converting into organic manure which may be two types by their origin animal manure and green manure. Animal manure has two types, one is farm yard manure (FYM), and another one is farm slurry or liquid manure. Farm yard manure formed of cattle excreta mixed with straw used as a fertilizer. Farm slurry or liquid manure is agricultural manure in liquid form known as slurry.

MATERIALS AND METHODS

The plant selected for the present study was *Amaranthus blitum* L. The seeds of the *Amaranthus blitum* L. was collected from the local raw drug market and were seedling in various plots based on the experimental design. The plots were properly maintained.

Experimental Design

Group I (N) - Normal Plant
Group II (T1) - *Amaranthus blitum* L. treated with ash for 36 days
Group III (T2) -*Amaranthus blitum* L. treated with onion waste for 36 days
Group IV (T3) - *Amaranthus blitum* L. treated with NPK for 36 days
Group V (T4) - *Amaranthus blitum* L. treated with tea powder for 36 days

Morphological parameters

The morphological parameters such as plant height, stem length, stem breadth, number of leaves, leaves length and leaves breadth were analyzed on12th, 24th and 36th days as per the standard textual procedure.

Biochemical Parameters

After 36 days the *Amaranthus blitum* L. leaves were shade dried and powdered. The dried plant powder was used for the estimation of macronutrients such as Carbohydrate and Protein. Micro nutrients such as Nitrogen, Phosphorus and Iron were also analyzed. Further the preliminary phytochemical screening was also carried out in the leaf powder.

- Estimation of Carbohydrates –Anthrone Method (Sathasivam and Manickam., 2000)
- Estimation of Protein –Lowry's Method (Lowrys *et al*., 1951)
- Preparation of ash in plant powder: 2g of plant leaf powder (*Amaranthus blitum L.*) was taken in a crucible. Then the crucible was kept in a muffle furnace at 600 °C for 3 hours. After the crucible was taken from the muffle furnace and taken the ash weight. The total ash was dissolved in 100ml of distilled water. From this, the different volume of sample was taken in test tubes and the following parameters were studied.
- Estimation of Iron (Miller *et al*., 1981).
- Estimation of Phosphorus (Fisk and Subbarow, 1925).
- Estimation of Nitrogen (Friedman & Boger, 1961).
- Preliminary Phytochemical Screening of Plant Powder (Brindha & Saraswathy, 1981).

Taxonomy

Botanical Name - *Amaranthus blitum* L.
Kingdom - Plantae
Subkingdom - Tracheobionta
Division - Magnoliophyta
Class - Magnoliopsida
Subclass - Caryophyllidae
Order - Caryophyllales

Genus - Amaranthus
Family - Amaranthaceae

Common name

Tamil - Mulai keerai

It is extremely consumed as a health vegetable, because it contains abundant beta carotene and other carotenoids, vitamins B1, B2, C and E, and minerals. It needs adequate moisture, sunlight and temperature and is negatively affected by low and high temperature.

RESULTS AND DISCUSSION

The experiment was conducted on `Growth and yield of *Amaranthus blitum* L. as influenced by organic manure and the results on effectiveness of various treatments including an untreated control for the management of amaranths have been discussed.

From the Table (1) it was noticed that the plants treated with onion waste showed increased plant height. From the Table (2) it was noticed that the plants treated with onion waste showed increased stem length. From the table (3) it was noticed that the plants treated with onion waste showed increased stem breadth. From the table 4 it was noticed that the plants treated with onion waste showed increased Number of leaves. From the Table (5) it was noticed that the plants treated with onion waste showed increased leaves length. From the Table (6) it was noticed that the plants treated with onion waste showed increased leaves breath. Table 7 indicates that the carbohydrate level in ash treated plants was found to be high. Table 8 indicates that the protein level in onion waste treated plants was found to be high. Table 9 indicates that the nitrogen level in onion waste treated plants was found to be high. Table 10 indicates that the phosphorus level in onion waste treated plants was found to be high. Table 11 indicates that the iron level in ash treated plants was found to be high.

CONCLUSION

Organic fertilizers are better alternative to chemical fertilizers due to fact that they are more eco-friendly. The major problem facing crop production in the tropics are low inherent nutrients and rapid soil nutrient depletion as a result of poor agricultural practices such as over grazing erosion, denitrification, deforestation and other human activities. From the study it was found that the highest values of carbohydrate, protein, nitrogen and phosphorus were recorded in *Amaranthus blitum* L. plant treated with onion waste whereas the least values are recorded in normal (manure untreated plant) plant. Plants treated with onion waste, tea powder and ash were more mucilaginous than normal (manure untreated plant) plant and NPK fertilizer. The increase growth, yield and quality, recorded in all the treated plants over the control suggest that fertilizer application is inevitable for a successful crop production. The significantly higher performance of onion waste, tea powder and ash treated plants over NPK on the growth yield and quality related characters is an indication that onion waste, tea powder and ash manure where available, can conveniently be used to replace NPK fertilizer in order to ameliorate the adverse effect of the use of chemical to ensure better environmental protection.

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Table 1: Plant height (cm) of *Amaranthus blitum* L. plant treated with various manure levels

Treatment	12th Day	24th Day	36th Day
N (Normal)	5.0	8.0	26
T1 (Ash)	4.5	9.3	16
T2 (Onion waste)	10	21	55
T3 (NPK)	4.1	7.5	20
T4 (Tea powder)	9.0	15	34

Table 2: Stem length (cm) of *Amaranthus blitum* L. plant treated with various manure levels.

Treatment	12th Day	24th Day	36th Day
N (Normal)	2.1	4.5	23
T1 (Ash)	3.0	5.4	14
T2 (Onion waste)	6.2	10.7	51
T3 (NPK)	2.0	5.4	15
T4 (Tea powder)	6.2	10	30

Table 3: Stem breadth (cm) of *Amaranthus blitum* L. plant treated with various manure levels

Treatment	12th Day	24th Day	36th Day
N (Normal)	0.3	0.6	3.0
T1 (Ash)	0.4	0.7	2.5
T2 (Onion waste)	1.3	2.1	4.9
T3 (NPK)	0.3	0.7	3.5
T4 (Tea powder)	1.0	1.7	4.7

Values were represented in cm.

Table 4: Number of leaves of *Amaranthus blitum* L. plant treated with various manure levels

Treatment	12th Day	24th Day	36th Day
N (Normal)	4	6	21
T1 (Ash)	3	5	10
T2 (Onion waste)	8	13	64
T3 (NPK)	3	5	15
T4 (Tea powder)	4	9	21

Values were represented in numbers.

Table 5: Leaves length (cm) of *Amaranthus blitum* L. plant treated with various manure levels

Treatment	12th Day	24th Day	36th Day
N (Normal)	1.2	2.4	11.5
T1 (Ash)	1.8	2.3	8.0
T2 (Onion waste)	4.5	8.0	15
T3 (NPK)	2.0	2.3	12
T4 (Tea powder)	3.5	6.1	14

Values were represented in cm

Table 6: Leaves breadth (cm) of *Amaranthus blitum* L. plant treated with various manure

Treatment	12th Day	24th Day	36th Day
N (Normal)	0.8	1.6	8.0
T1 (Ash)	1.0	1.7	4.0
T2 (Onion waste)	2.8	5.0	8.5
T3 (NPK)	0.8	1.2	6.0
T4 (Tea powder)	2.0	4.4	7.0

Values were represented in cm.

Table 7: Impact of organic manure on carbohydrate content in *Amaranthus blitum* L.

Treatment	Carbohydrate (mg/g)
N (Normal)	91.66
T1 (Ash)	165
T2 (Onion waste)	121.6
T3 (NPK)	60
T4 (Tea powder)	98.33

Table 8: Impact of organic manure on protein content in *Amaranthus blitum* L.

Treatment	Protein (mg/g)
N (Normal)	11.66
T1 (Ash)	18.33
T2 (Onion waste)	23.33
T3 (NPK)	5.0
T4 (Tea powder)	13.33

Table 9: Impact of organic manure on Nitrogen content in *Amaranthus blitum* L.

Treatment	Nitrogen (mg/g)
N (Normal)	16.28
T1 (Ash)	12.92
T2 (Onion waste)	17.42
T3 (NPK)	15.83
T4 (Tea powder)	13.75

Table 10: Impact of organic manure on phosphorus content in *Amaranthus blitum* L.

Treatment	Phosphorus (mg/g)
N (Normal)	15
T1 (Ash)	40
T2 (Onion waste)	45
T3 (NPK)	10
T4 (Tea powder)	40

Table 11: Impact of organic manure on Iron content in *Amaranthus blitum* L.

Treatment	Iron (mg/g)
N (Normal)	1.70
T1 (Ash)	1.80
T2 (Onion waste)	1.60
T3 (NPK)	0.90
T4 (Tea powder)	1.60

Table 12: Preliminary phytochemical analysis of *Amaranthus blitum* L. Leaves powder

S.No	Phytochemicals	N (Normal)	T1 (Ash)	T2 (Onion waste)	T3 (NPK)	T4 (Tea powder)
1	Saponins	+	+	+	+	+
2	Tannins	–	–	–	–	–
3	Sterols	+	+	+	–	–
4	Terpenoids	–	–	–	–	–
5	Flavanoids	–	–	+	–	–
6	Coumarins	+	+	+	+	+
7	Quinones	–	+	–	–	+
8	Lignins	–	–	–	–	–
9	Alkaloids	+	+	+	+	+
10	Glycosides	+	+	+	+	+
11	Sugar	+	+	+	+	+
12	Phenols	+	+	+	+	+

Fig. 1. *Amaranthus blitum* L.

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RESEARCH ARTICLE

Evaluation of *In vitro* Cytotoxic Effect of Aqueous Extract of *Hippeastrum puniceum* (lam.) Voss. Bulbs

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ABSTRACT

The bulbs of the plant *Hippeastrum puniceum* (Lam) Voss belonging to the family Amaryllidaceae is traditionally used in curing tumours and various inflammatory disorders. Some tribal communities are also using the bulbs in healing wounds and in treating piles. It is a perennial ornamental plant distributed worldwide. In the present study, initially brine shrimp lethality assay and a short term cytotoxic study using brine shrimp and Trypan Blue assay with DLA cells were carried out against aqueous extract of the bulbs and an appreciable result was obtained. Then the study was extended to five different cell lines employing MTT assay. In this procedure, the extract was subjected to treatment and cytotoxicity was measured using colorimetric methods based on the ability of metabolic active cells to cleave the yellow tetrazolium salt MTT to an insoluble purple formazan crystal. A concentration dependant activity was measured. To the best of our knowledge, this is the first attempt to study the cytotoxic potential of aqueous extracts of *Hippeastrum puniceum* bulbs.

Keywords: Cancer, Brine shrimp, Trypan Blue, MTT, Cytotoxicity, Cell lines

INTRODUCTION

One of the leading killer diseases of human beings is cancer and the important treatment methods of cancer include surgery, radiation, chemotherapy, immunotherapy and hormonal therapy. Biologically targeted drugs have become a new group of agents which are used in cancer therapy at present time. One of the major means for cancer treatment

is chemotherapy and is aimed to kill tumor cells in our body. Chemotherapeutic agents generally possess narrow margin of safety and usually are used in combination to achieve maximum ability to kill cancer cells. As the response rate of cancer patients to chemotherapy is always low, cancer is a serious and often life-threatening disease and the response rate to chemotherapy is low. So the patients experience significant drug induced toxicities and they seek alternative approaches and self medication with herbal remedies. Reports indicate that most of the adult cancer patients use at least one kind of complementary and alternative medicine and majority have reported the use of herbal products. The use of herbs or vitamins during chemotherapy is very common among cancer patients. In various folk medicines also the cancer patients use different types of herbal medicines [1].

Since herbal medicine have been reported safe and less or without adverse effects especially when compared with synthetic drugs, many developing countries started to make interest in the use of medicinal plants in recent years. In all over the world, the herbal medicines are considered as the most important field of traditional medicines. It is important to study medicinal plants which have folkloric reputation in order to promote the use of herbal medicine and to determine their potential as source of new drugs. The effort to find anticancer agents from higher plants was launched by US National Cancer Institute (NCI) in 1957. Plants have been proved to be a novel source of useful anticancer substances nowadays. Today many of the most useful and curative anticancer drugs are derived from natural products[2]. Many studies revealed the potential of the extracts as a promising agent as scavenging free radicals and treating diseases related to free radical reactions [3].

The Amaryllidaceae family is considered as one of the most important alkaloid-containing plant families. Amaryllidaceae alkaloids have structural similarities to the essential aminoacid phenylamine and related metabolites of tyrosine. Amaryllidaceae alkaloids have diverse and important pharmacological properties including acitivities such as anticancer, antiviral, immunostimulatory, antimalarial and acetyl cholinesterase inhibition. The bulbs of the plant *Hippeastrum puniceum* (Lam) Voss belonging to the family Amaryllidaceae is traditionally using in curing tumours and various inflammatory disorders. Some tribal communities are also using the bulbs in healing wounds and in treating piles. It is a perennial ornamental plant distributed worldwide [4-13]. Although this plant has been used in the tribal and folkloric medicine for many decades, no attempts were so far made to scientifically evaluate its therapeutic utility. Thus the present study is a step towards the anticancer evaluation of the aqueous extract of the bulbs of *Hippeatrum puniceum.*

MATERIAL AND METHODS

Plant Material

Fresh bulbs of *Hippeastrum puniceum* was collected from Kottayam, Kerala. The plant material was identified and authenticated by Department of Botany, CMS College, Kottayam. Voucher specimen of the plant (CMS 278) is deposited in the college.

Extraction of Bulbs

Fresh bulbs of uniform size were collected from the local areas of Kottayam, Kerala, after the leaves had fallen. The collected bulbs were washed thoroughly and sliced, shade dried and coarsely powdered. About 500 g of the powder was subjected to hot aqueous extraction for 6 hour at a temp below 60^0 C. The juicy solution obtained was filtered through muslin cloth and the marc was discarded. The solution was concentrated at a temperature below 60^0 C. The dried extract so obtained was then stored in a refrigerator for further studies.

Preliminary Phytochemical Evaluation

The preliminary phytochemical analysis was performed using the methods described by Harbone and Trease and Evans were used to identify the presence of alkaloids, terpenoids, carbohydrates, saponins, tannins [7,14-17].

In vitro Cytotoxic Studies

Brine Shrimp Lethality Assay

The extract was evaluated for lethality to brine shrimp larvae. Toxicities of the compound was tested at 6.25, 12.5, 25, 50, 1000 µ/mL, ten nauplii were drawn through a glass capillary and placed in each test tube containing 4,5 mL of brine solution. 0.5 mL of the bulb extract was added to 4.5 mL of brine solution to adjust the final volume to 5 mL and incubated at room temperature for 24 hours under the light. Test was performed in triplicates and the numbers of dead nauplii in each well were counted. Analysis of the data was performed by Probit analysis to determine the lethal concentration of half of the test organisms (LC 50).[18-21]

Short Term Cytotoxicity Study against DLA Cells

Trypan Blue Dye Exclusion

The extract was studied for short term in vitro cytotoxicity using Dalton's lymphoma ascites cells (DLA). The tumour cells were aspirated from the peritoneal cavity of tumour bearing mice and washed thrice with phosphate buffered saline (PBS). Short term cytotoxicity was assessed by incubating 1 x10^6 DLA cells in 1 mL phosphate buffered saline at varying concentrations (10 - 200µg/mL). The cells were incubated for 3 h at 37 ^{0} C. After incubation, the cell death was evaluated using Trypan blue dye exclusion method. To the cell suspension, 3 drops of 1% Trypan blue was added and the cells were loaded immediately on to a haemocytometer. The number of dead cells was calculated. The percentage cytotoxicity was calculated[22,23,24].

In vitro Cytotoxicity on Human Cancer Cell Lines

MCF-7, A549, HT29 and Hep G2 cell lines were purchased from NCCS Pune and was maintained in Dulbecco's modified eagles media (HIMEDIA) supplemented with 10% FBS (Invitrogen) and grown to confluency at 37^{0}C in 5% CO_2 in a humidified atmosphere in a CO2 incubator (NBS, EPPENDORF, GERMANY). The cells were trypsinised (%)) µl of 0.025% Trypsin in PBS/0.5mM EDTA solution) for 2 minutes and passed to T flasks in complete aseptic conditions. Extracts were added to grown cells at a final concentration of 6.25µg, 12.5 µg, 25 µg, 50 µg, and 100 µg/mL from a stock of 1mg/mL and incubated for 24 hours. The percentage difference in viability was determined by standard MTT assay after 24 hours of incubation [25-28].

MTT Assay

The cells were washed with PBS and then 30 µl of MTT solution was added to the culture. It was then incubated at 37^0 C for 3 hours. MTT was removed by washing with PBS and 200 µl of DMSO was added to the culture. Incubation was done at room temperature for 30 minutes until the cell got lysed and colour was obtained. The solution was transferred to centrifuge tubes and centrifuged at top speed for 2 minutes to precipitate cell debris. Optical density was read at 540 nm using DMSO as blank in microplate reader [29-34].

RESULTS AND DISCUSSION

Preliminary Phytochemical Screening

Aqueous extract of *Hippeastrum puniceum* bulbs were subjected to qualitative chemical test for identifying the class of compounds viz; alkaloids, glycosides, steroids, saponins, proteins, tannins, phenolics and flavanoids. The preliminary phytochemical screening of the aqueous extract of bulbs was carried out and the presence of alcohols, phenolics, flavonoids, carbohydrates, mucilage and starch were detected in the extract. The results are summarized in the following Table 1.

Cytotoxic Activity Studies

Brine Shrimp Lethality Assay

The results of the brine shrimp lethality assay using aqueous bulb extract is tabulated in Table 2. A graph was plotted with concentration versus percentage mortality to determine the IC_{50} of aqueous bulb extract by brine shrimp lethality assay (Fig 1).

Short Term Cytotoxicity Study Against Cells- Trypan Blue Dye Exclusion

The short term cytotoxicity study against DLA cells using Trypan blue dye exclusion test was performed with the extract and the results were tabulated in Table 3.

Determination of *in vitro* Anticancer Effect Of Aqueous Extract Of Bulb Using MTT Assay

The cytotoxicity of aqueous extract of bulb was determined using MCF-7, A549, HT29 and Hep G2 cell lines. A graph was constructed using percentage cytotoxicity and concentration in µg/mL to determine the IC_{50} using breast cancer cell line (MCF-7) (Fig 2), lung cancer cell line(A-549)(Fig 3), colon cancer cell lines (HT-29) (Fig-4), cervical cancer cell lines (HeLa) (Fig 5), hepatic cancer cell lines (Hep G2) (Fig 6). A comparison of the IC_{50} values of the five cell lines was also plotted in the graph (Fig 7).

It could be concluded that the aqueous extract of *Hippeastrum puniceum* bulb revealed to exhibit cytotoxicity towards the various human cancer cell lines. The comparison of the effect of extract towards different cell lines was tabulated in Table 4. In figure 7, a graph was also plotted indicating the effect and it was clear that the aqueous extract showed potent cytotoxicity against breast, lung and colon cancer cell lines. The aqueous extract showed low IC50 value againt breast cancer cell line. The findings of the study indicate that *Hippeastrum puniceum* herb is an antineoplastic agent and suggests that further studies evaluating the isolation of active antitumor compounds and their mechanism of action are necessary.

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Table.1. Preliminary Phytochemical Screening

Sl.No:	Phytoconstituents	HPB
1	**Alkaloids**	
	Mayer's test	+
	Wagner's test	-
	Hager's test	+
	Dragendroff's test	+
2	**Glycosides**	
	Legal's test	-
	Baljet's test	-
3	**Phenolics**	
	Ferric chloride test	-
	Lead acetate test	-
4	**Flavonoids and flavones**	
	Aqueous sodium hydroxide test	+
	Shinoda test	-
5	**Terpenoids**	
	Isoprenoid test	+
6	**Carbohydrates**	
	Molisch's test	+
	Benedict's test	+
	Fehling's test	+
7	**Saponins**	
	Foam/Froth test	+
8	**Proteins and aminoacids**	
	Millon's test	+
	Biuret test	-
	Ninhydrin test	-
	Mucilage	+
9	**Tannins**	+

(+) Presence, (-) Absence

Table.2. Percentage mortality in groups treated with HPB in Brine Shrimp Lethality assay

Concentration (µg/mL)	HPB
6.25	46.7
12.5	60
25	100
50	100
100	100

Table:3 Percent cell death using HPB aqueous extracts by Trypan Blue dye exclusion test

Type of cancer cells	Concentration of the aq. extract of HPB (µg/ml)	Percent cell death
Dalton's lymphoma as cites cells	200	23
	100	12
	50	8

Table:4. Comparison of IC_{50} values of HPB extract with five cell lines

Cell lines	IC_{50} values (µg/mL)	
	Standard	HPB
Breast cancer	37.37	15.51
Lung cancer	33.62	31.14
Colon cancer	32.65	28.18
Cervical cancer	31.27	54.38
Hepatic cancer	19.69	54.01

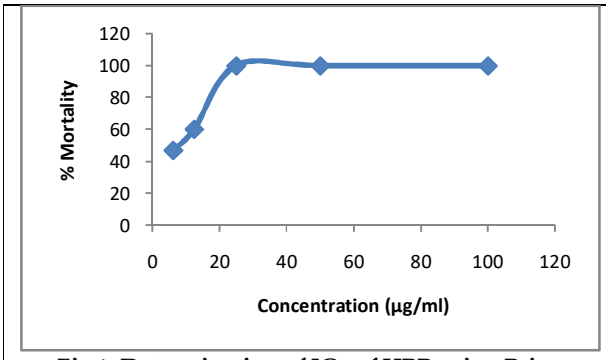

Fig:1. Determination of IC_{50} of HPB using Brine shrimp lethality assay

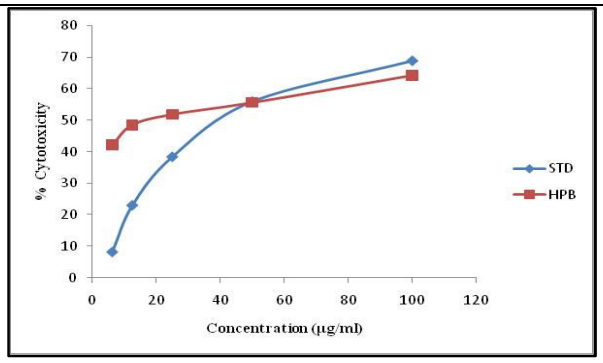

Fig:2. Determination of IC_{50} using breast cancer cell lines (MCF 7).

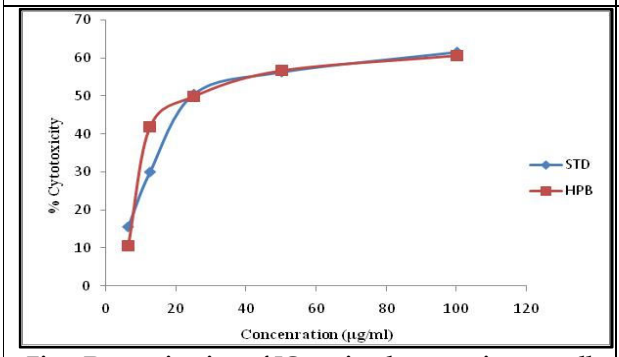

Fig:3 Determination of IC_{50} using lung carcinoma cell lines (A-549)

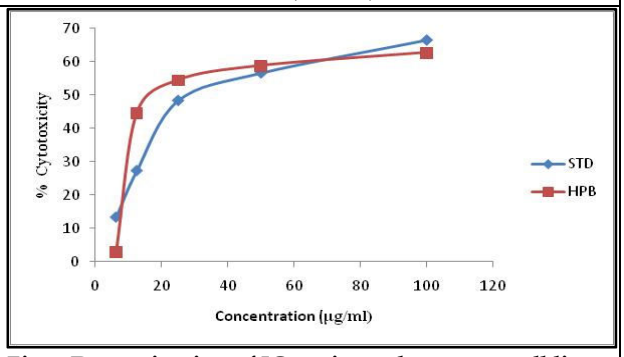

Fig:4. Determination of IC_{50} using colon cancer cell lines (HT-29)

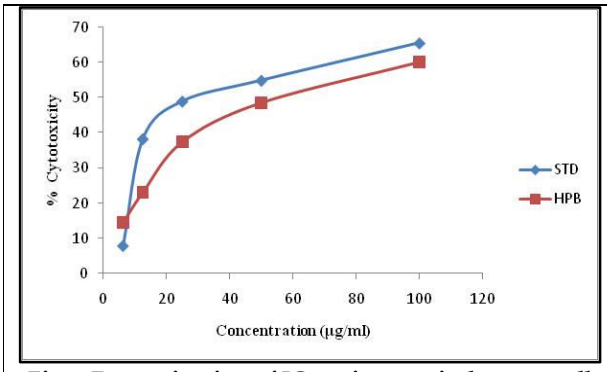

Fig:5. Determination of IC_{50} using cervical cancer cell lines (HeLa)

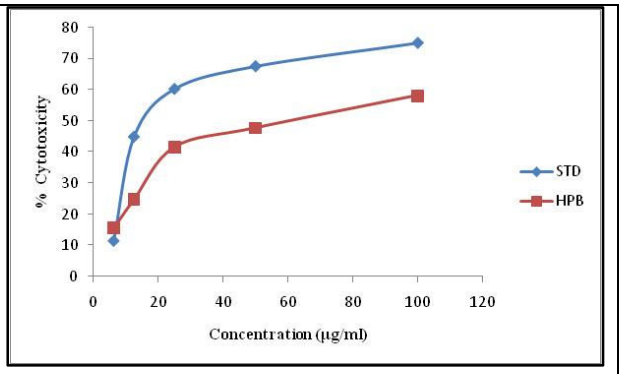

Fig:6. Determination of IC_{50} using hepatic cancer cell lines (Hep G2)

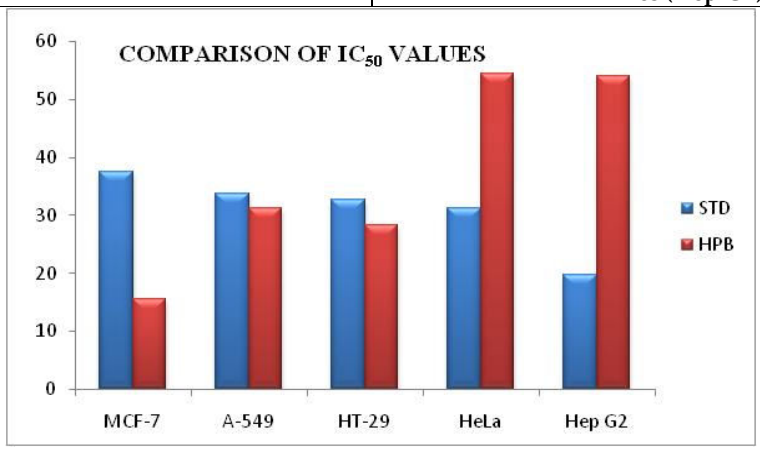

Fig:7. Comparison of IC_{50} values with standard and HPB in various cell lines

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RESEARCH ARTICLE

Performance Evaluation of Ice Plant Test Rig with R 404A Environmentally Friendly Refrigerant

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ABSTRACT

Cooling can be defined as the process of reaching and maintaining below ambient temperature, the purpose is to freeze into ice and cool some products or spaces. Refrigeration has found large-scale industrial applications in ice making, gas dehydration, household and commercial refrigeration. Ice plant used to produce refrigeration effect using vapour compression cycle, by using this cycle, we analyze the performance of the ice plant test rig using R404A environmentally friendly refrigerant. The test rig is analyzed for its cooling capacity assume per unit of mass flow rate of refrigerant. This test platform is used to calculate coefficient of performance. The actual coefficient of performance of the system found is 1.275, which directly depends on the cooling effect. The tonnages calculated by compressor and actual coefficient of performance calculation are 0.2 TR and 0.35 TR, respectively.

Keywords: Refrigeration, Coefficient of performance, R404A, Tonnage, Compressor, Analysis.

INTRODUCTION

R404A refrigerant is used to calculate the coefficient of performance. R404A is a mixture of HFC refrigerants and is commonly used in low and medium temperature refrigeration applications. Its composition includes: HFC-125 (44%), HFC-143a (52%) and HFC-134a (4%). The experimental device used to measure the coefficient performance and study the vapour compression refrigeration cycle, and on this basis during the cycle, we use R404 to perform the performance and analysis of the ice plant test rig. Dhamneya et al. [1] experimentally studied comparative analysis of ice plant test rig with TiO2-R- 134a nano refrigerant. This paper proposes and combines a vapour compression refrigeration system with vapour evaporative refrigeration pad and nano-refrigerant to improve the performance of the system in hot and dry weather, and conducts an experimental comparison. A proposal has been made to combine

the evaporative cooling system with the ice factory test bench to solve the problem of proper heat rejection provided in the condenser due to failure which operates under high pressure. Experimental research shows the characteristics of the evaporative cooling condenser have been significantly enhanced. Maximum coefficient of performance in hot and dry climate conditions, the increase is about 51% compared to the normal system. U.S.Wankhede [2], project aims to design an experimental test device for commercial use. It describes the design and selection criteria of refrigeration system components and concluded that model has satisfactory performance under various physical and atmospheric conditions, and can produce ice in the required quantity and quality within the required operating time. Hajidavalloo et al. [3], built and connected an evaporative cooler to the existing split air-conditioning air-cooled condenser to measure its impact on the cycle performance at various ambient air temperatures up to 49^{0}C. As the ambient temperature increases, the rate of circulation also increases. It was also found that by using an evaporative cooling air condenser in hot weather conditions, power consumption can be reduced by up to 20%, and the coefficient of performance can be increased by about 50%. Shailendra Singh Chauhan [4], experimentally investigated the performance of ice plant for composite nano particles (Al_2O_3-SiO_2) is dispersed in polyalkylene Glycol (PAG46) lubricating oil using R134a as working refrigerant with different volume concentration of 0.02%-0.1%.

The results show that the mixture of R134a/composite nano-lubricant (Al_2O_3-SiO_2/PAG) effectively plays a role in the rig, and it is found that its performance is better than that of any kind of nano particles dispersed in PAG alone. Power consumption in the compressor working with the composite nano-lubricant was 6.8% and 3.5% less than that of the dispersed Al_2O_3 and SiO_2 nano particles, respectively, while the COP was found to be 10.89% and 5.3% more than the separately dispersed Al_2O_3 and SiO_2 nano particles with 0.08% volume concentration. Nasir et al.[5], This article describes the design and performance evaluation of an ice maker that can freeze quickly with certain design considerations, such as the amount of water to be frozen, the choice of cooling system, and the method to achieve the desired result. The test result shows that the temperature in the freezer reaches -14^0°C, and the freezing time of 1 kg of ice cubes is 70 minutes. Yadav et al. [6] created a model to analyze the cooling capacity and coefficient of performance. Model compared by using refrigerant R 134A and R-22 for coefficient of performance and cooling capacity.

Researcher concluded that when the cooling water tank is completely insulated with plywood, the coefficient of performance value and cooling capacity increase and also found changes in coefficient of performance and cooling capacity are 0.12 and 0.042 TR per unit mass flow, respectively. Subramani et al. [7] investigated the vapour compression system using nano refrigerants. Experimental research shows that the refrigeration system using nano-refrigerant works normally. It was found that after replacing the POE oil with mixture of mineral oil and alumina nano particles the freezing capacity was higher and the energy consumption was reduced by 25%. Calculations show that when using nano-refrigerant instead of pure refrigerant, the enhancement factor of the evaporator is 1.53. Pande et al [8], this article introduces the research on different refrigerants and their combination refrigerants (HFC refrigerants). Use these refrigerants R-22, R-134A, R-410A, R-407C for refrigeration. They concluded that R-407C is a potential HFC refrigerant substitute for new systems and existing systems that currently use R-22, requiring the least investment and effort. The R-407C system with similar capacity and pressure as the R-22 can be designed. Due to all these characteristics, the R-407C can be used as a replacement product in the R-22 system without excessive redesign.

Experimental setup

The experimental device include the following parts-compressor, condenser, evaporator coil, filter drier, expansion valve, cooling box and various measurements equipment, such as digital temperature indicators, pressure gauges, electric energy meters, voltmeter, ammeter, etc. The construction of the system allows us to observe the Ice making process. The test rig shown in fig.1 with R404A used for measuring the coefficient of performance and studying the vapour compression refrigeration cycle. The cooling capacity of the analytical equipment is assumed to be a unit of refrigerant mass flow, which is directly measured using a tachometer.

Actual Process

In the ice factory, the water tank is filled with frozen brine. The salt solution is kept in constant motion through the stirrer to increase the heat transfer from the water in the tank to the frozen brine. The agitator can be horizontal or vertical, and can be operated by a motor. The temperature of the brine is maintained at -10ºC to -11ºc by refrigeration equipment. The high-temperature and high-pressure refrigerant vapour is condensed in the air-cooled condenser. The condensed liquid refrigerant expands through the expansion valve. Due to the expansion, the pressure of the liquid refrigerant is greatly reduced. The refrigerant then flows through the evaporator coil surrounding the brine tank, which is filled with brine solution. The low-pressure liquid refrigerant absorbs heat from the brine, the salt solution is equal to its latent heat of vaporization, is converted into a vapour state, and is sent to the compressor again to complete the cycle. The depth of the brine tank should be such that the brine level is about 25 mm higher than the water level in the tank. All four sides of the tank are insulated from the bottom. Provide an insulated wooden cover to cover the top of each section to facilitate the removal of the ice can. The ice can is made of galvanized steel and is chromium treated to prevent corrosion. In order to obtain transparent ice, low-pressure air is used to agitate the water in the tank through a pipe hanging from the top. Due to agitation, dissolved impurities (such as salt) and even colour will collect in the unfrozen water core. It is expected to be taken out and replaced with fresh water.

Thermodynamic Analysis

Heat to be removed from water [9]

$$Q = M_w (Cpw (T_1-T_2) + h_{fg} + Cpi (T_2-T_3) \quad (1)$$

Coefficient of performance of refrigeration system defined as [9]

$$COP = \frac{\text{Refrigerating effect}}{\text{Compressor Work}} = \frac{h_1 - h_4}{h_2 - h_1} \quad (2)$$

Where, h_1 enthalpy at compressor inlet in KJ/Kg, h_2 enthalpy at compressor outlet in KJ/Kg, h_3 enthalpy at condenser outlet in KJ/Kg, h_4 enthalpy at evaporator inlet in KJ/Kg.

RESULT AND DISCUSSION

According to the experimental analysis it is found that the actual COP of the system is 1.275, which directly depends on the cooling effect, which in turn depends on the work done by the system. If the cooling effect increases by a certain value, the actual COP of the system will increase, and vice versa. If the value of the work done increases the actual COP of the system will decrease, and vice versa. The actual COP is found by the p-h diagram (R-404A chart) of condenser pressure and evaporator pressure. If the condenser pressure (high pressure) or evaporator pressure (low pressure) increases or decreases, the COP of the system will change at the same time. The brine solution in the cooling tank and the fresh water level in the tank should be equal, otherwise the heat dissipation rate of the system will be higher and it will take more time to freeze. Similarly, if the water level in the tank is below the level of the saline solution, the heat removal rate will decrease and the time required to freeze will decrease. The tonnage calculated by the compressor and the actual COP are 0.2 TR and 0.35 TR respectively. This shows that we can increase the mass production speed of the system. The speed of making ice depends on the size of the refrigerator. If the size of the cooling water tank is small, it will take less time to freeze, and vice versa.

CONCLUSION

Ice Plant test rig with R 404A environmentally friendly refrigerant has been experimentally evaluated. The selection criteria for refrigerants and compressors were formulated, and other main components were selected on this basis, namely condensers, fans and motors, cooling boxes, expansion valves, rota meters, etc. With the help of PUF, the cooling tank is completely insulated, so there is no heat loss in the system. Through this performance, we got different readings. According to these readings, the refrigerant effect is 0.6804 KW, and the actual and theoretical COPs are 1.275 and 1.4. The efficiency of an ice plant is expressed by the coefficient of performance (C.O.P).

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Table 1- Technical Specifications of Ice Plant Test Rig using Refrigerant R-404A

Components	Specifications
Compressor	Hermetically sealed reciprocating compressor, 710W
Suction pressure (P_1)	1.5 bar
Discharge pressure (P_2)	20 bar
Condenser	Air cooled condenser
Expansion device	Capillary tube type
Refrigerant	R404A
Chilling tank material with dimension	Stainless steel (High in Nickel), 23*21*14.5 (in Inches)
Insulation Material	PUF Insulation
Insulation Thickness	2 (in Inches)
Number of Ice Cans	4 Nos.
Volume of Cans	1.25 ltr.
Rota meter	0.5-5 LPM
Brine solution	NaCl and water in the proportion of 1:3
Temperature sensors	Digital type thermocouples

Table 2- Content

Description	Symbol
Condenser pressure, bar	P_1
Evaporator pressure, bar	P_2
Compressor delivery/Condenser inlet Temp., °C	T_1
Liquid leaving Condenser Temperature, °C	T_2
Evaporator inlet Temperature, °C	T_3
Compressor suction/Evaporator outlet Temp., °C	T_4
Evaporator Temperature, °C	T_5
Temperature of Fresh water, °C	T_w
Temperature of Ice, °C	T_{ice}
Motor Compressor speed	rpm

All the enthalpy values are calculated from R404A chart at corresponding pressures and temperatures.

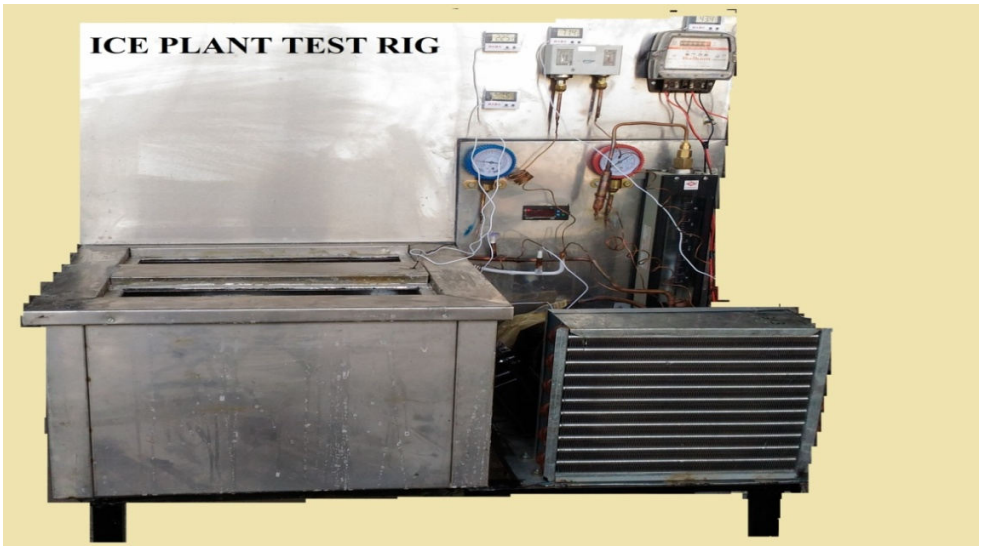

Fig. 1 Actual set up of Ice Plant Test Rig using Refrigerant R-404A

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RESEARCH ARTICLE

A Study Design to Overcome Content Uniformity Challenge by Multiple Sifting Techniques

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ABSTRACT

Tablet is made up of various excipients like Binding agents, glidants, etc. Partition coefficient, pH and UV spectroscopy are done for analysis of quality of drug. Angle of repose and Compressibility Index are some of the parameters for checking flow properties. Multiple sifting technique is performed by sifting acacia, maize starch, drug and Sodium Chloride through #100 mesh, Lactose and Magnesium stearate through #40 and #60 followed by blending for 5 minutes thrice at 10±1 RPM. For lubrication during optimization, sifted Magnesium stearate is added into the blender and lubricated for 5minutes at 10±1 RPM. The pre-formulation parameters show good flow properties and ideal quality of drug. Finished product formulations are evaluated for hardness, thickness, friability, disintegration and dissolution. F5 was considered to be better formulation with 81% of similarity factor compared to RLD product. The proposed design for the development of conventional tablets of highly potent low dose molecule extensively evaluated demonstrated to be flexible enough for improving the rate and extent of efficiency for even poorly soluble drug.

Keywords: Binding agents, glidants, Magnesium stearate.

INTRODUCTION

Oral administration is a distribution route where a product is delivered through the mouth. Per oral is sometimes used as an abbreviation for taking medication by mouth. Many drugs are taken orally because they are intended to have a systemic effect, reaching various parts of the body through the bloodstream [1]. Tablet is classified as a compressed solid dosage form which contains drugs with or without excipients. They vary in form and greatly differ

in size and weight, depending on the amount of medicinal substances and the mode of administration intended [2]. It is made up of various excipients like Binding agents, glidants, disintegrants, etc [3-5]. Various methods are available for preparation and formulation of tablets like granulation and direct compression [6]. There are various defects during formulation of tablet like chipping, lamination, cracking etc [7, 8]. To overcome these defects during formulation, new methods are developed continuously to improve quality of tablet. Freeze granulation, foam binder granulation, etc. are some of the modern formulation techniques currently in use [9,10]. MADG technology is commonly used in the granulation of active pharmaceutical ingredients which are immune to moisture, while, Fluidized bed processing is an air suspension technique that sprays binder solution onto the fluidized powder bed to obtain smaller, free flowing and homogeneous granules. It should be noted that the considerations and expectations of each manufacturing method is reproducibility and repeatability. The final product must be of proper quality and be devoid of high inter-batch and intra-batch variations [2,3].

MATERIALS AND METHODS

Preformulation Studies

Physical description / organoleptic properties

The drug and other excipients are checked for the organoleptic properties like odor and color of the raw materials to be used in the formulation.

Partition coefficient

Shake flask method was opted to determine the partition coefficient of the drug. Equal quantities of n-octanol (previously saturated with water) and Millipore water was taken in a flask & the drug was added. The equal quantity of solvents was shaken at 25°C for 24 h in an isothermal shaker. The two phases were separated carefully with separator funnel and drug content was analyzed. The experiment was carried out in triplicate.

pH determination of the drug

1 % w/v solution of the drug substance was dissolved in de-mineralized (DM) water and was evaluated for its pH by using calibrated pH meter and compared with the value given in the certificate of analysis (COA).

UV spectral analysis

The drug (5 mg) was dissolved in 500 mL methanol in a volumetric flask and the solution was scanned for the determination of λ_{max} (absorption maxima) in the spectral range of 225 nm of ultra violet visible region.

Loss on drying (LOD)

About 1 g of the drug was accurately weighed and evenly spread in an aluminum tray and placed in the LOD assembly for the determination of its water and volatile substance content under the pre-set conditions of 105ºC for 3 min and then the observed LOD was compared with standard range of LOD given in the COA (NMT 4 %).

Bulk Density

The model drug was introduced in a 100 ml graduated cylinder. Powder level was noted without compacting. Bulk density was calculated using the following equation,

Bulk density = M / V_o

Where, **M** = Mass of test sample, **V_o**= Unsettled apparent volume

Compressibility Index (Carr's Index)

The Compressibility Index and Hausner Ratio are measures of the porosity of a powder to be compressed. They measure the relative importance of interparticulate interactions. For poorer flowing materials, there are frequently greater interparticulate interactions and a greater difference between the bulk and tapped densities. These

differences are reflected in the Compressibility Index and Hausner Ratio. Compressibility Index and Hausner's Ratio was calculated using the following equation,

CI= V_0 - V_f / V_0 X 100

Where, **V_0** = Unsettled apparent volume, **V_f**= Final tapped volume.

Angle of Repose

Angle of repose of granules was determined by Fixed Funnel method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surface. The diameter the powder cone was measured and angle of repose was calculated using the following equation.

= Tan^{-}(h/r)

Where, h- Height of pile, r- Radius of the base of pile,θ- Angle of repose.

PROCEDURE

Humidity and temperature of area must be within the limit. Once the environmental conditions are favourable, the excipients must be weighed accurately using weighing balance (Sartorius model) after adjusting the bubble and formulated under monochromatic light. The equipments such as spatulas must be cleaned and dried prior to weighing.

Sifting process is done for acacia, maize starch, drug and Sodium Chloride through #100 mesh size. Lactose and Magnesium stearate are sifted through #40 and #60 meshes respectively. Co-sifted ingredients are mixed together in a homogenous manner. When Acacia and maize starch separately added and passed through sieve size #100 each time. This resultant mixture is loaded onto a blender. Divide sifted Lactose into three parts. Lactose is added in 3 parts with the preloaded mix in the blender and blended for 5 minutes thrice at 10±1 RPM. It should be noted that Samples were taken at 5 minutes interval to confirm the uniformity of content to optimize the process. The optimization of blending time is as given below:

For lubrication during optimization, sifted Magnesium stearate is added into the blender and lubricated for 5minutes at 10±1 RPM. It must be noted that samples were taken at 1 minute and 3 minutes to confirm the effect of lubrication to optimize the process. Prepared blend was processed for compression using 5.5 mm standard round punches and dies in 16 stations tablet compression. Each tablet was punched with the total a weight of 80 mg. Compression force and compression speed are performed as designed in the table below.

Evaluation studies for finished product

Hardness: The hardness of 20 tablets was determined using digital hardness tester (Electrolab) and the average hardness was calculated and expressed in N or kg/cm2.

Thickness: Vernier caliper (Mitutoyo) was used to determine tablet thickness. Average thickness was calculated by measuring thickness of 10 tablets.

Friability: The tablets of weight 6.5 g was taken and placed in Roche type friabilator (Electrolab). The machine submits the tablets to the combined influence of shock and abrasion by using a plastic chamber that spins at 25 rpm, where the tablets are dropped from a height of 6 inches for 100 revolutions. After 100 revolutions, the pre-weighed tablet sample was removed, dusted and reweighed. Percentage of friability should be not more than 1.0%.

Disintegration: The disintegration test was performed out on six tablets using disintegration test apparatus in DM water maintained at 37°C in 900 ml. The device is allowed to travel up and down at a frequency of 28 to 32 cycles per

minute, over a distance of 5 to 6 cm. At their upward movement, the tablet stays 2.5 cm below the liquid surface and not less than 2.5 cm from the beaker's bottom in their downward movement. The disintegration time of each tablet was recorded.

Assay: The sample is analyzed by injecting 20 µL of mobile phase as blank, standard solution and sample solution. The area of principal peak is recorded.

Content uniformity: (By HPLC) Content uniformity is evaluated by applying HPLC using 0.05 M sodium hydroxide solution. The concentration of standard & sample solution is set to be 4µg/mL for all 10 tablets.

Dissolution studies: Dissolution studies are carried by using Dissolution apparatus-II (Reciprocating Cylinder) for 60 minutes and drug content is checked at specific intervals using HPLC.

RESULTS AND DISCUSSION

Pre-formulation studies

Physical characterization and Drug Identification: The colour, odour, nature and taste of the API were evaluated and it was observed as specified in the monograph. Based on the observation, it was found satisfactory for the formulation of intended tablet dosage form and no discomfort likely to arise in patient compliance.

Partition Coefficient: The partition coefficient of the drug at 25°C for 24 h was found to be 1.0 for the drug, reported value: 1.04.Thus the drug is practically insoluble in water and it is well distributed in Octanol. Hypothetically, it is assumed it has higher permeability in GI tract.

pH determination of Drug: The pH of the given drug was found to be in the range of 7.1-7.6.

UV spectral analysis: The UV-spectrum of API using methanol as solvent is shown in Fig. The obtained spectrum was compared with standard API (225 nm) and confirmed that the drug shows maximum absorbance at 225 nm and was in good agreement with working standard.

Loss on Drying (LOD): The LOD was found to be 1.2% and found in line with standard range of LOD given in the COA (NMT 4 %). This infers that it has good stability in environmental conditions.

Bulk Density: Bulk Density of the formulation is determined as per instructions. The mean bulk density of the formulation is determined to be 0.431 g/ml.

Compressibility Index (Carr's index): The formulation is determined for Carr's Index as per instructions. The mean Compressibility index of the formulation is determined to be 12.85.

Angle of repose: As per instructions, the formulation is determined for Angle of Repose. The mean bulk density of the formulation is determined to be 33.1^0. This infers that the formulation has good flow property.

Evaluation of Finished Product

Hardness: The Hardness of the tablet was evaluated and is calculated to be 24 N. This shows optimal hardness property.

It is reported that F4 has the maximum hardness and F1 has the least hardness, when compared to other formulation batches and control.

Thickness: The thickness of the 5 batches is calculated and reported effectively. It is observed that F3 has the minimum thickness, while, F4 has the maximum thickness.

Friability: The formulations are checked for the friability and reported. The friability for 6 formulations including control is presented as follows:
Out of the given data, no formulation batch is near the control batch, which means that the formulation batches prepared by the multiple sifting techniques is more stable in comparison to the control batch. Out of the formulation batches, F4 is the least friable batch and is the more physically stable out of all formulation batches.

Disintegration: The formulation took 150 seconds to completely disintegrate with no palpable firm core. The disintegration time of the optimized formulation is slightly lesser than the reference product.

Assay: API was analyzed using ortho phosphoric acid in 300:700 v/v of Acetonitrile and Water as mobile phase with the help of Cosmosil CN 250mm x 4.6 mm, 5µm or Equivalent. Sharp and identical peaks of was observed at 13min at 225 nm with the flow rate of 1.0 mL/min detected by UV Visible detector.
The assay of 6 different formulation batches including control batch is as follows:
The assay shows drug content of nearly 101% for F5 which is the highest assay value excluding control batch, which is optimal by being within the range of 90.0 – 110.0%.

Content Uniformity: The content uniformity of the tablet formulations are checked by applying HPLC technique. It is observed that the content uniformity is 13%, which is lesser than 15%. Meanwhile, the formulation batch F1 shows maximum content uniformity, Reference Listed Drug formulation shows the minimum content uniformity.

Dissolution studies: From the dissolution profile, it was found that all the formulation pass the dissolution study and exhibits the dissolution limit NLT 70% (Q) at 30 mins. Challenge studies for formulation with variation in maize starch and magnesium stearate against dissolution are performed. The drug dissolution after 45 minutes is highest in F5 in case of prepared formulations excluding Control batch (96%). The dissolution profile for the study formulations F1-F5 exhibits release percentage of falling within the limits at 30 min. Thus, based on the similarity factor for the formulations F1-F5 in comparison to RLD it was observed that formulations F1, F2, F3 & F4 exhibited a comparable amount of percentage release difference from the RLD value, whereas F5 formulation showed a much closer release profile value. Therefore F5 was considered to be better formulation with 81% of similarity factor compared to RLD product.

Determination of Short-Term Stability Studies

The stability studies were performed for one month and the samples were analyzed to determine any change in physical and chemical properties of the drug. From the study, it is no significant changes were observed and found that all the parameters are within the limit and are stable.

CONCLUSION

Optimization always helps in improving the quality of the pharmaceutical product. Process optimization can help in incorporating the quality during the preparation phase, thereby facilitating Quality by Design (QbD). In this, optimization of process is performed by utilizing multiple sifiting techniques. Formulation of tablets using multiple sifting technique shows better performance and stability in comparison with Reference Listed Drug (RLD). So, we can confirm that this technique does not deteriorate (or) reduce the quality of final product. Overall, the proposed design for the development of conventional tablets of highly potent low dose molecule extensively evaluated demonstrated to be flexible enough for improving the rate and extent of efficiency for even poorly soluble drug.

Additionally, a cost-effective quality product can be delivered to the patients, which is equivalent to the reference standard.

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S.No	Factors	Unit	Levels		
			-5	0	+5
1	Blending/Mixing Time	Min	5	10	15
Responses		**Goal**	**Acceptable ranges**		
Y1	Blend Assay	Maximize	100% of label claim		
Y2	Blend uniformity	Maximize	AV NMT 15%		

S.NO.	COMPRESSION CHALLENGE	HIGH	OPTIMUM	LOW
1	Hardness	30-40N	20-30	10-20
2	RPM	15	12	10

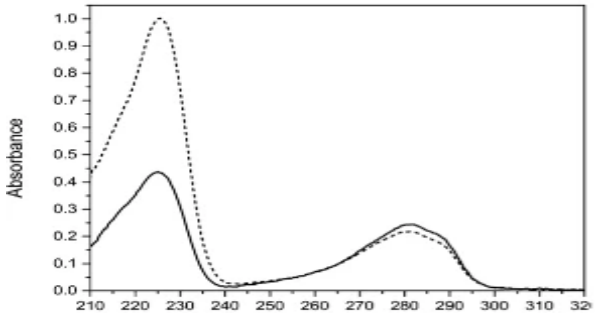

Figure-1: Ultra Violet Spectrum of drug (API)

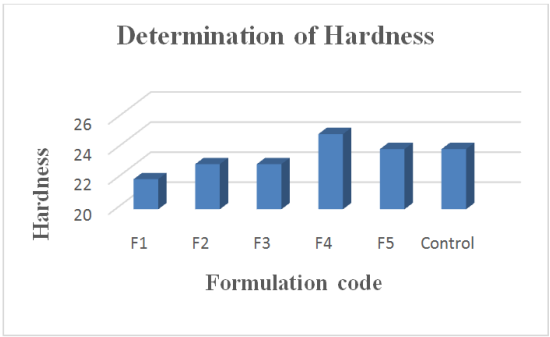

Figure-2: Graphical Representation of Hardness values of various formulation batches

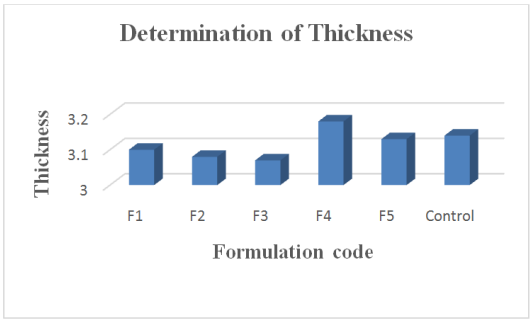

Figure-3: Graphical Representation of Thickness values of various formulation batches

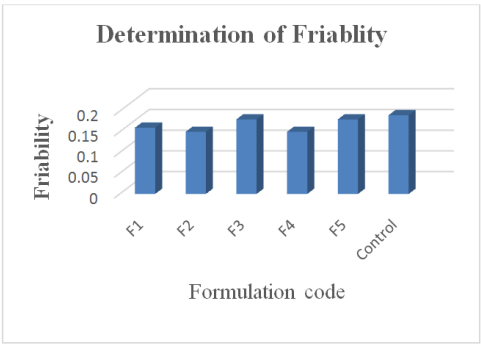

Figure-4: Graphical Representation of Friablility values of various formulation batches

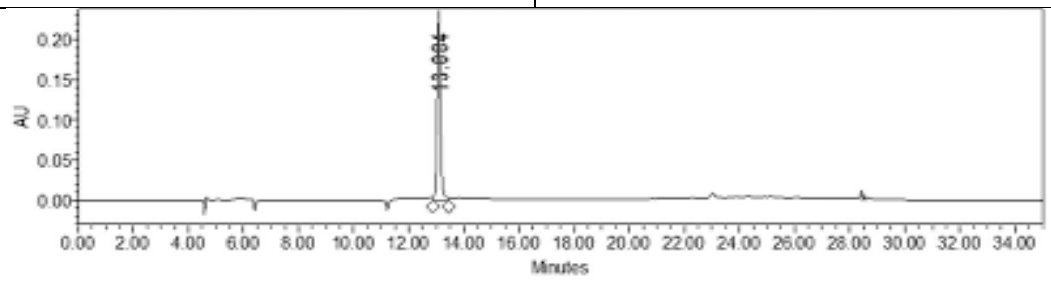

Figure-5: HPLC Chromatogram

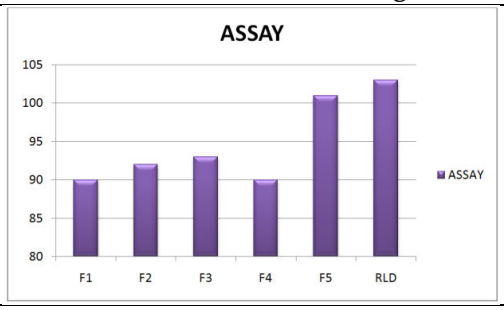

Figure-6: Assay values of various formulation batches

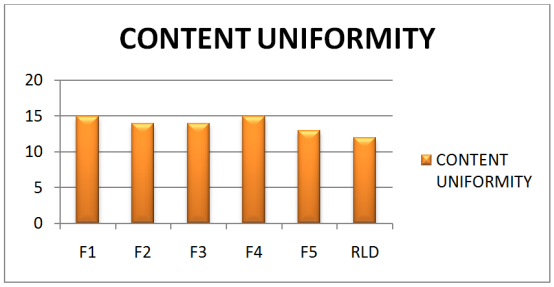

Figure-7: Content Uniformity of various formulation batches

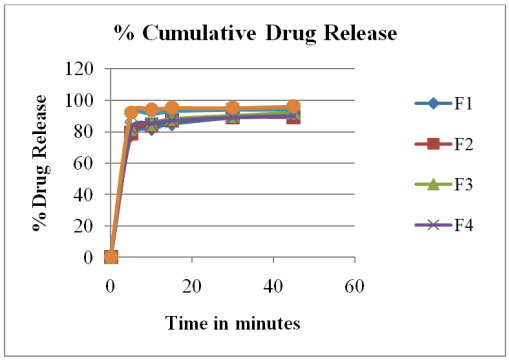

Figure-8: Result of dissolution studies of various formulation batches

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RESEARCH ARTICLE

Ethno Botanical Importance of Some Highly Medicinal Plants used by Indigenous Communities in Dang Region District of Dholpur, Rajasthan

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ABSTRACT

The present paper deals with an account of some highly medicinal plants with their name, family, plant parts which is used by indigenous communities to cure various aliments and ethnomedicinal uses in Dang Region District of Dholpur, Rajasthan. Dholpur is one of the tribal district of rajasthan. There are many tribal communities like Meena, Gurjar, Kanjar, Sahariya, Damor, Dhanka, Garasia, and Bhil which live in Dang area. Ethnomedicinal survey had been carried out in the Dholpur district from 2019 to 2020. Information collected has been obtained by personal contact during field trips with local communities.

Keywords: Ethnomedicinal; Aliments; Tribals; Indigenous; Communities.

INTRODUCTION

From time immemorial people have been using herbal medicines in India. The knowledge of these medicines, is being lost as traditional culture collapse and shifting of rural youngmen to urban areas. Thus there is an urgent need of conservation of this knowledge. Tribals residing in harmony with the vegetation around, know herbal remedy almost for every aliment. These folk medicines through not 100% effective strongly, they definitely help in relieving pains. Herbal medicines are in great demand in both developed and developing countries in primary healthcare because of their great efficiency and no side effects. The introduction of ethnobotany by Faulks (1958) wrote first on direct relationship between plants and human being new subject entitled "Introduction to ethnobotany". Ethno medicinal plants continue to play a central role in the healthcare system of large proportions of the world populations this is particularly true in developing countries where herbal medicine has a long and uninterrupted history of use. Continuous uses of herbal medicine by a large proportion of the population in the developing countries is largely due to high cost of Western pharmaceutical and healthcare. In addition, herbal medicines are more acceptable in these countries from their cultural and spiritual points of view. The tribals and rural population

of India are highly dependent on medicine plant therapy. Dang region is one of the most resource deprived, and arid region of Rajasthan state marked with degraded ravines, barren land and severe water shortage. All these factors together have created challenges for the community to even engage with basic livelihood activities such as agriculture and livestock rearing. Low farm yield and poor livestock productivity leads to pervasive poverty. Most farmers in the Dang region struggle hard even to fight hunger. Left with no alternative, many migrate as a wage labour and many work on daily wages in the stone mines. The main occupation of tribals in this dang regionis agriculture lands. Animal husbandry second largest occupation of tribals because of agriculture resources. Cows, Buffalos, Goats, sheeps, camels and Dogs are forms in domestic animals in this region. The tribal people mostly depend on forest and forest products for their needs and have sufficient knowledges about herbal medicines. Plants used and applied by tribals for treating their various types aliments. Dholpur is a city in the eastern most parts of the Rajasthan state of India. It is situated on the left bank of the famous Chambal river. Dholpur districr is among the largest dang region district in the state of Rajasthan. The geographical coordinates for Dholpur (Dholpur) are 26° 42' 0" North, 77° 54' 0" East. Total area of Dholpur district is 3,034 sq. kms. It is centrally situated in the eastern region in the state. It is bounded by Madhya Pradesh and Uttar Pradesh in the north. karauli district in the west.

MATERIALS AND METHODS

1. Discussion with villagers of tribal communities about different aspects.
2. Interviewing with 'Vaid ji' to know about ethno medicine.
3. Enquiry from oldmen about the ethno-medicines.
4. Interviewing with district forest officers at Dholpur.

Ethnomedicinal data was collected along with various in different manners by enquiry, observations, Interview, approach like through available literatute, library, herbaria on one hand and though Vadhyas, Hakims, Ojha and Homeopaths, Veterinary doctors.
Following villages of Dholpur (Raj) were visited for the ethnobotany medicinal plants studies. These are Basai dang, Leelauti, Rahrai, Pipron, Pattipura, Moroli dang, Kanchanpura, Nagla mau, Nadanpur, Noorpur, Mathara, Indora, Hingota, Gurha, Banora, Arjun pura, Bari and Baseri.

Climate Condition

The climate of Dholpur district is semi-arid and monsoonal with characterized by hot and dry summer. Dholpur recorded highest temperature at 50 °C on June 3, 1995. The hottest months are May and June, which mark the oppressive summer season. Temperatures in summers are normally higher than 40 °C. Coldest months are December and January where temperatures sometimes reach near-zero and subzero levels.

RESULTS

These selected 27 plants were found to be very important for ethnomedicinal purposes. Fresh plants parts were collected from the tribal village in Dholpur (Rajasthan). The ethno -botanical data (local name, mode of preparation and medicinal uses) were collected through questionnaire interviews and discussions among the tribal practitioner in their local language.

CONCLUSION

The present study reveals that the plant resources of Dholpur district are quite rich for using raw material needed for establishing and developing plants based small skill medicinal industries. Plants of medicinal value need to be investigated for pharmacological activity on the basis ethnotherapeutics being practiced by ethnic groups for their

safe use after having clinical trials. This will be certainly are very much helpful in evolving new sources of herbal drugs for pharmaceuticals industries. Search and efforts will provide employment in the area for economic upliftment.

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S. No.	Local Name	Botanical Name	Family	Aliment	Parts &Method of treatment
1.	Satyanasi	*Argimone Mexicana*	Papaveraceae	Protrusion	100 gm. roots of displant taken and mix with cow milk and prepare the paste and given orally for three days
2.	Babool	*Acacia nilotica (L) del. Subsp. Indica (Benth.)*	Mimosaceae	Immunization Inflammation Galactagouge	Seeds and fresh fruits pounded and given orally with water for seven days. Fresh unripe fruits given orally with grass for three days. Crushed leaves given orally with fruits of Acacia nilotica daily for a week.
3.	Oonga	*Achyranthus aspera L.*	Amaranthaceae	Cramps	Oonga in equal quantity, powdered and given to cattle in hot water twice or thrice in day.
4.	Adsuta/ Basouda	*Adhatoda vasiaca*	Acaanthaceae	Cough and Cold	Juice of leaves or hot water extract given orally (as expectorant) twice a day for three day
5.	Sitaphal	*Annona Squamosa L.*	Annanoceae	Wounds Insect bite	Paste of fresh leaves tied extremely for 3 days. Paste of fresh leaves tied externally for 3 days.
6.	Satavari	*Asparagus racemosus*	Liliaceae	Galactagogue / Lactation	The dried root and fruits or all plant with jiggery given orally as a fodder
7.	Hingota	*Balanites aegyptiaca L*	Balanitaceae	Haemorrhages	Crushed roots are soaked in water over night and given orally in next morning in

					fasting.
8.	Safed Aak	*calotropis gigentia L.*	Asclepiadaceae	Swelling	Heated leaves are applied locally three time a day for three days.
9.	Amaltas	*Cassia fistula*	Caesalpiniaceae	Diarrhoea	Stem bark crushed and soaked overnight given orally in next morning for 3 days.
10.	Panwar	*Cassia tora*	Caesalpiniaceae	Galactagogues	Crushed seeds are soaked overnight given orally in the next morning for 15 days.
11.	Bijoura Neebu	*Citrus maxima L*	Rutaceae	Emetic Abdomenal pain	Fruits given orally for emetic when ingestion of iron objects by the cattle. Powder of fruits mixed with black salt or common salt.
12.	Kana gokna	*Commelina benghalensis*	Commelinaceae	Eye problems	Leaf extract drop used three time in a day
13.	Kali Musali	*Curculigo orchioides*	Hypoxidaceae	Eye problems	Tuber juice dropped in open eye 2-3 time in day.
14.	Dhatura Datura	*Dhatura stramonium*	Solanaceae	Diarrhoea Lack of estrus	Fruits given orally for three days. Warmed fruits and seed powder given orally for three day
15.	Bhringraj /Bhangara	*Eclipta prostrate L.*	Asteraceae	Swelling	Paste of fresh leaves used locally twice a day
16.	Dandathore	*Euphorbia nerifolia L.*	Euphorbiaceae	Mastication problem	Paste of aerial parts given orally to the cattle's when they stop mastication.
17.	Ratan Jot	*Jotropha gossypifolia L.*	Euphorbiaceae	Injury	Locally applied the paste of roots.
18.	Mahndi	*Lawsonia inermis L.*	Lythraceae	Pain	Leaves crushed and make the paste apply locally for three days.
19.	Gheeya Torai	*Luffa cylindrical L.*	Cucurbitaceae	Dyspepsia	Smoke inhaled of the fibrous dry mesocarp of the fruits of the fruits.
20.	Neem	*Azardirecta indica*	Meliaceae	Loss of appetite Expulsion of worms	Leaves extract given orally twice a days. Fresh leaves & barks taken in equal quantity and prepare decoction and given to calf for expulsion of worm.
21.	Sahajana	*Moringa oleifera L.*	Moriginaceae	Rhumatism	Bark crushed and soaked in water over night next morning given orally
22.	Kaunch / Kounch Phali	*Mucuna Pruriens L.*	Fabaceae	Vermifuge	Pod's hairs given orally as a single dose.

23.	Har Singar	*Nytanthes arbor – Tristis L.*	Nyctanthceae	Vermifuge	Fresh leaves given orally in the morning.
24.	Arand	*Riccinus cummunis L.*	Euphorbiaceae	Vermifuge	Fresh leaves given orally for a weeks
25.	Kharanti	*Sida ovata*	Malvaceae	Rhematism	Stem bark crushed and soaked in water over night and given orally next morning.
26.	Brihati / Badi Kateri	*Salanum surrattanse*	Solanaceae	Rhematism	Fresh leaves given orally for three days
27.	Guduchi	*Tinospora cordifolia*	Menispermaceae	Blood purification Loss of appetite	Stem bark crushed and soaked in water over night and given orally next morning. Stem powder given orally daily in diet

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RESEARCH ARTICLE

Bluetooth Based Home Automation with Variable Controls using Power Electronics Device

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ABSTRACT

Innovation is a ceaseless cycle. To have the option to plan an item utilizing the current innovation that will be useful to the existences of others is a gigantic commitment to the local area. This paper presents the plan and execution of a minimal expense however yet adaptable and secure phone based home mechanization framework. The plan depends on a PIC and BT board and the home machines are associated with the info/yield ports of this board through transfers. The correspondence between the cell and the PIC Controller is remote. This framework is intended to be minimal expense and adaptable permitting assortment of gadgets to be controlled with least changes to its center. Variable control is likewise utilized by carrying out power gadgets in this undertaking.

Keywords: Bluetooth Wireless Technology, Smartphones, Home Automation System

INTRODUCTION

Remote innovations are getting more famous all throughout the planet and the purchasers like this remote way of life which gives them remember of the notable "link tumult" that will in general develop under their work area. Presently with the installed Bluetooth innovation, advanced gadgets structure an organization where the apparatuses and gadgets can speak with one another. Today, home robotization is one of the critical uses of Bluetooth advancement. Working over unlicensed, all around the world accessible recurrence of 2.4GHz, it can interface computerized gadgets inside a scope of 10m to 100m at the speed of up to 3Mbps contingent upon the Bluetooth gadget class. With this ability of Bluetooth; we propose a home robotization framework dependent on Bluetooth innovation. There are not many issues included when planning a home robotization framework. The framework ought to be adaptable so new gadgets can without much of a stretch be coordinated into it. It ought to

give an easy to use interface on the host side, with the goal that the gadgets can be effectively arrangement, checked and controlled. This interface ought to likewise offer some analytic types of assistance so that if there is any issue with the framework, it very well may be found. In addition the general framework ought to be adequately quick to understand the genuine force of remote innovation. At last the venture ought to be financially savvy to legitimize its application in home mechanization. In this undertaking we present a minimal expense secure cell based, adaptable home computerization framework. Apparatuses at home are associated with the PIC and BT board. The correspondence between the cell and the PIC is remote. Extra gadgets can be associated into the framework with little alterations. Figure 1 shows the outline of the generally speaking project's design.

METHODOLOGY

This framework just tells the best way to take care of home computerization issues at programming level and no equipment perspectives were thought of. It introduced a phone and PIC based controller framework where pin-check calculation has additionally been presented. Likewise to controller of home machines like stove, forced air system and PC by phones which offer simple use has been explored. With the progression of remote advancements such a WIFI and CLOUD network is the new past remote framework are utilized regular and all over the place. A few gadgets are left connected to control attachment though others should be connected to and yield of force attachment at various spans relying upon the time. This requires and individual to physically go to every one of the gadgets autonomously from an opportunity to time. All such checking and control should be possible without fundamentally being near or internal parts the home gadgets.

Working principle

The framework turns on by introducing the Android application in mobiles that work by android working framework. The android portable at that point sends orders through Bluetooth at whatever point it can't work in versatile. The Android application provides orders to run the fan (ON/OFF) from significant distances. This application sends the orders to the beneficiary Bluetooth gadget, the Bluetooth collector attempts to pass orders to the microcontroller, the microcontroller sends activities to run the TRIAC that gets the signs and send the PWM to the TRIAC to run ON the fan. Also, it has a temperature sensor which attempts to identify the temperature inside the room so as the temperature is expanding, the speed of fan naturally is expanding as well. Likewise, the LCD screen is associated with microcontroller that shows the temperature and fan speed.

Components Used

The various components which are used in automation systems are as shown in figure

REGULATOR IC 7805: Voltage controllers are normal in electronic circuits. They give a consistent yield voltage to a fluctuated input voltage. For our situation the 7805 IC is a famous controller IC that discovers its application in the greater part of the tasks. The name 7805 suggests two meaning, "78" infers that it is a positive voltage regulator and "05" infers that it gives 5V as yield. So our 7805 will give a +5V yield voltage. The yield current of this IC can go up to 1.5A. However, the IC experiences weighty warmth misfortune thus a Heat sink is suggested for projects that devour more current. For instance in the event that the information voltage is 12V and you are devouring 1A, (12-5) * 1 = 7W. This 7 Watts will be scattered as warmth.

DRIVER IC ULN2003: ULN2003 IC is quite possibly the most generally utilized Motor driver IC. This IC proves to be useful when we need to drive high ebb and flow loads utilizing computerized rationale circuits like Op-maps, Timers, Gates, DRIVERS, PIC, ARM and so on For instance a RELAY that requires 12V and 300mA to run can't be fueled by a PIC I/O henceforth we utilize this IC to source sufficient current and voltage for the heap. This IC is consistently used to drive Relay modules, Motors, high current LEDs and even Stepper Motors. The ULN2003 is a 16-pin IC. It has seven Darlington Pairs inside, where each can drive accumulates to 50V and 500mA. For these seven

Darlington Pairs we have seven Input and Output Pins. Adding to that we can a ground and Common pin. The ground pin, as regular is grounded and the use of Common pin is discretionary.

PIC16F886 – 8 Bit Microcontroller: PIC16F886 is microcontroller from 'PIC16F' family and is made by MICROCHIP TECHNOLOGY. It is a 8-Bit CMOS Microcontroller with Nano-Watt Technology. This microcontroller is famous among specialists and designers due its highlights and cost. PIC16F886 is a microcontroller useful for testing and creating applications since it has high blaze memory modify cycle. Additionally there are a great deal of instructional exercises and backing accessible on the web. The regulator has 16KBytes streak memory which is sufficient for some applications. Alongside 24 programmable Input/yield pins which are created to deal with 20mA current (direct LED driving ability) the framework can interface numerous peripherals without any problem. With Watchdog clock to reset under mistake naturally the regulator can be utilized to create utilizations of perpetual establishment.

LIQUID CRYSTAL DISPLAY (LCD): LCD modules are ordinarily utilized in most installed projects, the explanation being its modest value, accessibility and software engineer agreeable. A large portion of us would have gone over these showcases in our everyday life, either at PCO's or mini-computers. It is named as 16×2 LCD since it has 16 Columns and 2 Rows. There are a great deal of mixes accessible like, 8×1, 8×2, 10×2, 16×1, and so forth however the most utilized one is the 16×2 LCD. In this way, it will have (16×2=32) 32 characters altogether and each character will be made of 5×8 Pixel Dots

RELAY: Transfers are most normally utilized exchanging gadget in hardware. There are two significant boundaries of hand-off, first is the Trigger Voltage, this is the voltage needed to turn on the transfer that is to change the contact from Common → NC to Common → NO. The other boundary is your Load Voltage and Current, this is the measure of voltage or current that the NC, NO or Common terminal of the hand-off could withstand, for our situation for DC it is limit of 30V and 10A.

TRANSFORMER (CENTER TAPPED): A middle tapped transformer otherwise called two stage three wire transformer is typically utilized for rectifier circuits. At the point when an advanced task needs to work with AC mains a Transformer is utilized to venture down the voltage (for our situation, to 24V or 12V) and afterward convert it to DC by utilizing a rectifier circuit. In a middle tapped transformer the pinnacle converse voltage is twice as in connect rectifier henceforth this transformer is generally utilized in full wave rectifier circuits**.**

LM35 Temperature Sensor: LM35 is a precession Integrated circuit Temperature sensor, whose output voltage varies, based on the temperature around it. It is a small and cheap IC which can be used to measure temperature anywhere between -55°C to 150°C. It can easily be interfaced with any Microcontroller that has ADC function or any development platform like PIC.

FINGER PRINT READER: This is a fingerprint sensor module with a TTL UART interface for direct connections to microcontroller UART or to PC through MAX232 / USB-Serial adapter. The user can store the fingerprint data in the module and can configure it in 1:1 or 1: N mode for identifying the person.

Circuit Diagram: In the above circuit a PIC microcontroller is utilized, which deals with 5vdc as it were. In Power supply a Step-down focus tapped transformer is utilized, which changes a 220vAC over to 12vAC. As the entirety of the parts like PIC, LCD, Relay, CT are chips away at DC, thus D1 and D2 structures a rectifier which changes over a 12v AC in 12v dc with swell free yield with the assistance of channel capacitor C4. A controller IC 7805 is utilized to change over 12vdc further into a 5vdc. Capacitor C5 is utilized to store 5vdc, which will be utilized if unreasonable prerequisite of 5v. At first PIC microcontroller expects reset to flush its RAM area. A POWER-ON reset is framed utilizing capacitor C6 and opposition R1. In the above circuit, PIC estimates temperature and level of water. As PIC

can just gauge voltage somewhere in the range of 0 and 5v with the assistance of inner ADC (Analog to Digital Converter), thus a temperature sensor LM35 and attractive level sensor is utilized.

Different transfers are use is to work following tasks.
Gadget 1 and Device 2 ON/OFF relay.
Siphon ON/OFF transfer
Fan ON/OFF transfer.

All the hand-off utilized in our venture is of 12v and choice to ON/OFF the transfer is control by PIC. While PIC works on 5V and it gives greatest 5v, 20mA current sourcing in its yield port. The yield sourcing voltage of PIC isn't able to drive the 12v transfer which devours around 40 mA, subsequently a Driver IC ULN2003 is utilized. ULN2003 driver IC believers a 5v sign coming from PIC to 12v. This 12v is utilized to drive the transfers. In our task a variable fan speed controlling is likewise finished with the assistance of Power electronic gadgets like TRIAC. In the above circuit the primary point is to control the voltage across fan. At first regulator check the approaching voltage coming from line with the assistance of ADC (simple to advanced converter) present inside the Microcontroller. Our point is to control a +ve just as – ve half pattern of approaching AC for that a Firing point control technique is utilized. For controlling a terminating point of any AC voltage it is important to screen each +ve/ - ve half cycles, henceforth a Sine Wave Cycle Monitor(Zero Crossing Detector) block is utilized in our undertaking, which advises a regulator about start point regarding each cycle. When regulator knows the temperature and signs from sine wave cycle (zcd) screen, regulator compute the terminating point and gives terminating heartbeat to the AC to AC converter in which a static switch framed by a SCR/TRIAC is utilized.

Applications

- This undertaking can be utilized in home Industries, Office, Shops.
- We can handle machines from a specific spot by far off and furthermore screen the wellbeing
- By utilizing a home robotization framework, we can save a ton of time to work home machines from anyplace (without sitting around idly to move from office to home for simply opening entryway for relatives to enter the home).
- Home mechanization framework with computerized entryway locking and surveillance cameras works with greater security.
- People living with actual impediment may depend on the highlights of a home mechanization framework to achieve their undertakings.
- The most basic utilizations of home robotization are lighting control, HVAC, open air grass water system, kitchen apparatuses, and security frameworks.

CONCLUSION

This task proposes a minimal expense, secure, universally available, auto-configurable, distantly controlled arrangement. The methodology talked about in the paper is novel and has accomplished the objective to control home apparatuses distantly utilizing the Bluetooth innovation to interfaces framework parts, fulfilling client needs and necessities. BT innovation skilled arrangement has end up being controlled distantly, give home security and is savvy when contrasted with the already existing frameworks. Thus we can infer that the necessary objectives and goals of home robotization framework have been accomplished. The framework plan and engineering were examined, and model presents the fundamental degree of home machine control and far off checking has been executed. At long last, the proposed framework is better from the versatility and adaptability perspective than the industrially accessible home computerization frameworks.

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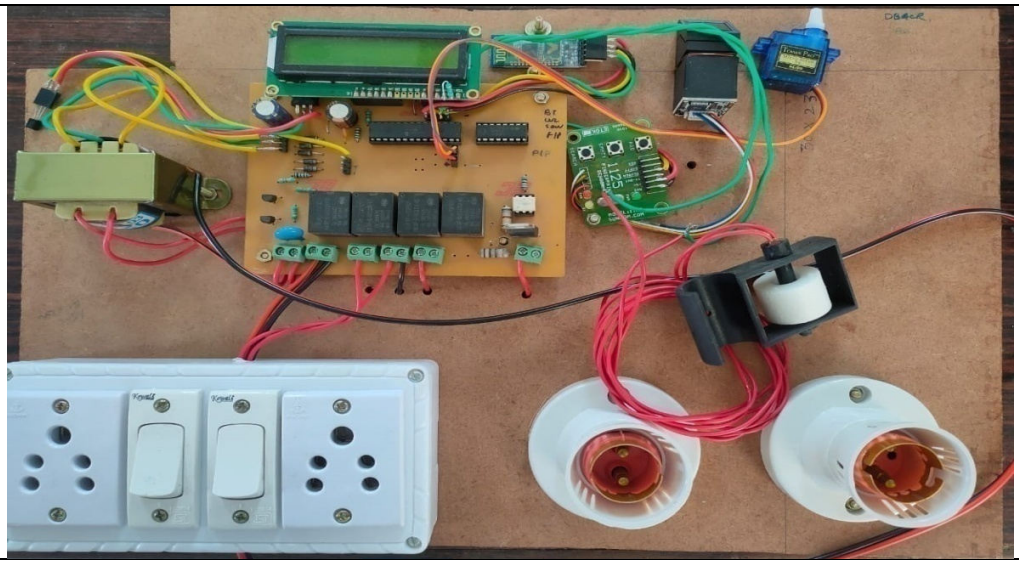

Fig. 1. Basic home automation system

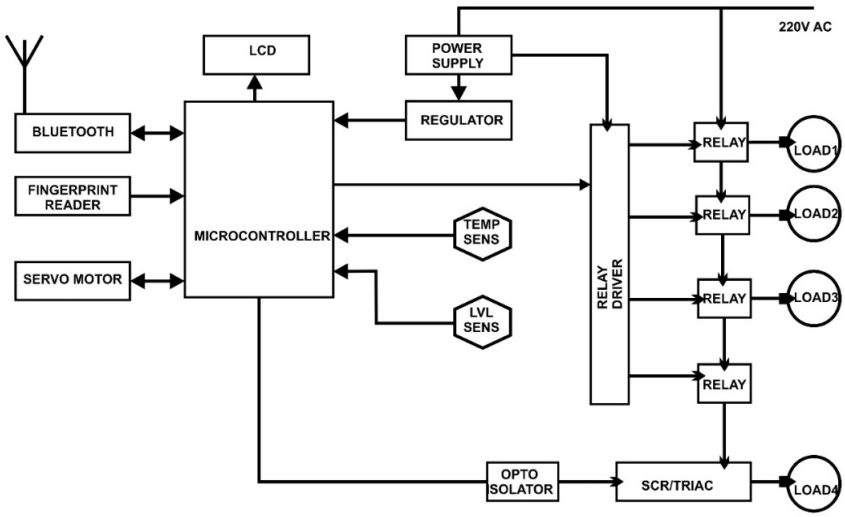

Fig.2 block diagram of automation systems

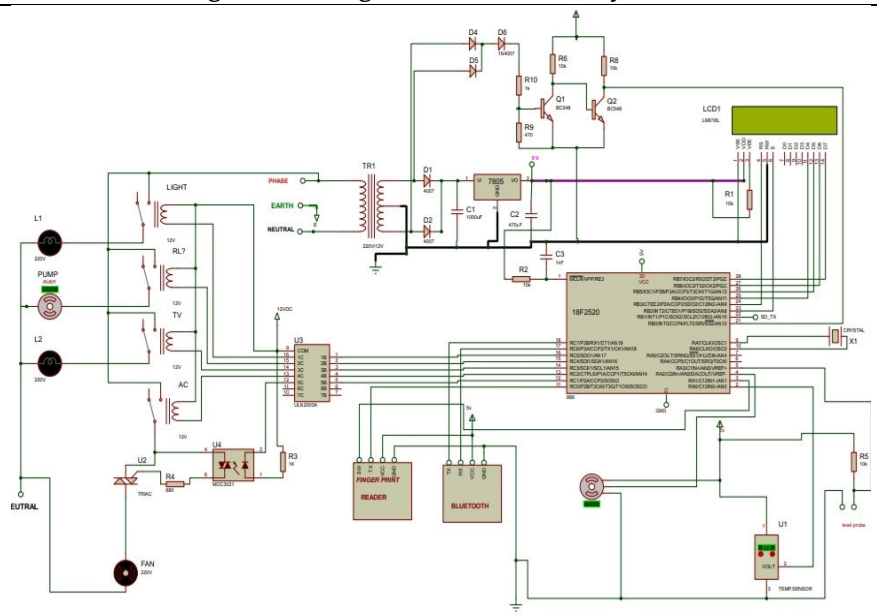

Fig.3. Circuit Diagram

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RESEARCH ARTICLE

Effect of Inspiratory Muscle Training to Improve Pulmonary Status in Asthma Patients

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ABSTRACT

The study is to find the effect of Inspiratory muscle training to improve peak expiratory flow rate and exercise tolerance (pulmonary status) in asthma patients. 20 asthma patients between 40-55 years of age were selected randomly using simple random sampling method. The pretest measurement of peak expiratory flow rate and exercise tolerance was measured using the peak flow meter and six minute walk test for all the subjects. After the pretest assessment the subjects received Inspiratory muscle training for a period of 8 weeks and on the end of 8th week posttest measurement of peak expiratory flow rate and exercise tolerance was done using the peak flow meter and six minute walk test for the group in a similar fashion as that of pretest measurement. The results of the study concluded that Inspiratory muscle training improved peak expiratory flow rate and exercise tolerance in asthma patients.

Keywords: Asthma, Inspiratory muscle training, Peak expiratory flow rate, Exercise tolerance test.

INTRODUCTION

Asthma is an important health and socioeconomic issue occurring all over the world, which is been affecting more than 300 million lives of human being. This disease is considered as an inflammatory disease in the airway, thus resulting in increased airway responsiveness, obstruction, mucus hyper-production and involvement in the airway wall repairing. Asthma has been interchangeably called as bronchial asthma (BA) as the anatomical involvement specifies. The management of Bronchial asthma had always been a challenge to the physicians and the physiotherapist as it involves an extensive pathological dysfunction.

There has always been dilemma in the classification of bronchial asthma in obstructive lung diseases and restrictive lung disease. People claim that bronchial asthma is a combination of both as there is reduced patency of the airways along with restriction in chest wall expansion when it manifests chronic asthma. As it is associated with allergies, it's very common among developing countries with poor ecological conditions and pollution. For this India is a no exception. There are many types of asthma like Adult-Onset Asthma, Allergic Asthma, Asthma-COPD overlap, Exercise Induced Bronchoconstriction (EIB), Nonallergic Asthma, Occupational Asthma .Asthma is identified by the movement of airways , thus resulting in the reversible airflow obstruction associated with the increased airway responsiveness (AHR) and airway swelling (1). The disease is affecting greater than three hundred million individuals all over the world, with around two lakhs fifty thousand yearly deaths (2). In the last twenty years , the corticosteroid [inhalers] has become the great therapy agent for asthma, the death rate of asthma has decreased (3). Meantime , allergic diseases, such as asthma, have increased in the past fifty years associated with urbanization (4). Childrens have the greater ratio of asthma when compared with other generation groups (5). Then, it is expected that the number of the cases will get increased by more than hundred million by 2025 (6). Basically , most of the asthma disease gets initiated from childhood in relation with sensitization to usual inhaled allergens, those are house dust mites, cockroaches, animal dander, fungi, and the pollens. These inhaled allergens encourages T helper type 2 (Th2) cell multiplications , later the Th2 cytokines, interleukin (IL)-4, IL-5 and IL-13 gets created and release. Many basics and clinical education suggests that the airway swelling was a main key to the disease pathophysiology.

The continuation of the chronic airway swelling in asthma has been accepted over a century.(7). The Symptoms of asthma involves repeated episodes of wheeze, cough, breathlessness and chest tightness, altogether with the episodes of marked worsening of the symptoms, that is known as exacerbations (7) . The swelling is induced by the releasing of potent chemical mediators from the inflammatory cells. Resulted of chronic airway swelling , airway repairing , featured by thickening of all the compartments of the airway walls, is appeared and this might have intense consequences on the mechanics of airway constriction in asthma and contributes to the chronicity and development of the disease. As the allergic sensitization, the allergen could be taken up by the dendritic cells (DCs), which processes the antigenic molecules and then presents them to simple T helper cells. So the activation of the allergen specific Th2 cells is happened , the cells plays an vital role in the development of the asthma. Allergic diseases are created by improper immunological responses to the allergens without any pathogenesis operated by the Th2-mediated immune response. The hygiene theory had been used to explain about the raise in allergic diseases because of the industrialization and urbanization, and the greater incidence of allergic diseases are numerous in developed countries. The theory has now been enlarged to involve the exposure to symbiotic bacteria and the parasites are as main modulators of the immune system , along with the infectious agents (8). Recently, the asthma has not been acknowledged as a simple Th2 disease, which is featured by IgE upgrading and somewhat eosinophilia.

The Th17 and Th9 cell subtypes are well known to contribute the swelling or increasing the smooth muscles contraction or stimulating the mast cells. Asthma is a chronic airway swelling disorder of the lungs that leads to structural and functional changes, thus resulting in increased bronchial responsiveness and the airflow stoppage. .Exacerbations might be fatal and these are more repeated and more serious in high-risk clients or clients with uncontrolled asthma. Factors involves viral infections, allergens, tobacco smoke, physical exercise, stress, some medications like non-steroidal anti-inflammatory drugs and beta-blockers might trigger or even worsen asthma symptoms. Some of the phenotypes are identified, such as allergic asthma, non-allergic asthma, and late arising asthma. During quiet breathing, the primary muscle responsible for ventilation is the diaphragm .Inspiratory muscle training showed a significant improvement in inspiratory muscle strength and an increased exercise tolerance (9). . Bronchodilatation, gaseous exchange improves peak expiratory flow rate and exercise tolerance. The aim of the study is to find the effect of Inspiratory muscle training to improve pulmonary status in asthma patients. The study is essential as most of the general population suffers from this problem and also to make physiotherapists to realize

the benefits received from the alternative approaches like Inspiratory muscle training to improve peak expiratory flow rate and exercise tolerance in asthma patients (10,11).

MATERIALS AND METHODOLOGY

20 acute asthma patients attending Vinayaka Missions KirupanandaVariar Medical College, Salem between 40 and 55 years of age were selected randomly using simple random sampling method are included for the study. Patients having cardiac and psychiatric problems are excluded from study. The group underwent a pretest assessment of exercise tolerance and peak expiratory flow rate with the help of six minute walk test and peak flow meter . Exercise tolerance test was measured using six minute walk test . Materials like chalk powder, stop watch, whistle, meter tape were used to collect the data for this test. A hard and flat 200 meters walkway was marked for six minute walk test. Subjects were asked to stand in the start line and were instructed to walk in their self pace and rest as needed back and forth along the marked walkway for a period of six minutes following a whistle blow. Stop watch & whistle were used to start and stop the test. The distance walked was measured by multiplying the number of times of full completion of marked walkway with 200 meters and the excess using a meter tape. The distance walked in six minutes was recorded with a help of a meter tape in meters. Peak expiratory flow rate of the subjects was measured using peak flow meter . The sliding pointer was set to zero before the start of the procedure. The subjects were asked to stand straight and hold the handle of the peak flow meter. They were further asked to take a deep breath and put the mouth piece in their mouth and seal their lips and teeth tightly around the mouthpiece, following which they were asked to blow out as hard and as fast as they can. The number on the scale corresponding to the sliding pointer was noted. The pointer was rest to zero every time and the best of three recording was taken into account. The numerical value corresponding to the slide pointer was taken as the score. After the pre test measurement was over, the subjects received Inspiratory muscle training for 8 weeks and then posttest measurement was taken.

Inspiratory muscle training was done for a period of eight weeks once a day in the morning session between 8.30 am and 9.30 am. The training was given for six days in a week. Inspiratory muscle trainer is a device which consist of mouth piece and with adjustable resistance. Inspiratory muscle trainer resistance is altered according to patient condition from acute to severe. Place nose clips to close the nose. Inspiratory muscle trainer is placed in mouth started with minimal resistance and gradually resistance is increased. Treatment time is 10 to 15 minutes.Inspiratory muscle training is defined as a course of therapy consisting of a series of breathing exercises that aim to strengthen the bodies' respiratory muscles making it easier for people to breathe. Inspiratory muscle training is normally aimed at people who suffer from asthma, bronchitis, emphysema and chronic obstructive pulmonary disease. . Inspiratory muscle training (IMT) has been shown to improve inspiratory muscle strength, reduce dyspnoea and improve exercise tolerance and peak expiratory flow rate in both healthy people and patients with COPD . Reviews of work done on training the respiratory muscles using inspiratory muscle training reduce bronchospasm ,improve exercise tolerance(9,10,11).Patients with asthma resort to complementary and integrative applications (such as breathing techniques, yoga, herbal products, Inspiratory muscle training) for asthma treatment. Inspiratory muscle training using Inspiratory muscle trainer is one way to improve pulmonary functions (9,10,11). Non-pharmacological treatment methods are as important as pharmacological treatment in asthma patients in order to take symptoms under control and to prevent the frequency of exacerbation. . After Inspiratory muscle training the collected data was subjected to statistical analysis using paired 't' test .

RESULTS AND DISCUSSION

The results of the study were derived from the statistical analysis using the paired t-test . The results using a paired t-test revealed that there is a significant improvement in peak expiratory flow rate and exercise tolerance in asthma patients. The results of the study showed that difference between the pretest and posttest mean values were

statistically significant thereby indicating that peak expiratory flow rate and exercise tolerance had significantly improved following Inspiratory muscle training for a period of eight weeks .The improvement in peak flow rate and exercise tolerance may be because due to increased capillary density, myoglobin content, mitochondrial enzymes and the concentration of glycogen. Inspiratory muscle strength is improved which prevents alveolar collapse and respiratory muscle performance is increased. Lucas ramos.,*et al.*(1998) studied Inspiratory muscle training exhibited improvement in exercise tolerance and peak expiratory flow rate. TD Mickleborough, LA Turner (2011) studied Inspiratory muscle training attenuates inspiratory muscle fatigue, reduces the perception of dyspnoea, and increases exercise tolerance.

CONCLUSION

The results of the study make us to conclude that Inspiratory muscle training improved Peak expiratory flow rate and Exercise tolerance in asthma patients.

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Table. 1. The collected data were analyzed using paired'ŧ' test

S. No	Variables	Pre test Mean	Post test Mean	Mean difference	Standard deviation	'ŧ' calculated value	'ŧ' tab value
1.	Peak flow rate scores (liters/minute)	374.5	393.5	18	6.95	11.61	2.09
2.	Exercise tolerance test scores (meters)	372.3	395.85	22.55	5.826	17.346	2.09

t calculated value > t table value.

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RESEARCH ARTICLE

Radar Frequency Double -Band U- Structured Aperture Reinforced Sky Wire for Communication Applications

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ABSTRACT

This research paper signifies the designing and result observation of compact umbrella shape slotted patch antenna regarding dual band applications resonating at WLAN (2.4 GHz) and Lower WiMAX (2.9 GHz). Design is simulated on simulator software with FR4 substrate dimensions of 30×30×0.82 mm^3. The simulated S-parameters and VSWR parameters are analyzed for operating range 2.35-2.62 GHz and 2.81-2.99 GHz concerning S band applications. In terms of the stable realization of efficiency, gain and patterns, the results have been identified and simulated.

Keywords: Dual-band, Umbrella shape slotted Patch antenna, WiMAX, WLAN.

INTRODUCTION

In present scenario MPA (micro strip patch antenna) are demanded regarding applications in the field of wireless communication because of various characteristics of MPA such as compactness, broadband, stable gain and efficiency. Wireless communication is more popular and demanding over the wired network communication due to various advantages such as ease of mobility, affordable cost, sharing the band with multiple users, data transmission by utilizing the radio waves, ease of installation, flexible in use and virtual access. Many common applications of wireless communication in daily life are Bluetooth, cordless and mobile phones, ad hoc networks, WLAN, Wi-Fi and Wi-MAX [1]. Multiband antennas are widely used in the field of various wireless communication technologies. To

cover all the desired wireless communication frequencies, multiband antennas can be used which function in the multiple frequencies simultaneously. Multi radio platform require multiband antennas for obstacle free communication [2]. A multi-band antenna is demonstrated by utilizing a triangular micro strip patch for many applications. The antenna consists of a fragment of capacitor and groove having shape of T. Input reactance of demonstrated structure varying with T grooved fragmented capacitor. The multiple resonant modes are achieved with elemental frequency range of 1.97–2.16 GHz [3].

Dual band antenna is framed by using a rectangular micro strip patch which consists of internal radiating patch of pentagonal shape which built on glass epoxy dielectric material because easily available with lower price. For the applications of Wi-Fi to maintain the linear polarization, consider dual band operation. The pentagonal patches were used to attain the respective resonator of circular shape. The designed multiband antennas are embedded on a router. A good agreement with the operating frequency is achieved. It has been observed that the antenna functioning satisfactorily in the dual band mode for WLAN and WiMAX Applications. The measured results are compared with mono polar radiation patterns [4-5]. In this paper proposed a dual band antenna structure to cover the wireless standards at WLAN and lower WiMAX at 2.4 and 2.9 GHz respectively. An umbrella shape radiating section is choose to improve the radiation characteristics at desired resonant modes.

Designing of Proposed Antenna

This part focuses on designing of proposed umbrella shape slotted dual band antenna. Figure 1 represent the layouts of the proposed structure with front, side and bottom view. Antenna is designed on FR4 dielectric material having depth of 0.82 mm, $\varepsilon r = 4.4$ and dissipation factor $\tan\delta = 0.02$. The dimension of the design is 30 × 30 × 0.82 mm^3. Proposed design is fed by rectangular shape feed line (characteristics impedance of 50 ohm). Antenna consist radiating part of slotted circular shape (radius 7.5 mm) attached with circular ring (radius 6 mm) in upward direction which makes an umbrella shape with radiating section as reference of Figure 1 (a).

Extracted values (in mm) of recognized structure are:- $L_S = 30$, $W_S = 30$, $h = 0.82$, $R = 7.5$, $R_1 = 5$, $R_2 = 6$, $L_{SL1} = 0.25$, $W_{SL1} = 8$, $L_{SL2} = 2.25$, $W_{SL2} = 4$, $L_1 = 9$, $W_1 = 1.5$, $L_2 = 5$, $L_{SLT} = 1.4$, $W_{SLT} = 4$, $W_f = 4$ and $L_f = 18$. The antenna parameters used in simulation are analyzed by applying transient solver of simulator CST Microwave Studio (MWS-version 2014) [6].

Figure 1 Layout of proposed design (a) Top view, (b) Side view, (c) Bottom view.

In proposed design the radiating section is in circular shape, so the required parameters are obtained by using following equations:

Radius of circular patch can be calculated as

$$a = \left[\frac{F}{\left\{1+\frac{2h}{\pi\varepsilon_r F}\left[\ln\left(\frac{\pi F}{2h}\right)+1.17726\right]\right\}^{1/2}}\right] \quad (1)$$

Where

$$F = \frac{8.791\times 10^9}{f_r\sqrt{\varepsilon_r}} \quad (2)$$

h is depth of dielectric material (in mm).

ε_r is relative permeability of dielectric material.

f_r is fundamental frequency.

RESULT ANALYSIS

Proposed configured antenna indicates the dual operating bands with impedance bandwidth of 5.43 % (2.35-2.62 GHz) and 3.10 % (2.81-2.99 GHz) during simulation mode as represented in S-parameter and VSWR analysis as shown in figure 2 and 3. The Figure 4 represents the variation in the radiation efficiency with respect to the operating frequency for proposed antenna. The maximum efficiency of 78% and 88% is achieved at resonant frequency band at 2.41 GHz and 2.92 GHz respectively. The simulated antenna gain is indicated in Figure 5, represents the variation in the antenna gain with respect to the operating frequency for proposed antenna. The peak gain of 2.49 dBi and 3.52 dBi is observed at wireless communication mode at 2.41 GHz and 2.92 GHz respectively. Figure 6 showing the 3D plot of proposed structure at resonant frequency 2.42 GHz and 2.91 GHz. It is identified that at higher frequency side gain is improved.

For better observation of the proposed design another parameter radiation pattern are studied. Patterns are investigated for E and H plane in simulation as well as measurement mode. There is a fair matching between the simulated and experimented analyzed parameters. Figure 7 represents the comparison of patterns regarding proposed design at distinct resonant frequencies 2.42 and 2.91 GHz. As observed from Figure 7, the patterns like as Omni directional and dipole like/ bi-directional in H and E plane respectively [7-8]. The simulated surface current distribution of proposed umbrella shape dual band antenna at wireless standards 2.4 GHz and 2.9 GHz is anticipated in Figure 8. It is noticed that the current exists around the periphery of U-shaped slot on the ground plane for resonant frequency 2.4 GHz for WLAN application. For upper resonant band 2.9 GHz (Lower Wi-MAX), the current is present across the part of the slotted circular shape radiating section and umbrella shape section, provides the enhanced radiation parameters [5].

CONCLUSION

In this research proposed, antenna has been designed/analyzed for wireless application standards at 2.4 GHz and 2.9 GHz to facilitating various wireless frequency band applications. The above incurred bands are useful for respective application in wireless communications: WLAN (2.4 GHz) and Lower WiMAX (2.9 GHz) for RFID services. The radiating part comprising the slotted circular shape with integration of umbrella shape circular part and defected ground plane which results the dual resonating band configuration for wireless applications. Proposed design specifies the radiation characteristics in consistency and improved formation.

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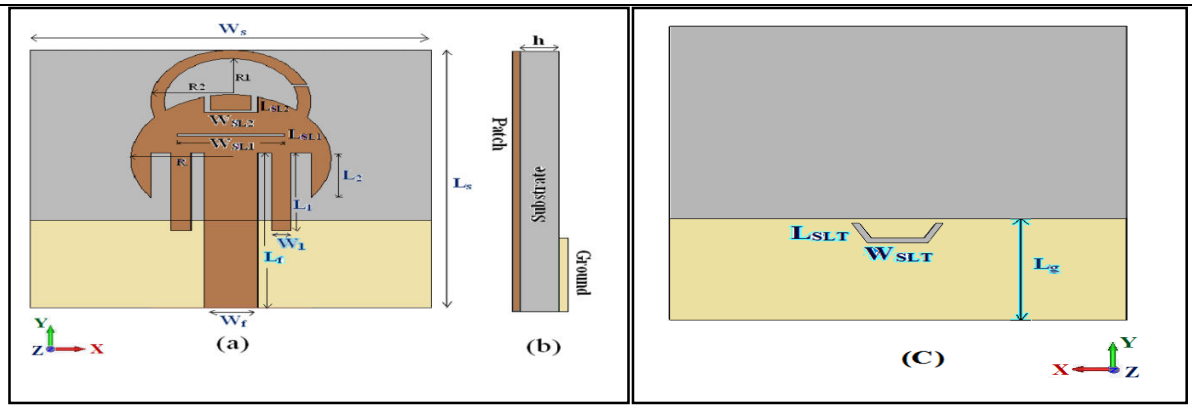

Figure 1. Layout of proposed design (a) Top view, (b) Side view, (c) Bottom view.

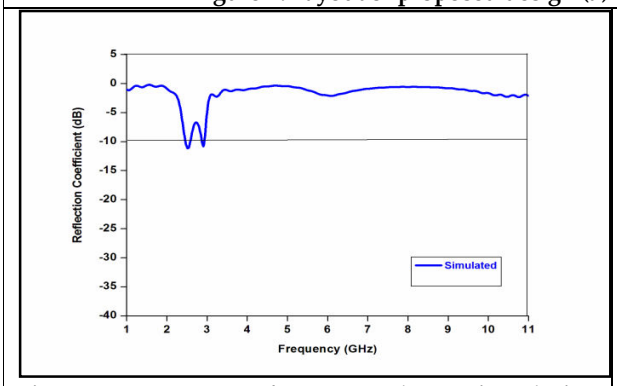

Figure 2. S_{11} versus frequency observation during simulation process.

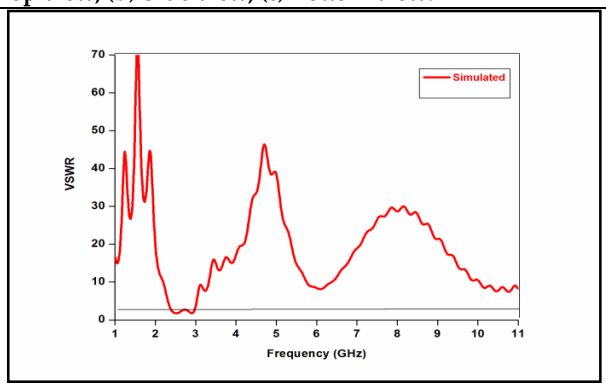

Figure 3. VSWR versus frequency observation during simulation process.

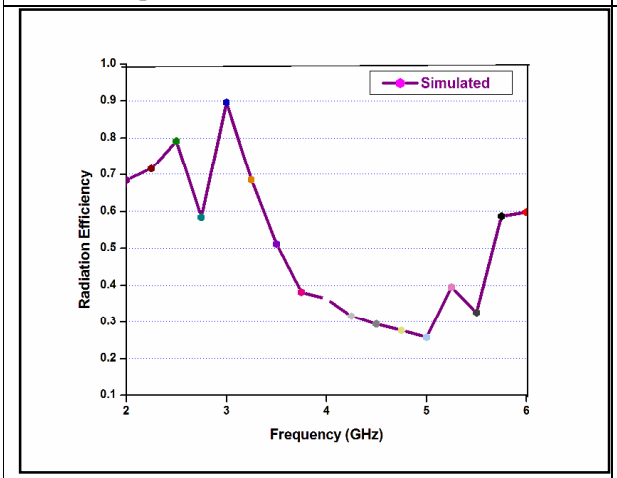

Figure 4. Simulated antenna radiation efficiency

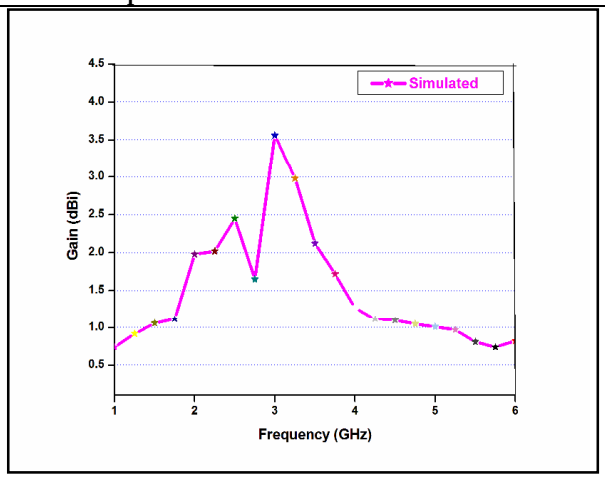

Figure 5. Simulated antenna gain.

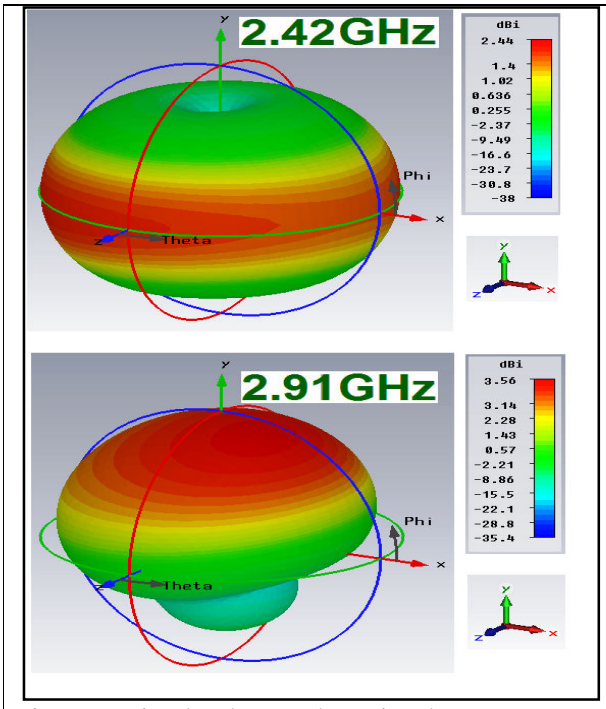

Figure 6. Simulated 3D polar gain plot at 2.42 GHz 2.91 GHz

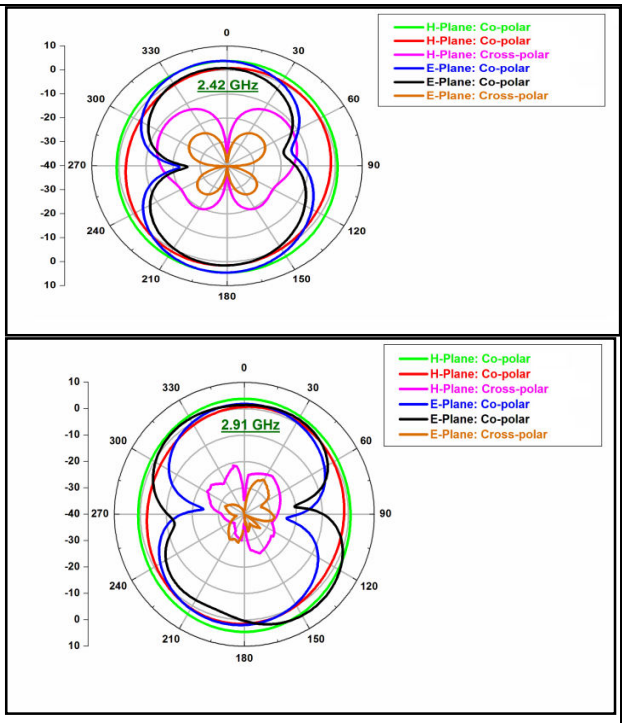

Figure 7. Radiation Patterns at 2.42 and 2.91 GHz.

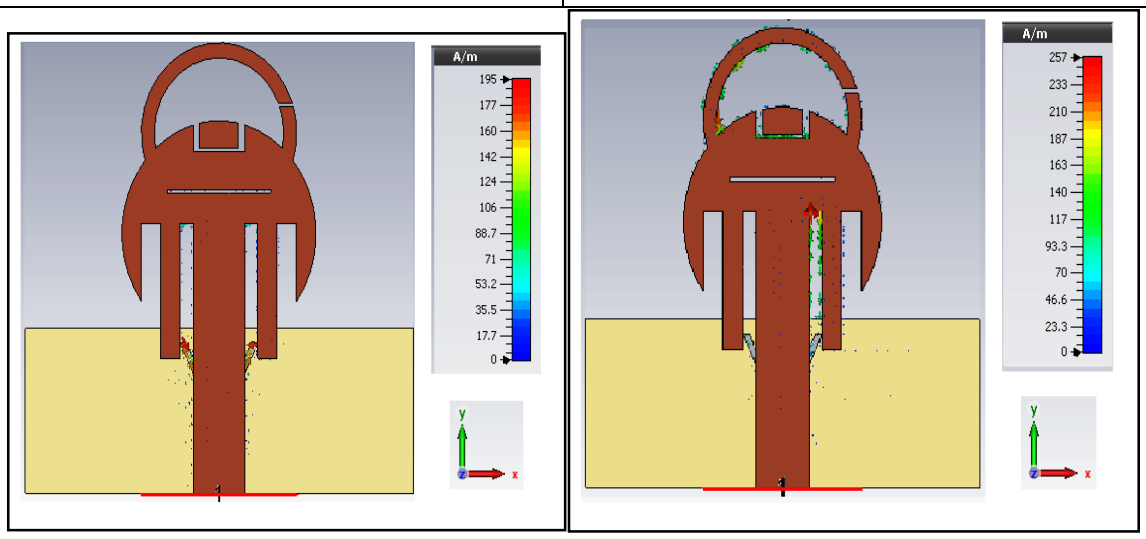

Figure 8. Current distributions at 2.42 and 2.91 GHz.

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REVIEW ARTICLE

Mesenchymal Stem Cell Therapy in COVID 19

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ABSTRACT

COVID-19 is caused by the SARS-CoV-2 virus, which is a positive stranded RNA virus. By allowing its surface spike protein to interact with and bind to the host ACE2 receptor, the virus primarily targets pulmonary epithelial cells as its initial site of infection. The virus's internalization and incremental replication triggers an exaggerated immune response, resulting in the release of a slew of pro-inflammatory cytokines and chemokines. This immune storm causes a slew of health problems in the host, eventually leading to multiple organ failure. Mesenchymal stem cell therapy is a promising treatment option for COVID-19 patients who are experiencing delirium due to the infection. In COVID-19 patients, this therapy has been shown to reduce the expression of pro-inflammatory cytokines while also repairing damaged tissues. The aim of this review is to present the promising evidence and implications in support of mesenchymal stem cell therapy as a necessary treatment option for COVID19 patients.

Keywords: COVID-19; SARS-CoV-2; Mesenchymal stem cell; Immune storm; Treatment

INTRODUCTION

Present enormous public health crisis and the pre-eminent threat to the human race is the COVID-19 outbreak. COVID-19 is preferably an enclosed RNA virus, which is clearly found in humans and animals. The virus is of zoonotic nature and belongs to the corona viridae family. This virus exhibits symptoms such as extreme pneumonia, myalgia, headache, high fever, tiredness, dry-cough and dyspnea [1]. Pathogenesis of corona virus involves ACE2 (Angiotensin converting enzyme 2) receptor conversion by its spike protein and the cellular priming of the spike protein, and TMPRSS2 (transmembrane protease serine 2) which facilitates entry and distribution of host cell [2,3]. Still, however the immense challenges to understand the biology and pathophysiology of corona virus have contributed to an accelerated global mobilization of the scientific community to establish a successful care and vaccine protocol. Innumerable experiments and research papers related to COVID-19 were published and are predicted to grow exponentially. Stem cells represent valuable properties, offering inexpensive and ethnic for

cruelty-free animal trial studies. In this way, research papers have already explained the use of stem cells to produce new data on many aspects of corona virus [4].

Like what has been done with other viral diseases previously, these stem cells can also be a desirable method for immune regulation [5-12], as well as re-formation of tissue with a lot of cumulative information about the fundamental mechanism of operation and decades of clinical experiences [13-18]. In addition to the potential use of stem cell in primary science. It is well know that the roles of most immune cells can be mediated by mesenchymal stem cells (MSCs) that can be regulated by a network of mechanism including direct cell interaction and secretion of solutionic factors with an immunodomestic role [19,20]. Henceforth, MSCs may be promising instrument of treating conditions involving deregulation of immune system which might the situation of COVID-19.

Mesenchymal Stem Cells

Stem cell therapy has been demonstrated to be one of the best treatment strategies and offers a chance to cure a variety of diseases that were historically thought to be incurable [21]. In spite of the major advancement of the stem cell-based therapy field, the key shortcomings of this technique have not yet been solved such as immunogenicity, small cell source and ethical challenges. Among others, MSCs have Drawn interest due to the possible causes like high rate of dissemination, the minimal invasive technique and the lack of ethical concerns.

In contrast with other therapies, there is a great deal of superiority in the usage of MSC therapy, including:

1. They are readily available and can be separated from different tissues including fetal liver, umbilical cord, dental pulp, buccal fat pad, menstrual blood, etc.
2. Stem cells are multipotent.
3. In a proper period of time MSCs could quickly extend to the clinical volume.
4. MSCs can be processed for repetitive medicinal use.
5. Until now no adverse reactions of MSCs have been shown by clinical trials to allogenic MSC.
6. Several clinical trials have specifically recorded the safety and efficacy of MSCs [22].

Mesenchymal Cells Therapy in COVID-19

MSCs' ability to differentiate into multiple lineages and modulate immune responses indicates that these somatic progenitor cells have a wide range of therapeutic applications [23]. Figure 1 describes cascade of SARS-CoV-2 and the intervention by MSCs. The immunoregulatory effect of mesenchymal stem cells on COVID-19 is led by cytokines storm. SARS-CoV2 when enters the lungs, in infection areas it activates immune cells and localizes inflammation. The devastating uncontrolled systemic inflammatory response is triggered by the secretion of high levels of pro-inflammatory cytokines such as interleukin, interferons, chemokines, and other factors by the immune effector cells in this infection. After MSC treatment, these cells invade the lung tissue and secrete factors that can modulate the immune system; ROS and even lung tissue fibrosis can also be suppressed [24].

Experimental models tend to show the protection and efficacy of transplanted MSCs for the treatment of inflammatory lung diseases [25]. From basic science to clinical trials, MSCs have been widely used in cell-based therapies [26,27,28]. Inflammation has been shown to affect many pulmonary morbid processes, including obstructive diseases like chronic obstructive pulmonary disease (COPD) and asthma, as well as restrictive diseases like idiopathic pulmonary fibrosis (IPF) and lung cancer (ARDS). Acute and chronic lung injury are often associated with impaired immune function and fibrosis, either as a cause or as a result of these diseases [29,30]. MSC therapy, like most cell therapies, may be beneficial in lung disease because it has been shown that many intravenously administered MSCs (80–90%) enter the lungs quickly when injected intravenously [31]. The majority of MSCs lodge in the pulmonary vascular bed after systemic administration due to unknown interactions with capillary endothelial cells. Most MSCs are cleared within 24–48 hours, according to tracking studies using labelled MSCs, though they can linger for longer in damaged or inflamed lungs [32]. The detection of cellular transmembrane protease serine 2 (TMPRSS2) and angiotensin I converting enzyme 2 receptor by SARS-CoV-2 allows it to enter cells (ACE2). The heart (coronary artery endothelium, myocytes, fibroblasts, and epicardial adipocytes), blood vessels (vascular endothelial

and smooth cells), gut (intestinal epithelial cells), and lungs (tracheal and bronchial epithelial cells), kidney (luminal surface of tubular epithelial cells), brain, and testis all have ACE2 receptors [33]. The large surface area of alveolar epithelial cells in the human lung may explain the organ's susceptibility to COVID-19 infiltration's negative consequences. A key argument is that ACE2 receptors are primarily expressed in type II pneumocytes, which are small cylinder-shaped cells that make up 5% of all pneumocytes [34] and are responsible for alveolar surfactant production while also serving as "stem" cells and progenitors of type I pneumocytes (which make up 95% of pneumocytes) that conduct gas exchanges in the lungs [35,36,37]. SARS-CoV2 bind to ACE2 receptors, allowing membrane fusion and virus penetration into the cell [33, 38]. As a result, these receptors are downregulated. In other words, the virus appears to penetrate the cell along with the membrane receptor, which is then separated from the membrane's external surface.

RESEARCH FINDINGS AND DISCUSSION

SARS-CoV-2 has a high transmission capacity, travels quickly around the world, and kills a lot of people. Since the pathogenesis of this disease has been partially identified in previous studies and there are similarities between its pathogenesis and that of other viruses in this family that can cause lung injury in patients with ARDS [39,40,41], research into therapeutic approaches that can suppress inflammation, cytokine storm, and ARDS can aid in the development of novel therapeutic approaches for this disease. As a result, MSCs may be considered as one of the immunomodulating and tissue-regenerating cells that have previously shown to be effective in the treatment of ARDS and cytokine storms [42-46,48]. Exosomes can have anti-inflammatory effects on lung tissue by moving mRNAs, miRNAs, and various proteins from the secretory cell to the target cell [49]. Since these cells exert their effects in a number of ways, including exosome secretion, the use of their exosomes can be called a cell-free therapy [47]. These exosomes can reduce inflammatory cytokines, increase regulatory cytokines, and suppress inflammation, as previously demonstrated [50]. MSC-exosomes were also shown by Monsel *et al.*, to improve alveolar type II cell survival by increasing intracellular ATP levels [51].

CONCLUSION

SARS-CoV-2 (novel corona virus) infects by binding the spike protein on the viral surface to the ACE2 receptors on the surface of the host cell. As a result, SARS-CoV-2 infection will affect any tissue or organ that expresses the ACE2 receptor. Since alveolar epithelial cells have a high proclivity for ACE2 receptors, they are the ones that suffer the most when SARS-CoV-2 infects them. The SARS-CoV-2 infection causes a debilitating cytokine explosion, resulting in extreme shock, oedema, and multiple organ failure. Giving COVID-19 patients an infusion of multipotent MSCs will help them fight the disease since these cells can suppress the overactive immune response and promote lung epithelial cell endogenous repair by improving the microenvironment. We have outlined all of the consequences associated with MSC therapy application in the case of COVID-19 in this review.

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Conflict of Interest

The authors do not have any conflict of interest.

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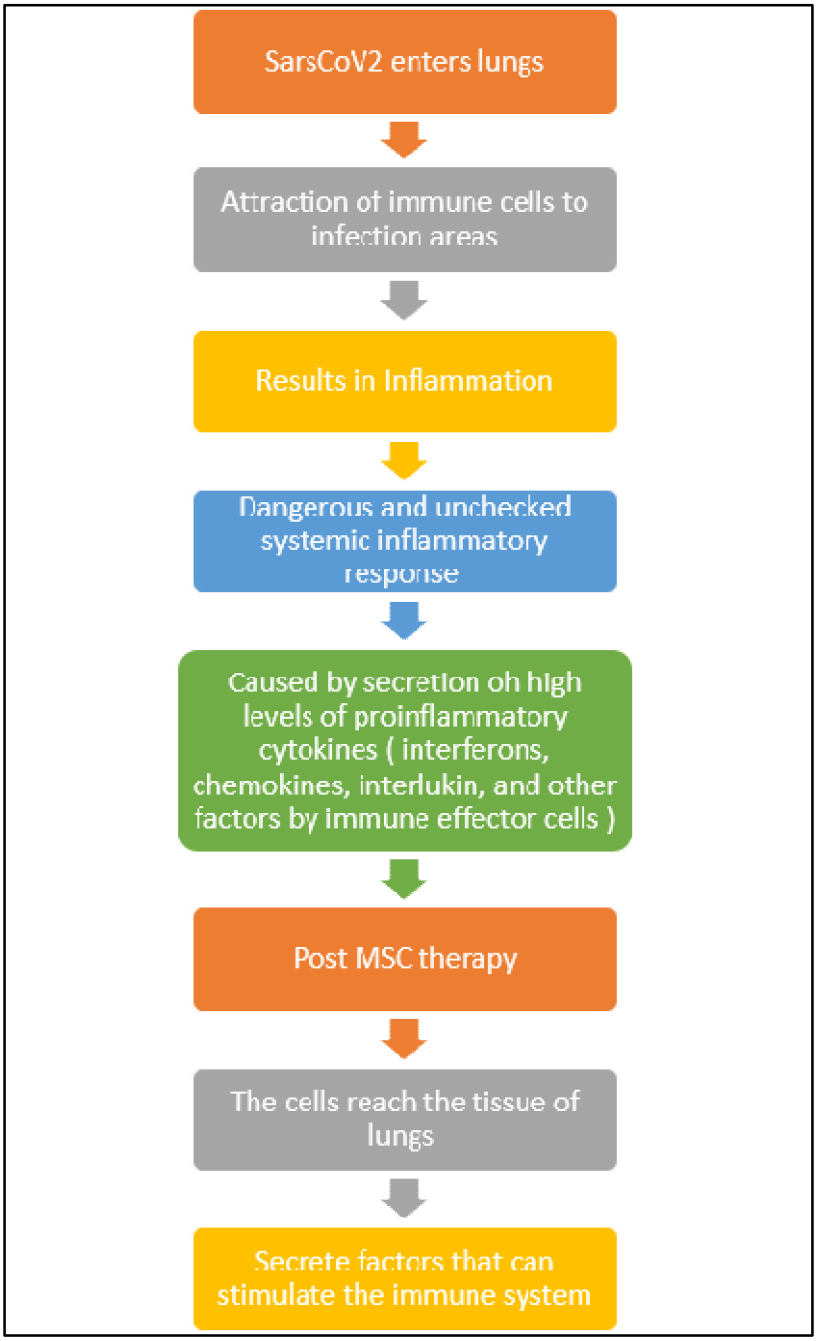

Figure 1: Cascade of MSCs treatment
Note: MSCs also prevent the lung tissue damage caused in ROS and Fibrosis

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RESEARCH ARTICLE

A Study to Find Out The Effect of Land Based Exercises on Improvement of Cardiorespiratory Functions Among Chronic Obstructive Pulmonary Disease Subjects.

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) is a lung disease characterized by chronic obstruction of lung airflow that interferes with normal breathing and is not fully reversible. Symptoms will be mild at first with intermittent coughing and shortness of breath. COPD is the major cause of morbidity and mortality worldwide and results in an economic and social burden that is both substantial and increasing. Various studies have been conducted for the management of COPD. This study investigates the effects of land-based exercises in the improvement of cardiorespiratory functions among COPD patients. Total of 20 subjects participated in the study. With the help of Peak flow meter, the lung function of the participants was measured prior the treatment. The subjects were taught to perform diaphragmatic breathing exercise, pursed lip breathing and segmental breathing exercise for a period of 6 weeks with 2 sets each day. PEF values were measured after the intervention and the statistical analysis were done using paired 't' test. The Paired 't' test revealed a significant difference in the respiratory parameter (PEF) of the chronic obstructive pulmonary disease patients.

Keywords: chronic obstructive pulmonary disease, peak expiratory flow, peak flow meter, diaphragmatic breathing exercise, pursed lip breathing and segmental breathing exercise

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a lung disease characterized by chronic obstruction of lung airflow that interferes with normal breathing and is not fully reversible. COPD is the major cause of morbidity and mortality worldwide and results in an economic and social burden that is both substantial and increasing. The airflow limitation is both progressive and associated with an abnormal inflammatory response of the lungs [1, 2]. Cigarette smoking or exposure to noxious agents induces an inflammatory response in the lungs that leads to small airway disease and parenchymal destruction. It is characterized by a specific pattern of inflammatory process involving increased cytotoxic level Tc1 lymphocytes. Symptoms will be mild at first with intermittent coughing and shortness of breath. It is a slowly progressing disease with a long asymptomatic phase, during which lung functions continue to decline. Persistent cough particularly with mucus production is a common symptom. Dyspnea, especially with exercise, wheezing and chest tightness may also be present. End-stage COPD is characterized by severe airflow limitation, limited performance and systemic complications [3, 4] and considerable reduction in the PEF rate. At present, there are major difficulties with the quantification of emphysema and small airways disease during life, so clinical investigators study COPD by measuring the degree of lung function abnormality, notably the impairment in FEV_1. This is justified on the basis that both emphysema and small airways obstruction reduce maximum expiratory flow, so that the FEV_1 represents some kind of sum of the two influences. Patients with COPD, the FEV_1 is, besides age, the single best predictor of mortality. Exercise intolerance is another troubling manifestation of this disease [5, 6]. There are pieces of evidences point to the fact that features of impaired exercise tolerance are not simple consequences of loss of pulmonary functions but because of combination of exertional dyspnea, cardiovascular limitation, nutritional impairment, psychological factors and skeletal muscle dysfunctions which are commonly encountered in COPD patients [7- 9] Because of exercise intolerance patients typically limit their activity to avoid these uncomfortable sensation of dyspnea, leg fatigue and discomfort . Activity limitation reduces social interaction and promotes depression and anxiety which further worsens the impact of dyspnea. This vicious cycle of exertional dyspnea, immobility, social isolation, depression and lack of fitness in COPD is responsible for morbidity [10-12]. People suffering from severe form of this disease usually spent their remaining years of life in bed and have impaired health related quality of life and high utilization of health care resources [13-15]. This study was conducted mainly to determine the effects of land-based exercises and its effect in improving the PEF of COPD patients.

MATERIALS AND METHODS

Sample Size

A total of 20 subjects participated in the study

Inclusion Criteria

Age group between 30 to 50 years
PEF < 70 liter/minute

Exclusion Criteria

Unstable cardiac disease
Long term oxygen therapy
Inability to complete exercise training

Materials Used

Peak expiratory flow meter
Cotton
Couch

Sterilizer alcohol based
Pillow

Procedure

The study was carried out Aarupadai veedu medical college hospital and ethical clearance was obtained. Patients who visited the outpatient department and satisfied the inclusion and exclusion criteria were included in the study. Prior informed consent was obtained from the participating subjects. The participants were assured that the data would be kept confidential and the nature of study was explained. Adequate care was taken to avoid any bias. The peak expiratory flow rate of the patients was measured prior the treatment and the values were recorded. The participants were then taught to perform diaphragmatic breathing exercise, pursed lip breathing and segmental breathing exercise for a period of 6 weeks with 2 sets per day. The PEF rate was measured after the completion of 6 weeks. The Peak flow meter is a calibrating device that could generate accurate flows between 0-900 L/minute, with 30 milliseconds rise time and 10 milliseconds dwell time, with an abrupt fall of flow after reaching the PEF, the subjects performed at least three acceptable blows into the peak flow meter until the two highest PEF values were reproducible within 40 L/minute. The pre- and post-values were measured and recorded by using peak flow meter.

Data Analysis

Analysis of data was performed based on the value the participants obtained by using the peak flow meter. The effect of intervention on the changes from pre to post test values were analyzed using Paired 't' test. And the significance of the values were determined.

RESULTS AND DISCUSSIONS

The study was conducted with a sample size of 20 subjects in the age group between 30 to 50 years who visited Aarupadai Veedu Medical College and Hospital. Severity of condition was assessed using peak flow meter. The pre- and post-test values were analyzed using Paired 't' test.

Analysis of PEF Value

While comparing the pretest and post test value of the peak expiratory flow using paired 't' test, the calculated paired 't' value is 10.8. The 't' table value is 3.250 at 0.005 level of significance. From the results the calculated 't' value is greater than the table 't' value, which inturn implies that there is significant difference in pre- and post-PEF values following land-based exercises among COPD patients.

CONCLUSION

The calculated 't' value is extremely significant, which in turn confirms that there is a significance difference in the peak expiratory flow rate of the patients, who have performed land based exercises. The land based exercise includes diaphragmatic breathing exercise, pursed lip breathing and segmental breathing exercises. These exercises improves the lung capacity and increases the thoracic expansion and also decreases the lung hyperventilation. Which in turn enhances respiratory muscle function, and increases the exercise tolerance. Hence incorporation of land based exercises should be considered from the cost benefits perspective. The monetary and temporal cost of performing this exercise is minimal. Incorporating this exercise into home exercise is cost effective and improves patient function.

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Conflict of Interest

The authors declare that they have no conflict of interest

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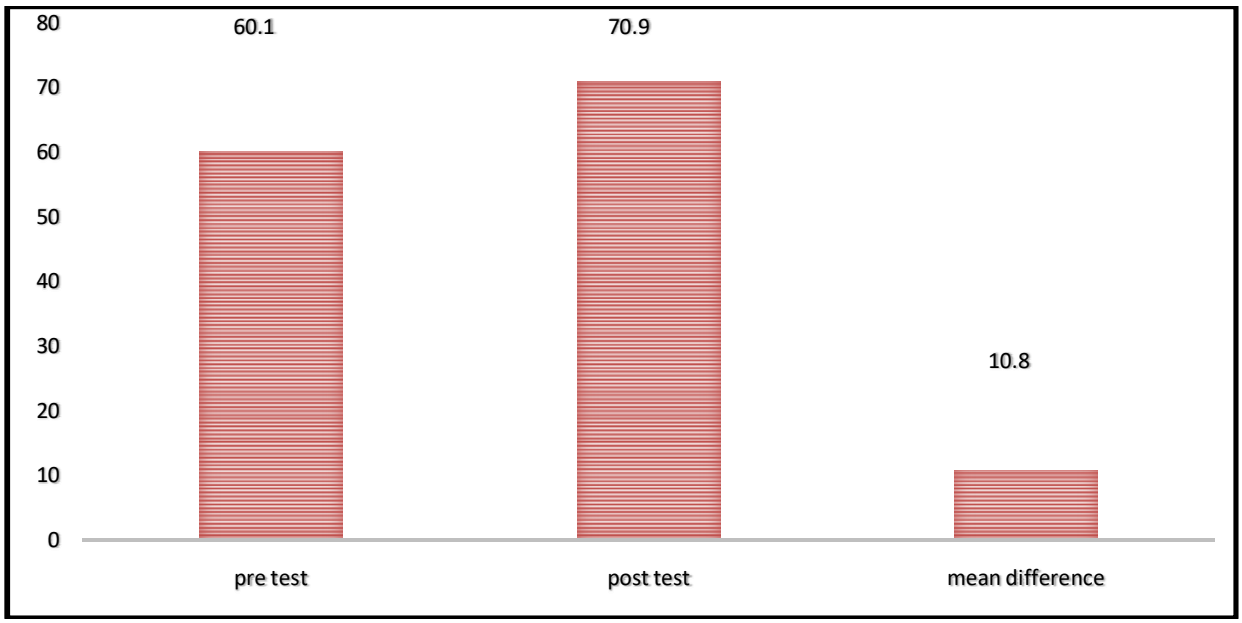

Fig. 1. Analysis of PEF Values

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RESEARCH ARTICLE

A Smart Shopping with an Automated Billing using Mobile Application

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ABSTRACT

In Today's life people going to malls for shopping is increasing rapidly. People purchase the item. After completed the shopping they go for billing at the billing counter but as there are many people standing in queue for billing purpose, so lots of time is required for the individuals for billing. The main objectives of this proposed system are to eliminate time taken in billing counter in shopping mall and Increases customer satisfaction. It reduces manpower required in billing section. Increase productivity time. The admin will make use of the webpage to add new super market product category. The new offer details such as big offer, seasonal offer and current offer are notified to the customer. The user can view overall list of super market products under the corresponding brand (vegetable, kitchen items, and snacks). The list of products can be filtered by using size, price and ratings. The camera helps to scan the QR code of the product to fetch the product details in the smart manner. The lists of items are added to the cart and proceed for payment. The admin will receive the order notification and status of the delivery gets updated after sending the order package. As soon as the order placed, the admin will get the notification regarding the order placing. The admin can view the overall order and as per the request, the confirmation will be fixed. The user can track the current location centre of product through Google Map to deliver the product.

Keywords: QR Code, mobile Application, GPS.

INTRODUCTION

In Today's life people going to malls for shopping is increasing rapidly. People purchase the item. After completed the shopping they go for billing at the billing counter but as there are many people standing in queue for billing purpose, so lots of time is required for the individuals for billing. The main objectives of this project are to scan the QR code of the product and the purchased products are added to the cart. After purchasing the product the customer can go for payment section. In payment section there are various options available like paytm, stripe, Cash on Delivery and to satisfy the customer we provide door delivery option. In covid situation customer can place the order from home itself using Mobile Application

The project is designed to satisfy the needs of both admin and customer to get the needed super market items in low cost and low time from anywhere. The admin will make use of the webpage to add new super market category. The new offer details such as big offer, seasonal offer and current offer are notified to the customer. The user can view overall list of super market products under the corresponding brand (vegetable, kitchen items, and snacks). The list of products can be filtered by using size, price and ratings. The user can view the super market item offers and make use of the coupon for order placing. The lists of items are added to the cart by using QR code Scanner through camera and proceed for payment. The admin will receive the order notification and status of the delivery gets updated after sending the order package. As soon as the order placed, the admin will get the notification regarding the order placing. The admin can view the overall order and as per the request, the confirmation will be fixed. The user can track the current location centre of product through Google Map.

LITERATURE SURVEY

Dylan Hicks *et.al* [1]. developed an android application that can help the shoppers in searching for items in the store. The application has two screens corresponding to searching and map. The user can type in the products in the search bar. A centralized server returns available results for the search. On selecting the preferred search result, the map screen displays the location of the chosen item on the floor plan of the store. Reetesh V *et.al* [2]. built an android application for an educational institute. The software android studio is used to develop the application. Android Studio has a large number of diverse views available for the development of the application. Some of the common views are button, scroll view, list view, checkbox, search view etc. A layout editor that supports drag and drop of components makes the app more user-friendly.

Chandrasekhar *et.al* [3]. proposed that Ever since the debut of wireless technology, electronic commerce has developed to such an extent to provide convenience, comfort, and efficiency in day-to-day life. The main purpose of this system is to provide centralized and automated billing system using RFID and ZigBee communication. Each product of shopping mall, super markets will be supplied with an RFID tag, to identify its type. Every cart contains PID (Product Identification Device). Zhenhai Mu *et.al* [4]. describes a bookstore management application which is used to administrate the transaction of books. Users have to register and make an account during the first time login. A mobile application to evaluate English pronunciation skills is reported in research work. RizqiMutqiyyah *et.al* [5]. developed the app, the user is provided with random English words which are fetched from the SQLite Database. The user has to pronounce the words. The system compares the received input with the database and notifies whether the pronunciation is correct or incorrect. Deepali Bajaj *et.al* [6]. developed an android application which can track the nutritional consumption of the users. The application was developed using Android Studio. The app can provide tips to the user for improving his/her diet.

Kin Chi Chan *et.al* [7]. introduced a location based application for shopping assistance. The users can search for nearby shops where a particular product is available. The location of the user is determined by the GPS (global positioning system) system of the mobile phone.

Ruinian L *et.al* [8]. identified the design requirements of a smart shopping cart which uses RFID readers and tags for the total price calculation. The RFID reader enables the user to pay the bill using the cart itself and thus avoids the tiring billing queues. The entire setup was made and they have also designed secure communication protocol to make the system more secure. Sayali Bhagat *et.al* [9]. Propose system effectively used in mall for notify towards expected product. It also reduce affords of customer and shopper at the time of bill payment. It could be used in shops for billing purpose. Propose system could be used for product recommendation and rating that could play an important role in Indian society as a whole. The usage of Pocket PC mall navigator as a shopping mall navigator, in addition to helping the users to find shops efficiently and effectively, were able to create awareness in using smart mobile devices for flexibility in almost every task among the shopping.

Proposed System

In existing system the public need to use common online shopping server to buy super market related products which won't be flexible. All category of person can't make use of the application in effective manner in searching the needed item. The admin need to reach the public by giving various offers and coupon which is applicable in existing application. The live tracking of delivery product can't view by the user. Problems identified in Existing System: i) selling a super market items in offline will get only local customers and user won't have a option in comparing the cost and rating of items with other company band items.ii)The order maintenance and sales billing records are carried out in manual process which leads to mismatch in order and sales entry.iii)The admin can't analyze the sales range and profit prediction in quick manner.

In proposed system the public can connect customers directly without any third party dealers which help to get the items from super market related product companies in low cost. The public can connect to the customer through the android application. The customer can view the items in the list and as per the need; the items can be placed for order. The admin can make use of the application by providing various offers and coupon for the customer. This helps to bring various customers to use the application and thus the profit of the company will rise. The user can filter the needed products by cost, company, offers and color and thus as per the needs, the products can be fetched from the database. After placing the order, the customer also has facilities to track the order by knowing the current location of the truck though google map. The QR scan using camera helps to fetch the product details in smart manner.

Novelty of Proposed System

- The public can get the conducts of the customers directly from the android application.
- The cost of the items from company to customer will become less due to absence of third party dealers.
- The admin can get the conducts of the customers directly from the android application which helps to send of notification of offer directly to the customers.
- The admin can get a notification once the order placed by user through android application.
- The order can be processed for delivery, as per the season the cost of the farm items can be updated by the admin.

RESULT AND DISCUSSION

The Smart Super Market product Shopping Application can be implemented in any platform and thus all category of user can utilize the process and thus all process can be carried out in a secure and in quick time. This Smart Super Market Product Shopping Application can implement in any Android Version such as Kitkat, Lollipop and so on. As it overcomes all type of testing, there won't be any error in implementing the software. As per the needs of the admin and customer, this application is designed which will definitely overcomes the existing system. As a rule, system implementation takes, as its input, all of the integrated software components that have successfully passed integration testing. The user can install the application in any Android application and it also supports tamil font therefore any one can make use of the application in an effective manner to place the order. The admin module

consists of several sub modules like Admin login, manage product category, add new product, offer notification, sales coupon allocation, view order and sales report generation.In figure 2 shows the admin can add any number of categories such as Prevention, Protection, snacks, grains, etc., the products are added under the corresponding category. Figure 3 displayed the details of the super market product such as product name, description, cost, selling cost, offer cost, product image, GST details and other attributes are stored in the database under the corresponding category selection. The admin can provide offers for the products to reach the customer. The admin can upload offer banner and offer details which get viewed to the customer app. The offer will be categorized as big, summer and seasonal offers shown in the figure 4.

The order placed by the customers is viewed by the admin. The admin webpage will get a notification alert with sound while receiving the order. The admin will view the order statement and proceed for delivery. Once the order is confirmed by the admin, the user will get notification from shopping app which is shown in figure 5 Figure 6 shows the user can make use of the camera to scan product QR code which helps to fetchthe product details in smart manner. The code retrieves the corresponding product details from database. The necessary product can be added to the cart. The cart contains the list product name, quantity and cost details. After checking the details, the user can proceed for placing an order is displayed in the figure 7 and 8.

CONCLUSION

Thus the application is designed to fulfil the needs of both product company and pubic in an effective manner. The android application is designed in a user friendly manner therefore all category of person can make use of the application in an effective manner. The public can get all super market related products from a single application. People purchase the item. After completed the shopping they go for billing at the billing counter but as there are many people standing in queue for billing purpose, so lots of time is required for the individuals for billing. The main objectives of this project is to eliminate time taken in billing counter in shopping mall and Increases customer satisfaction and During this pandemic time, this application helps to fulfil the needs of customers to get super market related products in quick manner.

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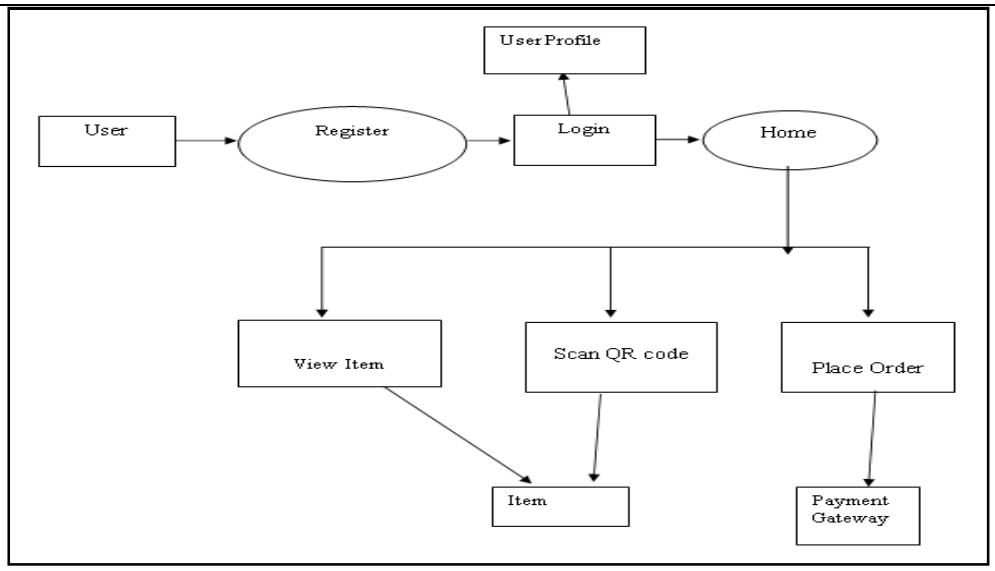

Figure 1. Work flow of the Proposed System

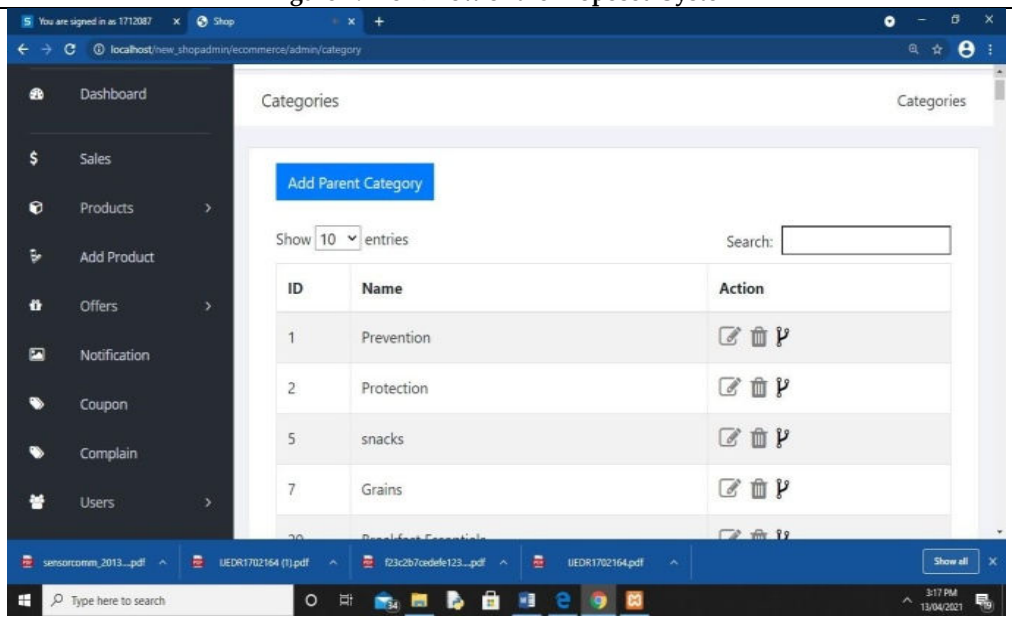

Figure 2. Manage Product Category

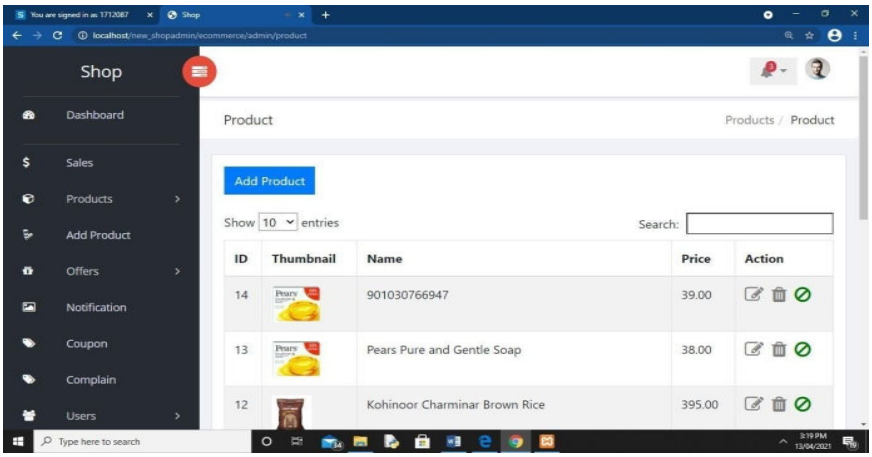

Figure 3. Add New Product

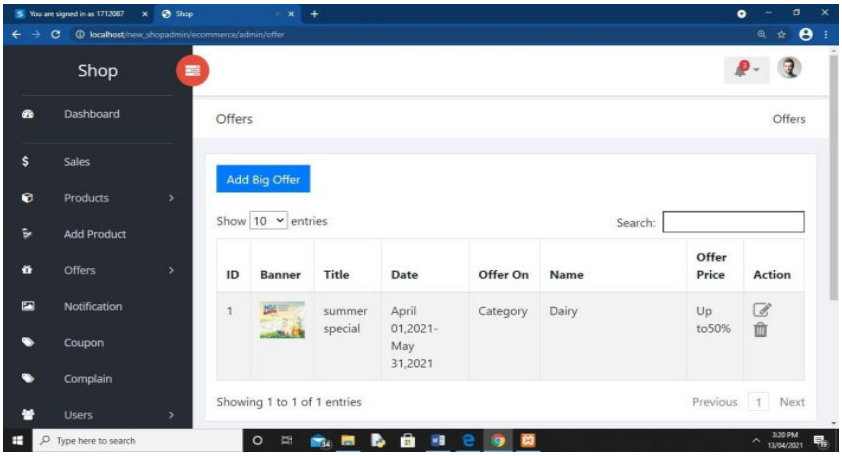

Figure 4. Offer Notification

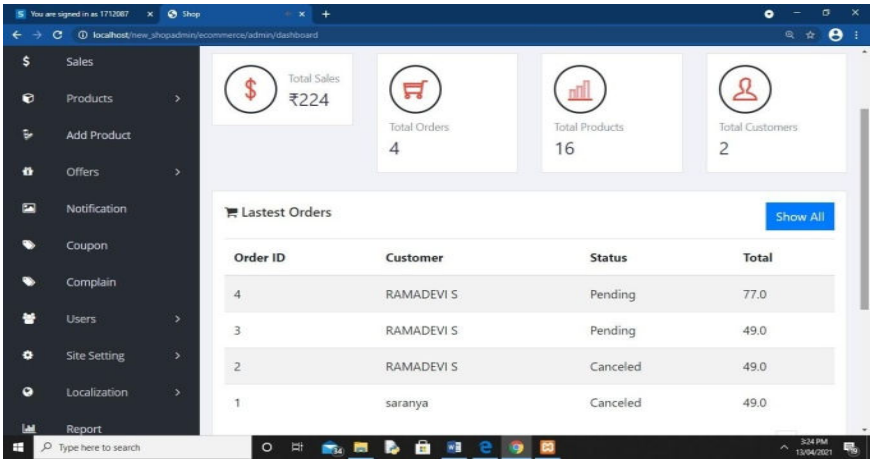

Figure 5. View customers Order

Figure 6. Scan Product using QR Code

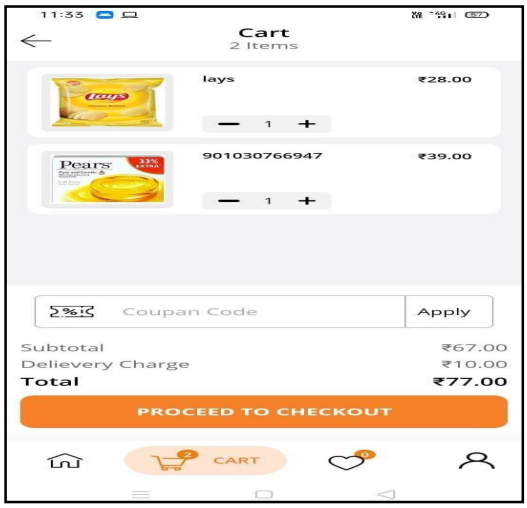

Figure 7. Add products to Cart and Proceed Payment

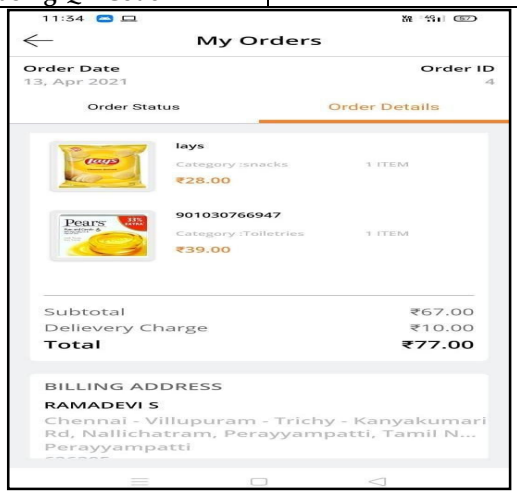

Figure 8. Order Status

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RESEARCH ARTICLE

Emotion Detection in Classroom Teaching

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ABSTRACT

At present, the one-to-many teaching is quite popular and implemented in all classrooms. This strategy is yet embraced among the vast majority of the instructing classrooms in current colleges. Restricted by the assets of instructors, the quantity of students in some fundamental courses could be all the way into the hundreds. In such circumstances, it is hard for educators or lecturers to take input from all the students right away. This paper proposes a framework dependent on the cluster camera to get outward appearances; identify the emotions of the students, and judge the instructing impact of the teaching process. This framework can help the educator handle the learning state of the students powerfully, with the goal that the instructing techniques or progress can be acclimated to accomplish better educating impact.

Keywords: Emotion Detection, Classroom teaching, HAAR classifier, Python

INTRODUCTION

Intellectual brain science shows that psychological handling and feeling preparing are coordinated at different levels in cerebrum [1].For instance, some cortical structures (for example or bito frontal cortex) coordinate psychological and feeling data in learning progress by communicating with neural designs of emotional processing (for example amygdala) [2].Drugs can decrease or expand the ruinous impact of nervousness on learning [3]. Experiments on animals explore have shown that the learning of the mouse will be influenced on the off chance that the amygdala preparing the first nonpartisan tangible sign into an undeniable passionate sign with appalling data [4]. The significant job of enthusiastic involvement with learning illuminates us that: students can learn and see all the more adequately with a homeroom climate which can prompt for positive feelings.

To more readily incite students' positive feelings, educators may need to get a handle on the students' learning states precisely. Be that as it may, in current classroom, particularly the fundamental courses, students are frequently packed to a large numbers, that make it hard for instructors to screen students' emotion in learning environment thoroughly. In any case, with the improvement of PC vision as of late, the precision of emotions dependent on face location has been persistently improved. Along these lines, it gives an amazing assurance to us to assemble a continuous input arrangement of students' classroom learning feeling. In view of the enthusiastic group of learning feelings, this paper explains how a camera can be installed in a classroom to obtain pictures of students. Then these images can be fed to the classifier to perceive feelings; sum up distinguishing proof data to give factual outcome and present the emotions of the students to the lecturer.

Emotions and its Types: An overall meaning of emotion is: emotion is an intricate condition of feeling that outcomes in physical and mental changes which affect our mind and then our body. These progressions can likewise influence thought and practices in our day to day life. Emotions are classified in various categories. Paul Ekman first and foremost classified emotions into six fundamental categories: Anger, Disgust, Fear, Happy, Sadness, and Surprise [5]. He additionally extended different feelings like Shy, Satisfied, Pride, Pleasure, and so on [6] Robert Plutchik [7] summed up eight unique feelings and their relationship through wheel of feeling. He Wei [8] set up a student feeling model dependent on three-dimensional feeling model, and measured the six unequivocal emotions.

Procedure: Emotion Recognition is done with the help of Open cv and Python. Open CV has a lot of face recognizer classes. The process is as such -

- Capture images of student
- Extract face from the images.
- Creation of Training set and classification set
- Identify the emotions of students
- Judge whether student has learnt or understood the concept via the emotion captured.

We are installing Open CV and Python language along with numpy in our PC.

Numpy –This is a package which works well with all programming languages and is basically used for mathematical calculations..

OpenCV-This is a software which is used to identify emotions of a student and in the end to identify whether the student has interest in the class. Various face recognizer classes are present in Open CV which is used to identify the face and the emotions. Fisher face algorithm is used to identify the emotion. Firstly the digital image of students is captured and kept in the source images folder. Then the python code is executed and it sorts the images according to the emotions. In this proposed system we need a digital camera to capture images and a personal computer. We are going use python snippet and Open CV. The advantage of python is that it works well with high level language.

HAAR classifier is used to detect faces. This classifier is based on Paul Viola and Michael Jones machine learning based algorithm. This classifier is trained several times with a lot of images and thus it starts predicting the classification. This classifier is used to detect objects in an image.

The overall procedure uses Viola-Jones Haar-like classifier is used to distinguish faces just as eyes and mouths. Distinguished features are trimmed, resized, and mean deducted; at that point PCA is performed. Utilizing the reduced dimensionality preparing dataset Fisher LDA is performed to extricate Fisher faces on which we can project test information. Moreover during preparing, eye and mouths are recognized utilizing Haar-like feature. Based on whether students are able to understand, we set up three classifications of emotional states for learning which are positive, neutral and negative. Later after identifying the emotions of students a questionnaire is distributed to the students. This questionnaire helps in identifying whether the student has understood the concepts and whether the emotion is related to the understanding.

Camera Installation: To progressively distinguish every student's understanding state, it is needed to recognize every students' head picture data continuously and capture images. In light of the chose cameras' visual point, goal, size of diverse classroom, students' number, the ideal camera establishment area can be plan out.

RESULTS AND DISCUSSION

The dataset was for 350 students .A questionnaire was distributed to all the students and their images were also captured and fed into the python snippet. Various graphs were plotted to identify the relationship between the emotions and understanding level. It was observed that majority of the students express positive emotions like joy when they understand a topic and are not able to control impulsive feelings in a class. They also express boredom and interest in the class. Students also express surprise if they discover some new concepts in the class. So this graph in figure 2 clearly depicts those students emotions are related to their understanding level. Scatter plots figure 3 , 4, 5, 6 were plotted among student depicting joy emotion when he understands a topic, surprise when a new topic is understood and confused/disgust/anger when students don't understand a topic. Here we could conclude that most of the students show various kinds of emotion in the class according to their understanding level.

CONCLUSION

Lecturers can improve student's concentration and interest by utilizing a few positive measures like playing, experimentation, demonstration, posing questions, group discussions. This paper presents a multi-camera-based feeling identification framework in classroom environment. The framework can recognize and record changes in students' emotions, and report to the lecturer in considerable time. By contrasting the consequences of ideal and non-ideal feelings, it is shown that the aftereffect of this framework can accurately mirror the genuine circumstance. This motivates us that instructors can progressively change the teaching plan as indicated by the framework. Additionally it gives reference to making changes in encouraging arrangement when students' feelings change, with the goal that the teaching quality can be improved.

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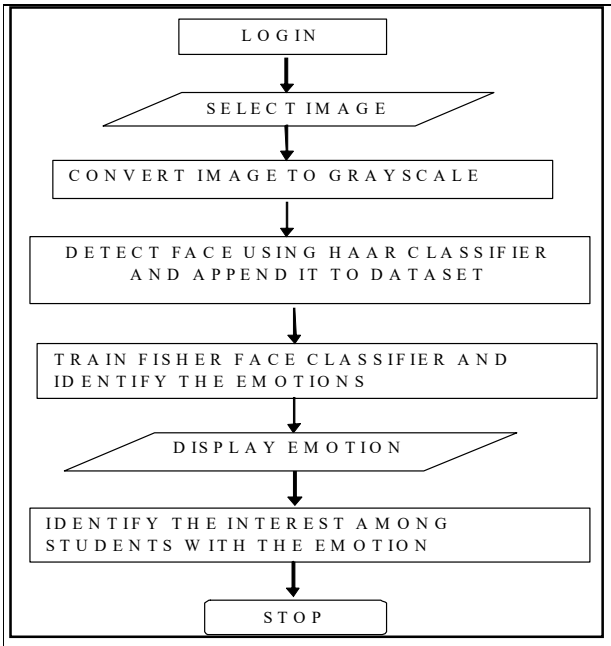

Figure 1 : Flowchart Of The Proposed System

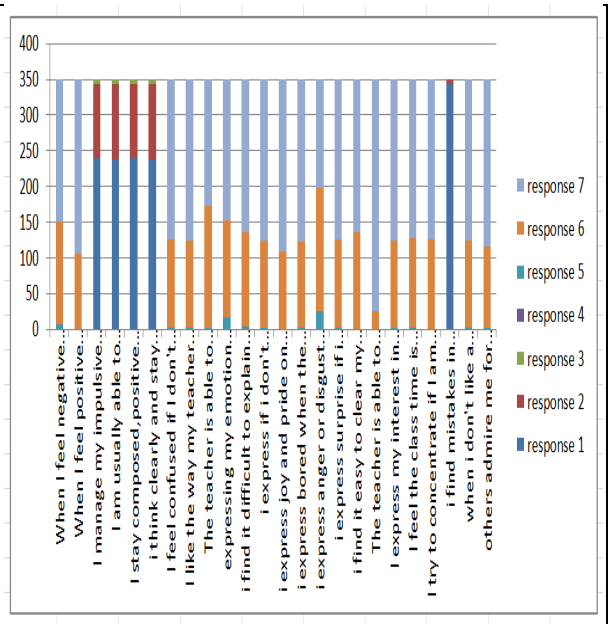

Figure 2: Graph Depicting Emotions And Self-Awareness Among Students

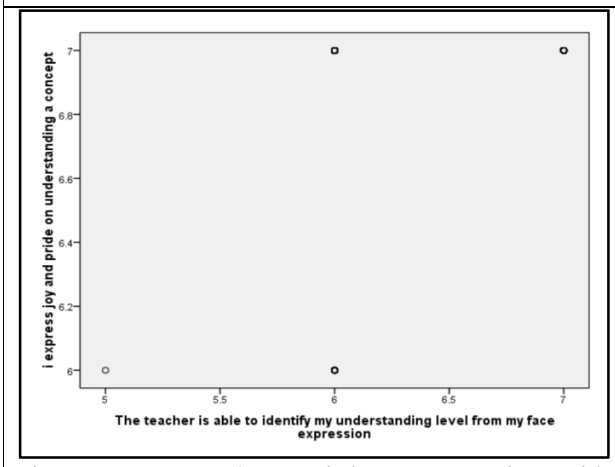

Figure 3: Scatter Plot Depicting Joy Emotion With Understanding

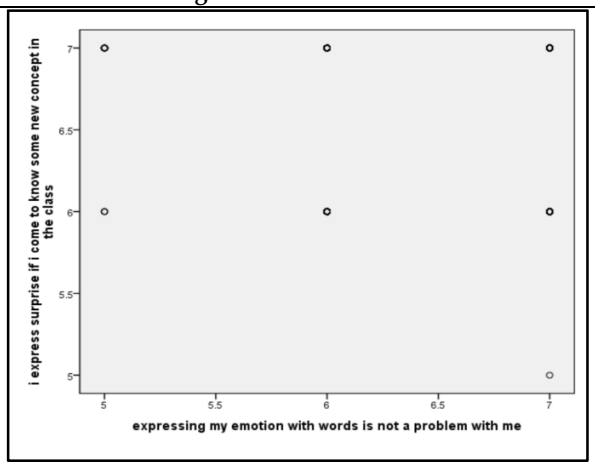

Figure 4: Scatter Plot Depicting Surprise Emotion On New Topic With Words Spoken

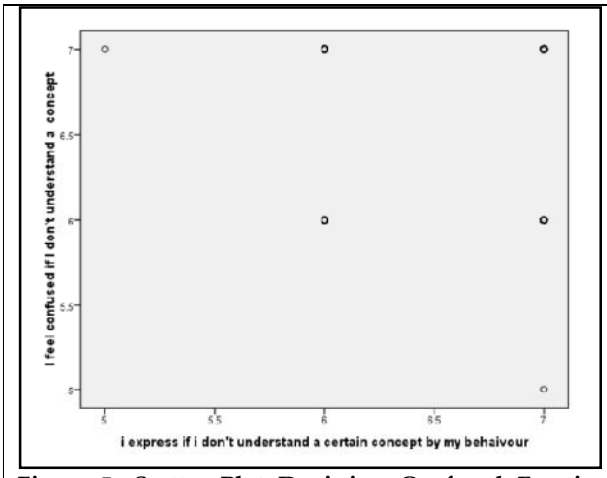

Figure 5: Scatter Plot Depicting Confused Emotion When Topic Is Not Understood

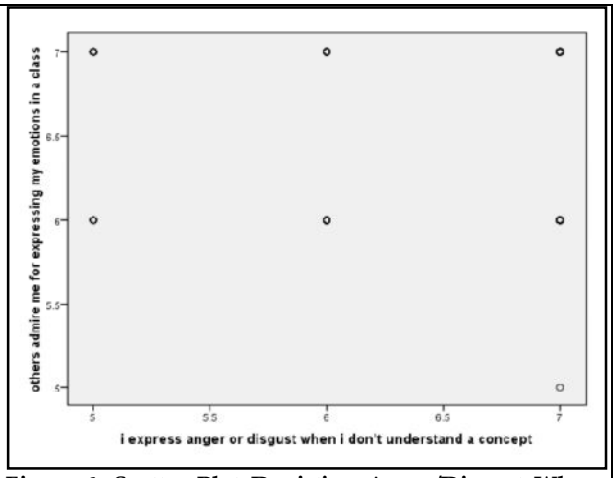

Figure 6: Scatter Plot Depicting Anger/Disgust When Topic Is Not Understood

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RESEARCH ARTICLE

Feasibility Analysis on Implementation of Enterprise Resource Planning (ERP) Packages In Small and Medium Enterprises (SME)

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ABSTRACT

This paper examines the environment which is feasible to implement ERP packages in Small & Medium Enterprises. The feasibility analysis was conducted in 40 Small & Medium Enterprise out of which 32 has reported. A structured questionnaire was administered for which the managers in the organization has answered it. Some of the key findings includes vender selection, opting for generic software, willingness to spend. The scope of the study includes application of artificial intelligence in decision making.

Keywords: ERP, SME, Feasibility study

INTRODUCTION TO ERP

Enterprise resources planning refers to combination of both system and software used to aid the smooth functions of organisational activities which involve primary activities managing human resources, financial activities, production planning of monitoring manufacturing, quality audit distribution of products and management of supply chain. ERP has the aid from both system and software support. The combination of both system and software helps the organisation to connect the communicate with the business process which includes [3].

1.Integration of company departments
2.Establishing communicate within organisation.

It also connects the external source like banks, customers, suppliers, government from the company departments as shown in Fig. 1. Thus, the smooth way of communications is established within the organisation and with external source. ERP is the smart system which integrates the department in the organisation along with the external source like vendor, supplier and banks. It comprises of centralized database where information is shared with various department. It monitors and keeps tracks on real time company operations. It is capable of generating various reports namely sales report, financial, labour turn over, employee performance report etc.

REVIEW OF LITERATURE

Economic development in a country is very much dependent on regional development which includes small and medium enterprises, some of the critical success factor of implementation depends on in-department interview and observation of organizational requirement, change in management practices, provision of training are some of the successful implementation factors [1].There is a vast change can be seen while implementing ERP in small and medium enterprises while compares to large organization. Some of the finding indicate educating and training the employees, framing of high power project team with best IT service engineering skills [2,4].

Implementation of ERP is costlier for any organization which require to go for socio – technology endeavours. Affordability of the organization has to be considered while going for implementation. most of the organization adopt existing Enterprise Resource Planning software's for the sake of saving the cost , many ERP packages are validated by the SMEs for module confirmation[3].This paper examines post implementation of ERP based on the 3 quality dimension which includes system quality , information quality and service quality has important place in post implementation analysis [5].This paper compares the traditional ERP with technologically driven ERP. Earlier packages were designed for larger organization and now it is focusing to serve small & medium enterprises. The business process and workflow of different business have driven a demand for it irrespective to large, small or medium enterprises.

Enterprise Resource Planning

ERP is evolved in many forms and its adopted and implemented according to the company names. The implementation process rigorous study and only after that it can be successfully implemented.
Some of existing forms ERP are

1. The premises ERP
2. Cloud based ERP
3. The hybrid ERP

This study is intended to the implementation of ERP system in the organisation which is having the Net worth of less than 1 crore. As the business formats are transforming from traditional model to the adoption of modern technology, so does the operation and business flows. The primary transformation occurs in the way of connecting the various department in the organization with the external factors which also contributes or influences the business operations. The transmission occurs for the betterment and here comes the crucial role of ERP system which integrates various departments [1].When it comes to implementation of ERP there is a wrong assumption that is suitable for bigger organisation and it is difficult for small organisation to adapt it. Another reason for such assumption is scalability of operation [6]. In order to study the feasibility for implementing ERP in SME, certain questions are framed in data is collected from the SME of Coimbatore city. The responses given by this enterprise is given some insides regarding the opinion of implementing the ERP in the organisation. First of all the concept of ERP has to be studied which includes study of infrastructure of organization. The study of implementation starts with answering the following questions. most of the questions comprises of the awareness level of Enterprise Resource Planning [2].

RESEARCH METHODOLOGY

The total number of organizations taken for the study is 40 and the response was received from only 32 organisations. The above questions were asked to the middle level managers who were trained in using the packages and who were all responsible for implementation,

Findings

Some of the key findings includes

Interpretation

Findings indicate some of the key insights like: Awareness of system integration software and is known to most of the respondents (Table1), the respondents are aware of the popular ERP software in the market (Table 2), What ERP package the company has implemented (Table 3).It also gives the information on what kind of ERP system is implemented and whether it is a generic or customized one(Table 4). The study also provide information of the awareness of some popular ERP packages among the response were tally and Microsoft NAV has been known to all of the response (Chart 1). The study gives the rough idea about how much the company is ready to invest in ERP packages (Table 5). Many of the response of are not ready to invest more than 60,000. It also gives information on duration of usage of ERP (Table 6). The Fig 2indicates some of important issues faced by the small and medium enterprises which implement in ERP. The issues listed out are both micro and macro level issues are the ones which occurs within the organization. Some of the issues includes: Investor budget for ERP, how much money the company is willing to speed for purchasing ERP packages. Another issue is the selection of ERP or choosing the right vendor who can give the suitable module according to company needs. Training the employees will be tedious task initially, as they are prone to exhibit resistance for learning the software and another technical aspect of the software [5]. Macro level organizational issues includes volatility of business profits will affect the implementation cost of the ERP as well as the budget allocation of the company. Scalability of usage of ERP software and determining the usage of software. It depends on both internal and external use ability of the software.

Choosing the right vendor contributes 90% of solution for problem in vendor support. Vendors with wide experience and could reputation and customer good will place crucial role in choosing the right vendor. Future up gradation to new version helps in enhancing the utility of ERP software in long run. It is the duty of vendor to provide security patches and software updates from time to time. The above standard issues are some of the practical problems faced by the companies. While implementing ERP are some of the aspects in which any organization as to prepare ahead with these aspects. This study can be used for making decision for ERP implementation it also support the organization feasibility to study before deciding to go into implementation. It helps to study both existing internal and external environment by considering some of the critical factors.

CONCLUSION

There are large number of resources available but it requires a great deal of time and analysis to seek out critical factors which contributes to the successful implementation. In future more advanced factors or modules can be added up to the ERP package where it is ready to handle robust data and has ability to solve the organization work flow. Artificial intelligence also plays important role in enhancing the ERP software, where it is capable of taking decision to the critical problems.

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Table 1: Integration Module

Awareness of system integration of business management.	
Yes	20
No	12

Table 2: Awareness of ERP

Awareness of ERP – enterprises resource planning	
Yes	30
No	2

Table 3: Packages

ERP packages known	
Tally ERP	27
SAPERP	3
MICROSOFT	2

Table 4: Customised or Generic

ERP packages customised or generic	
GENERIC	32
CUSTOMISED	0

Table 5: Willingness to Invest

Companies' willingness to invest in Enterprise Resource Planning	
BELOW 60,000	29
60,000 to 2,00,000	3
2,00,000 to 10,00,000	0
10,00,000	0

Table 6: Usage

Duration of ERP usage	
Not implemented	5
Less than 2 years	27
Less than 10 years	0

ANNEXURE

Table 7: Questionnaire

S.No	**Questions**
1	Are you aware of system integrated way of managing enterprises? Yes No
2	Are you aware of the concept ERP enterprises resource planning? Yes No
3	What ERP package is your company has implemented _____ Yes No
4	Is the ERP package is customised or generic software? Customised Generic
5	Are you aware of any of the ERP packages? a) SAP business one ERP b) Tally ERP c)Sage ERP d)Marg ERP e) Strategic ERP f) Epicor ERP g) Microsoft dynamic h) All the above
6	How much does your company ready to spend on ERP implementation, price ranging from? Below 60,000 60,000 to 2,00,000
7	Is the training provided to the employees are adequate? Yes No

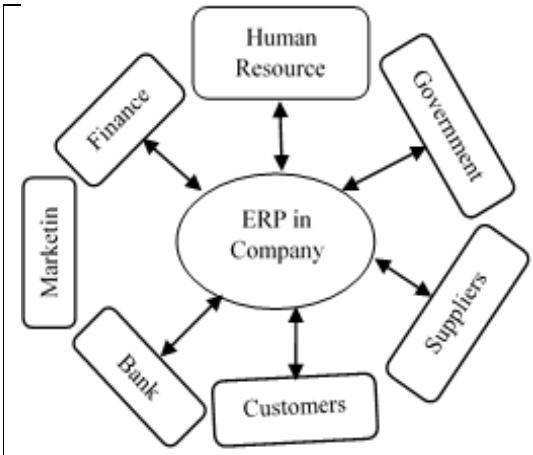
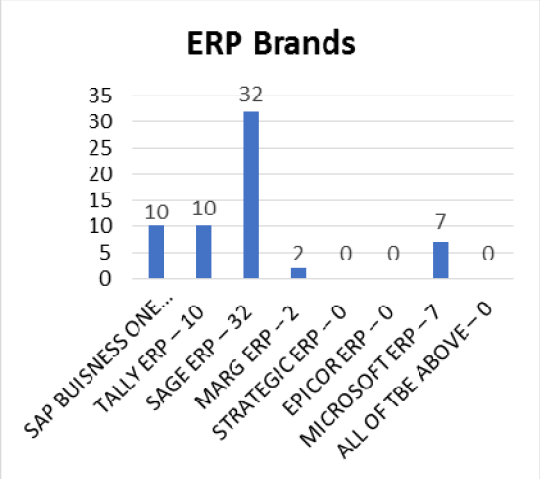


Figure 1: ERP Integration

Figure 2:Small and Medium Enterprises Implementation Issues



Graph 1: ERP Brands

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RESEARCH ARTICLE

Privacy Model For "Like" Button on Facebook

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ABSTRACT

The "Like" button is the most effectively perceived feature of the Facebook. We can "like" pictures, status updates etc. using this feature. "Likes" can show sensitive private data such as our characteristics of personality, IQ, ethnicity, gender, how pleased we are, and whether or not we use addictive drugs etc. Misusing the sensitive personal information of the Facebook users increases people's privacy concerns. This paper presents a privacy model for "Like" button on Facebook that enforces a user's private data security technically. The implementation of the privacy model for Like button in the Facebook, Privacy Enhancement Tool has also been discussed in this chapter.

Keywords: "Like" button, Privacy risks, Privacy model, Facebook Privacy Enhancement Tool.

INTRODUCTION

The Facebook Like button is a function that enables users to positively acknowledge a post, image, or video without participating in any meaningful form of conversation or dialogue. It enables users to express support for the images, statuses, comments, wall posts and fan pages. The "Like" button added in February 2014 enables users to express their content fulfilment without having to comment in writing. While the websites initially given users the chance to become a supporter of them, in April 2010, Facebook replaced this choice with a "Like" button. The "Like" button also reveals the number of users who liked every part of the content. [Techtarget, 2019]. The sensitive personal information about us can be revealed by our "likes." Such private data will be disclosed to unknown users of Facebook when we "like" a post. As a consequence, the users of Facebook are exposed to various privacy hazards. The privacy model which is suggested in this paper enables regulate who can see his likes by the Facebook user.

Thus the Facebook users' privacy could be enhanced. This paper also presents the implementation of the privacy model.

Privacy Risks of Facebook "Like" Button

The "Like" icon is a feature on the Facebook that significantly influences our privacy. Facebook "Like" icon is an easy Facebook user-friendly "thumbs-up" icon. However when we press the "Like" button, all our likes would be placed on all our friends' newsfeeds. These readily available digital documents of our behaviour can be used by Facebook users to obtain sensitive private data relating to us. Moreover, we do not want to share such sensitive private data even with our close friends. Facebook "Likes" pose severe hazards to the privacy of the users [Francesco Buccafurri, 2014]. Mark Zuckerberg, Chief Executive of Facebook, launched the "Like" function button that could be easily placed on web pages. Facebook users can press "Like" in the other websites also. Facebook monitors individuals by switching their "likes" from one page to another. Liking something or someone has spread to distinct websites beyond the boundaries of Facebook. "Liking" shows the purchaser's satisfaction with the item or substance. "Likes" reveal more information in relation to us. "Likes" of the Facebook users turn into a prime data source. "Likes" also predict psycho-demographic profiles of the users. "Likes" of Facebook users in News Feed also reveal more information about them.

Facebook "Like" button can be found in almost every popular website. A great many individuals press "Like" button each day, uninformed of the full results. Nicole Ozer, an attorney with the ACLU of Northern California says that "If you put a Like button on your site, you're potentially selling out your users' privacy even if they never press that button". Nicole Ozer also includes that "If an organization puts a Like button on their site, they're potentially telling Facebook about everyone who visits their Web site, every time that person visits their Web site". Whenever a Facebook user clicks on the like button, it reports the details of the pages to the Facebook. The websites which are visited by individuals could be easily collected by Facebook using the reports. Facebook can easily track the URL of web pages visited by individuals and the IP address of individuals - tapping on the Like icon isn't required, regardless of whether the guest isn't a Facebook client or isn't signed in. On the off chance that enough destinations take part, Facebook can without much of a stretch gather a tremendous measure of information about Internet clients' perusing propensities. Facebook "Like" icon allows the users to share their opinions about the products which they preferred. Users who clicked on "Like" catch for certain products could see their private data used to promote such products. Various privacy models have been presented to implement the protection of the individual data of a client [N. Jayalakshmi, 2016]. But in order to address the privacy issues raised by the Facebook "Like" button, a privacy model has been suggested.

Proposed Privacy Model for "Like" Button on Facebook

The content that we posted on the Facebook, could be concealed by us. However, when a Facebook user likes on a companions' photograph, that companion controls that who can see his "likes". By placing the cursor on the privacy of the photograph, it will at that point unveil who can see that photograph. In the event that it says:
Public - Our likes could be viewed by any user of Facebook.
Friends - Our likes could be viewed by the friends of the user who posted that photograph.
Friends of Friends - Our likes could be seen by the friends and friends of friends of the user who posted that photograph.

Our likes can uncover the delicate individual data relating to us. When a Facebook user likes a post, (with the privacy preferences Public, Friends or Friends of Friends) it would be revealed to the other users also. It leads to critical users concerns over their privacy [N. Jayalakshmi, 2015]. We cannot regulate the viewers of our likes on Facebook. In any case, the suggested privacy model allows the Facebook client to regulate who can view his likes. Figure 1 demonstrates a suggested Privacy Model for Facebook Like button.

As indicated by this model, the user A uses the privacy setting private to send a friend request to user B. The user B accepts a friend request with the privacy setting private and uploads some photos. The user A likes the photos which were uploaded by user B. If the user A sends a friend request with the privacy setting public, depending on the privacy setting of the photo, his likes would be viewed by other users. If the privacy setting of the photo is public, his likes would be viewed by any one on Facebook. If the privacy setting of the photo is Friends only, all the friends of user B can view the likes of user A. As the user A chose the privacy setting private, his likes on photos would only be viewed by user B even though the privacy setting of the photo is public. His likes cannot be seen by others without his permission. Thus it improves the privacy of the users. "Like" button privacy model is shown in figure 2. As the user A chose the privacy setting private, his likes on photos would only be viewed by user B even though the privacy setting of the photo is public. His likes cannot be seen by others without his permission. Thus it improves the privacy of the users. "Like" button privacy model is shown in figure 2.

Implementation of the Proposed Privacy Model

The proposed privacy model is implemented in the Facebook Privacy Enhancement Tool. A profile of the Facebook user Ram is created using the tool. Figure 3 shows the setting up of a profile. Once the profile is created, the user Ram is sending friend request to another user Kavitha with the privacy setting private. Figure 4 shows the privacy settings of send request. The user Kavitha views the request and confirms it. She is uploading a photo. Figure 5 shows uploading a photo. The user Ram likes the photo. As the privacy setting of send request is private, the likes of Ram would only be viewed by Kavitha. Despite the fact that the privacy preference of the photograph is public, other users can not view the likes of Ram. Thus, the Facebook Privacy Enhancement Tool secures the private data of the Facebook users. The likes viewed by the other user Raja is shown in figure 6.

CONCLUSION

This paper initially clarifies the distinctive hazards of "Like" icon on Facebook. Our likes reveal sensitive personal information about us on the Facebook. These sensitive data can prompt privacy floats, for example, harming the notoriety and noteworthiness of the client. The principle objective of this chapter is to suggest a privacy model for "Like" icon on Facebook that protects the private data of the clients and to implement this model in the Facebook Privacy Enhancement Tool. With the interpersonal interaction assaults expanding step by step, usage of this proposed model will definitely lessen the quantity of private data taking and spillage occurrences.

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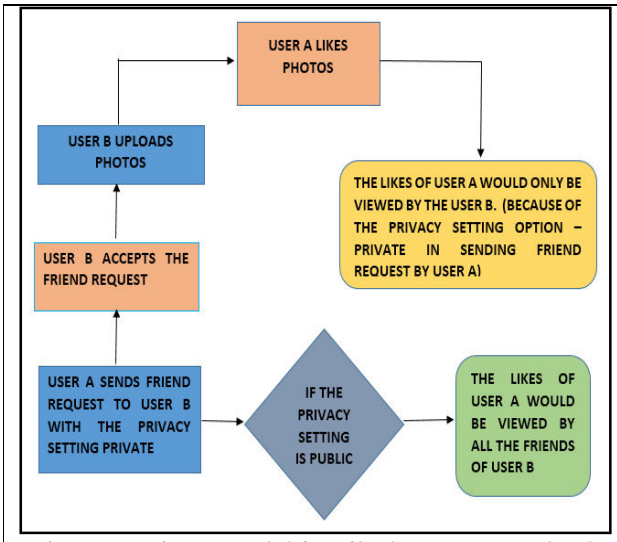

Figure 1 : Privacy Model for Like button on Facebook

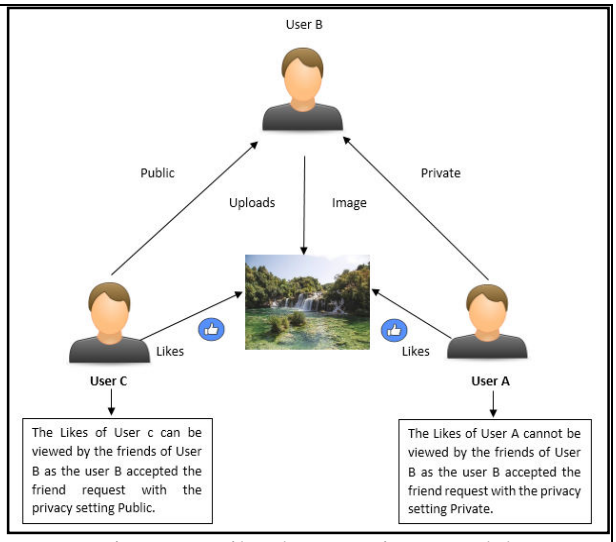

Figure 2 : "Like" button privacy model

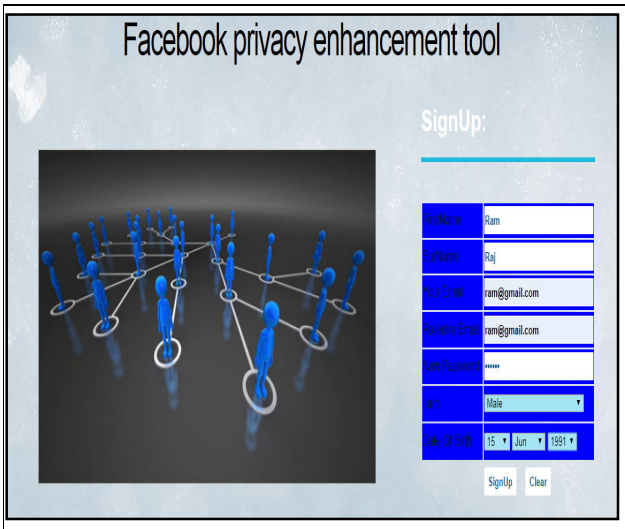

Figure 3 : Setting up of a profile

Figure 4 : Privacy setting of Send Request

Figure 5 : Loading a Photo

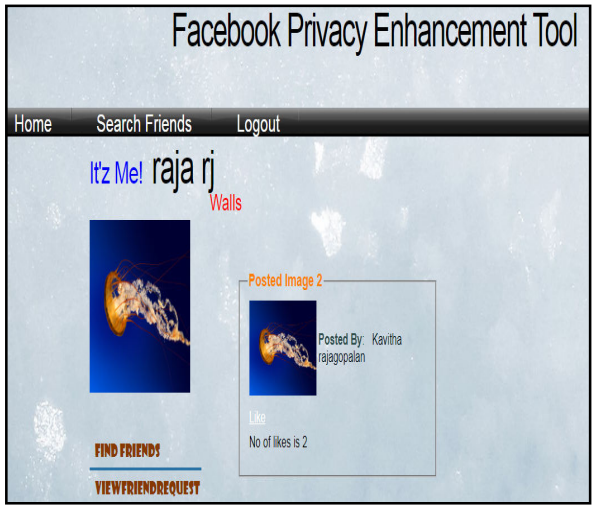

Figure 6 : View Likes

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RESEARCH ARTICLE

An Evaluation of Potential Threats of Ransom Ware Attacks

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ABSTRACT

Ransom ware in recent years has turned to be the highest extortions to strike the business. Ransom ware is a category of malignant program's which is planned to an deny entry to a machine or certain files as far as some ransom is paid to lift the restriction. Financial gain is the main motive behind these attacks. Usage of ransom ware encourages more criminals to exploit victims. As the attacks become epidemic, the payoff to criminals also increases. Most affective fashion of restraint is encryption of significant factual information on networks or software systems that allows the assaulter retain user data. This paper presents some important issues related to ransom ware attacks, analyses the algorithms used in launching ransom ware attacks and does an experimental evaluation of the proposed method.

Keywords: malware, ransom ware, WannaCry virus, NotPetya, encryption, decryption, hybrid algorithm

INTRODUCTION

The new-fangled cryptography uses cosmopolitan mathematical algorithms and secret keys for encryption and decryption. Encryption is used to secure electronic transactions like bank details and digital transactions. Digital signatures are replaced by handwritten signatures or credit card authorizations and publickey encryption provides secrecy. Ransom ware is a type of malignant software's which is designed to an deny access to a machine or certain files up to the payment is done. So, if the victim denies to compensate the assault the access to his system and data is further not obtainable. Shortly after sometime the ransom ware high-risks rose as the cybercrime found much variant vulnerability for corrupting this malware. Ramifications of a thriving assault are more expensive than the malware's

expense. Companies endure lost turnout, undergo losses, hindrance caused to customers and also prospective loss of data permanently. These can be caused from a simple probing port scan to sophisticated malware attacks. Even though intruders get a lot of attention, most of them use this to make money as soon as possible. But this crime is many a times safer than a robbery, with an advantage of no weapons, not getting caught, disguises, no risks at all. Some of the prone sectors to this attack are health care providers, educational institutions and legal firms. Figure 1 shows an overview of the process for a ransom ware attack.

Related Works

The attack vector of the ransom ware is more interesting than the ransom ware itself. The Wanna Cry is a malicious ransom ware worm that hastily spreads through several number of networks. The susceptibility that Wanna Cry exploits lies in the Windows implementation of the Server Message Block (SMB) protocol. Petya and Not Petya are the malwares which ambitious in encrypting the hard disk of infected computers, but initially the Not Petya was just seen as a variation on a theme. But it has much more available tools to help it infect and attack hardware. Petya is a usual piece of ransom ware which is ambitious to make few swift Bitcoin from victims targeting only windows computers. The abstraction of data from the system is highly threatening. The major ransom ware attacks among all are the Petya ransom ware attack [1]. If one agrees to the request which triggers Petya to reboot your system. After this you see is a normal window which appears after the system crashes This only could encrypt files <100MB. It uses AES and RSA encryption. Crypto locker emerged around 2006 which eventually enters the organisation by emails. If the user clicks on the executable files, it immediately starts to scan the network drives, renames all the files & folders and encrypts them. As ransom ware attacks emerged recently there is lack of awareness about its affects. This malware initialises by directing e-mails which has this scornful code that affects the system. Once the attachment is downloaded and open it the working of this malware starts abruptly which gains access of the victim's system to a remote attacker's machine. In order to avoid the effects of ransom ware few methodologies must be accompanied such as- to the windows system, the institutes and organisation must apply patches [2][3].

Bitcoins are crypto currency which can be sent from one user to another user on the peer-to-peer Bitcoin network without the need for intermediaries. These networks are quick, stable, and verifiable. The attacker can confirm through the public block chain when a victim has made the payment; she can make a distinct payment details for each victim and self-operates the process of unlocking their files upon a confirmation of bitcoin transaction to that distinct detail. As now cyber criminals moved from cyber vandalism to cybercrime as a major business, ransom ware emerged as the go-to malware to feed the money-making machine [4]. Backing up significant data regularly is one of the best ways to secure data which can reduce the effects on the recovery process and also system loss . The backed-up data must be stored on a system which is out of reach of networks. Beware of attachments in the unprompted URLs, links and e-mails. Update antivirus systems on all the networked systems. Download software from trusted websites exceptionally free software. For operating systems and web browser enable automated patches. It is feasible to develop a functional security mechanism that can avoid a large number of ransom ware attacks, including those that use advanced encryption capabilities, by monitoring suspicious file system behaviour [5].

METHODOLOGY

Enhancing online security in anyway meaning reducing the threats to zero, but you can plug the main gaps to reduce the largest potential issues. Changing social media settings which allow access for direct connections only. Beware of your activities online and while login with other devices. Even the largest cloud providers are hacked on daily basis. Smart protection practices as in the password which are used to secure your accounts must be complex and not easy to guess by the hacker. Usage of anti-malware software which has to be given equal preferences as the anti-virus software. Anti-virus software can prevent malware but not all of them. Malware bytes can be used to secure these and updating for latest versions is ideal. Regularly backing up your data is the most efficient way to avoid future risks by such attack. Also, the hardware used for backup must be out of networks. Among the network of systems,

one system must be allotted to monitor other systems in the network. This must monitor any suspicious activities in the networks [6]. Ransom ware also has grabbed the attention of cloud service providers and its users, as it is effortless to pervade malware to victim as an intruder. Assaulter with comprehensive platforms encourage ransom ware to grow extensively in wide domain. Therefore, it requires for a user to know the functionalities of these attacks and their working. Figure 2 demonstrates the block diagram of entire process encryption and decryption. The first thing ransom ware does is it sneaks into your system and find files for encryption. It then spots the files; this program then encrypts them using python programming. The actual files are vanquished with encrypted bytes. Invisible payment instructions exist which needs to be found. Usually, this malware gives every detail as to how to acquire a "decryptor" to retrieve the files after decrypting them. Besides some shared network resources, there are extended features which are not utilized and are hidden. Figure 3 depicts the methodology implemented in this paperto analyse the ransom ware attack. The proposed algorithm to demonstrate the process of encryption and decryption of these ransom ware attacks is given below .

Algorithm1: Encryption and Decryption In Ransom Ware Attacks.

Step 1: First a 128-bit key know a session key is generated by the sender which is later going to use to encrypt and decrypt the data (symmetric).
Step 2: Sender then encrypt the 128-bit key known as session key using asymmetric (public key) will be used to encrypt the session key.
Step 3: Now the encrypted key will be transmitted so that no one can intercept the key.
Step 4: The receiver receives the encrypted session key and decrypt the session key using asymmetric (private key) to decrypt the session key.
Step 5: An AES encrypted verification message will be sent to the sender to ensure that the correct key is received.
Step 6: Then the sender encrypts the data using the session key (for symmetric).
Step 7: The receiver receives the encrypt data and decrypt the data using the available Session key.

RESULTS AND DISCUSSION

To implement this hybrid algorithm, python code was run in the terminal which the prompts the choice to encrypt or decrypt. The name of the file to encrypt / decrypt. Need to be specified in the encryption process the code will ask the user to enter a custom password and it will create an encrypted file of the same name concatenated with the keyword "encrypted". The encrypted file will have 16bytes and remaining will be the encrypted characters. For decryption, enter the file name to be decrypted and enter the same login credentials. if the credentials match the file will be decrypted. The below Screenshots depicts the working demo of the methodology of hybrid encryption implemented in this paper.

CONCLUSION

The paper analyses the concept of ransom ware and their affects and to make aware of what can be the preventives measures. So, there are many ways for a ransom ware to affect our data it can be either by hardware devices, software issues, or even through shared networking. This approach can be widely used among small scale industries to secure their data from these ransom ware attacks who cannot afford to expensive methodologies. Integration of the proposed methodology with enterprise content management solution and block chain technology on a secure solution to mitigate ransom ware attacks. Samples of ransom ware can be collected, analysed and their behaviours can be monitored from which a suitable software can be developed to look up to these attacks.

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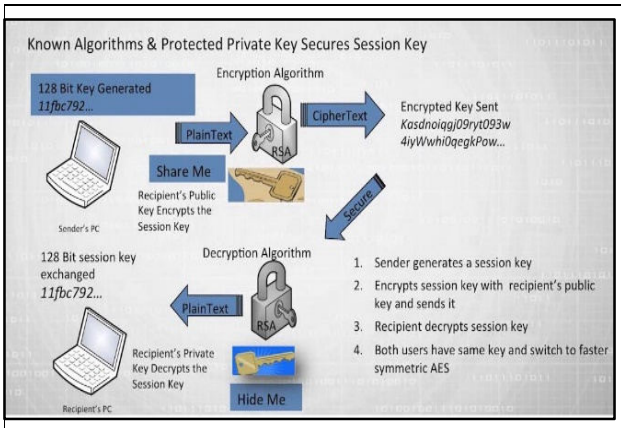

Figure 1: Ransom ware Attacks

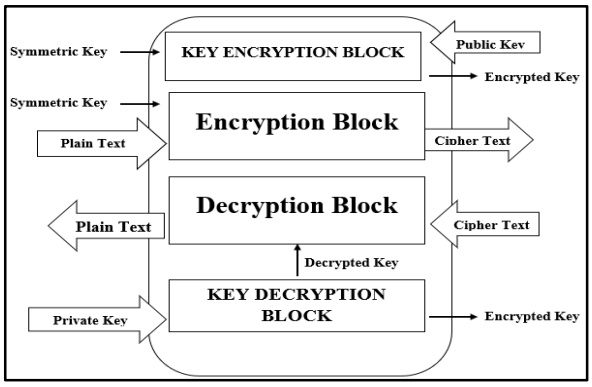

Figure 2: Block diagram of encryption and decryption of the ransom ware attacks

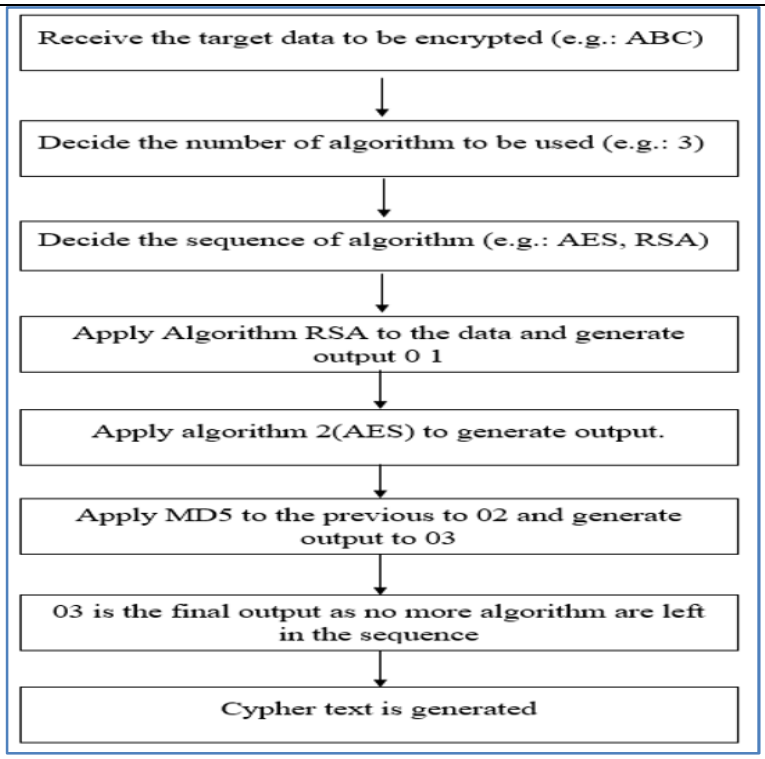

Figure 3: Flow chart of Encryption and decryption process

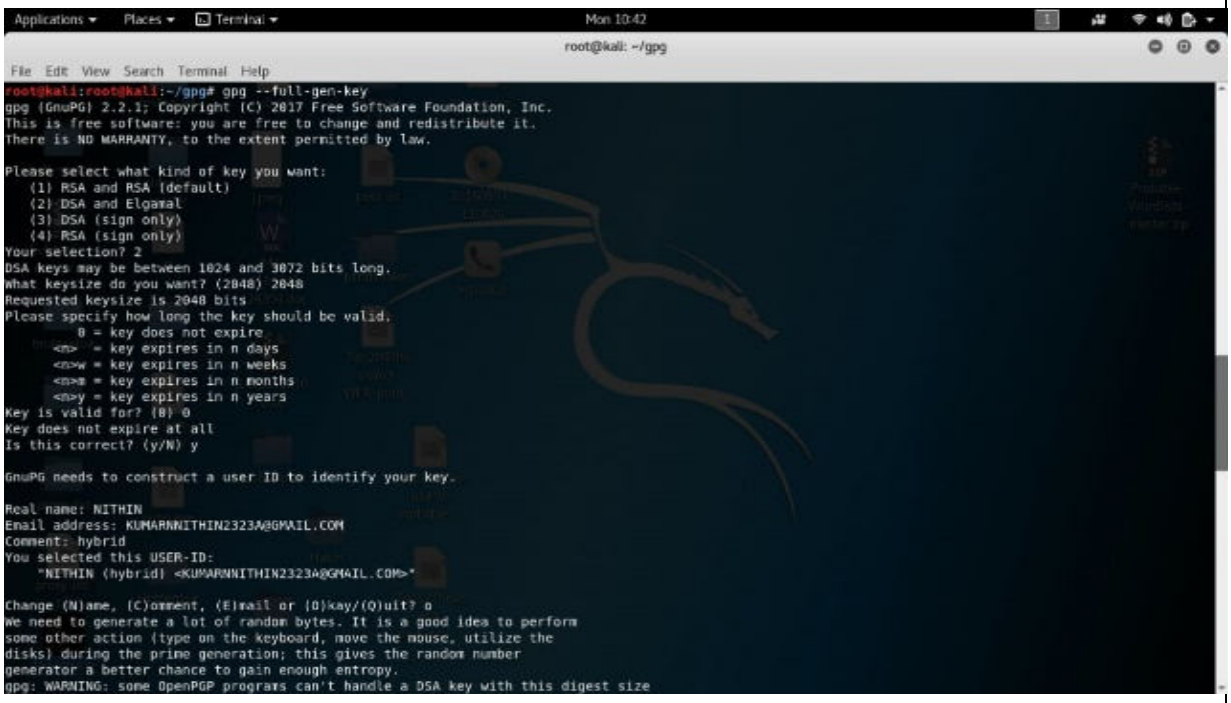

Figure 4: Contents of the text files that we are encrypting now.

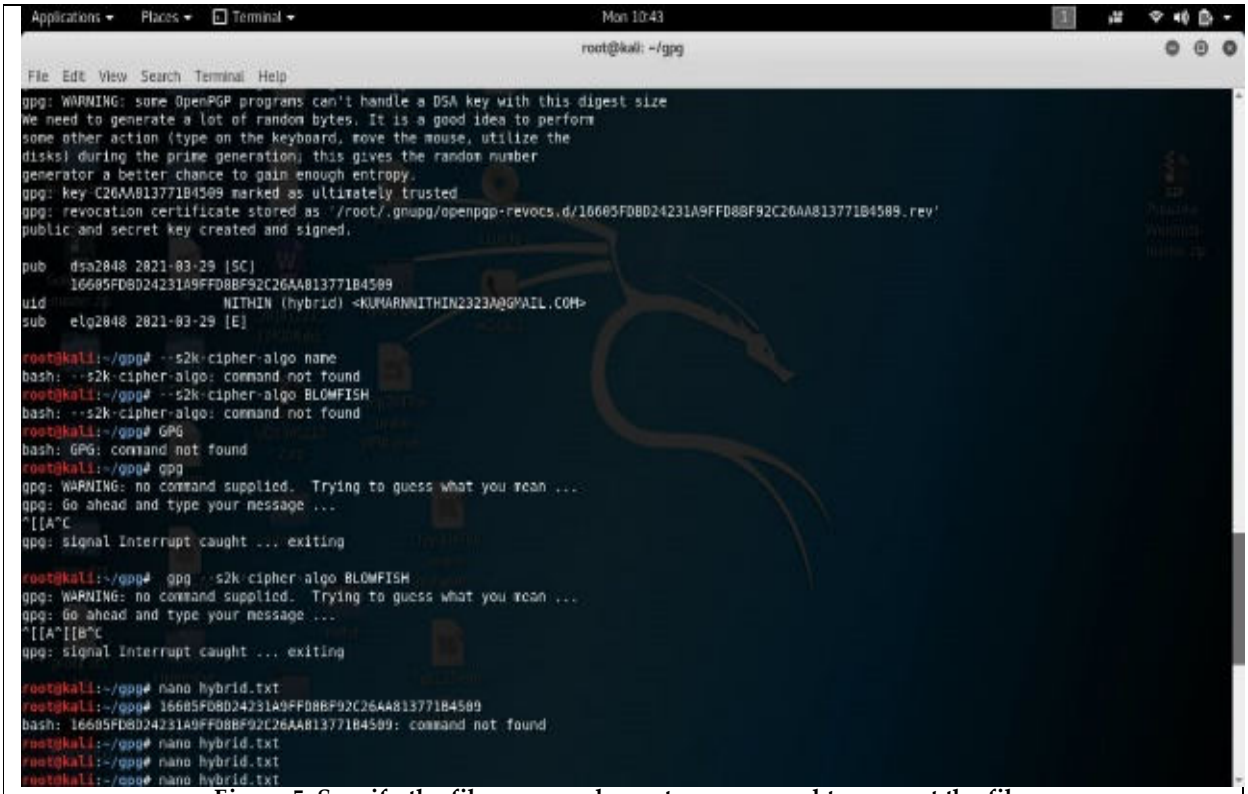

Figure 5: Specify the file name and a custom password to encrypt the file.

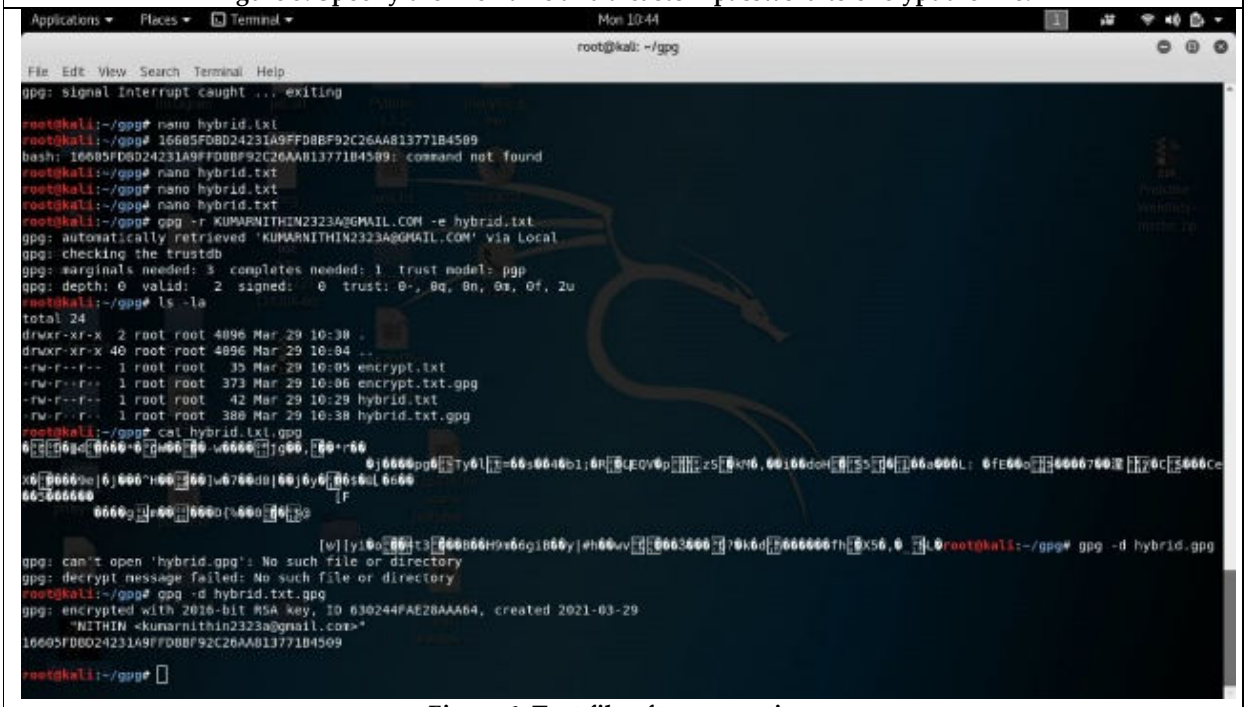

Figure 6: Text file after encryption.

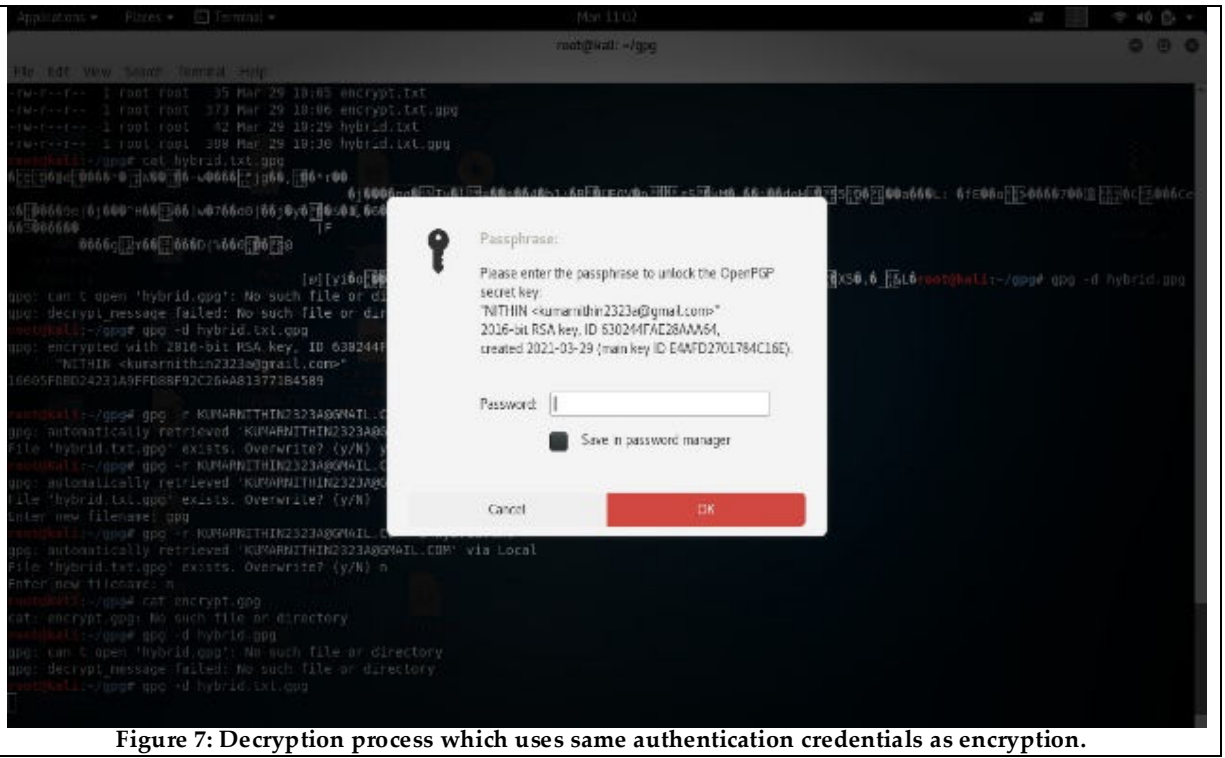

Figure 7: Decryption process which uses same authentication credentials as encryption.

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RESEARCH ARTICLE

Cyber World

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ABSTRACT

This paper presents a Web Based attacks which is a part of Cyber World. It is all about how attackers can misuse the website or web application and how attacks can be prevented from attackers[1]. It consists of various attacks like SQL Injection Attack, File Inclusion Attack, Cross-Site Scripting, DoS, Brute Force, Dictionary attack, Session Hijacking, Man in the Middle (MIM) Attack, Phishing, Spear Phishing, Whaling.

Keywords: This paper presents a Web Based attacks which is a part of Cyber World. It is all about how attackers can misuse the website or web application and how attacks can be prevented from attackers [1]. It consists of various attacks like SQL Injection Attack, File Inclusion Attack, Cross-Site Scripting, DoS, Brute Force, Dictionary attack, Session Hijacking, Man in the Middle(MIM) Attack, Phishing, Spear Phishing, Whaling.

INTRODUCTION

Cyber security can be defined as to protect data, computers, networks, programs from attackers or from unauthorized content, so attackers will gain the targeted information. We need cyber-security, because everything is going on the web and the main computers will be connected to the internet.
Cyber security is classified into two types:
*Web based attacks
*System based attacks
Web based attacks can be performed on website or web application.
System based attacks can be performed on computer or computer network[2].
This paper describes about web based attacks and how it can be prevented.

They are:

- Injection attack.
- File Inclusion attack.
- Cross-Site Scripting
- DoS
- Man-In-The-Middle(MITM) attack.
- Brute Force
- Dictionary Attack
- Session Hijacking
- Phishing, Spear Phishing
- Whaling.

Literature Survey

Web Security plays major role in application deployment and has a lot of challenges and complexity. The web developers may not be to implement or fulfill the security practices. Web based attacks use malicious code to manipulate the web application or website where attackers gain the information which is needed [3]. Security is the most important for web application or website, so that we can protect data against theft or malware.

Working of the Project

We have chosen different types of web based attacks like:

Injection Attack means where the data is inserted to website or web application, so that it will manipulate whole web applications. There are different types Injection attacks like: SQL Injection, XML Injection, Code Injection, Log Injection etc [4].

- The most frequently used attack is SQL Injection(SQLi).
- SQLi can be corrected by validating the data for input and output.
- SQLi can be prevented by using:

***Parameterized Query**

Snippet code for Parameterized Query

```
Protected void btnGetEmpbyName_click(object sender, EventArgs e)
{
 String cs = ConfigurationManager.ConnectionStrings["DBCS"].ConnectionString;
SqlConnection con = new SqlConnection(cs);
SqlCommandcmd = new SqlCommand("SELECT * FROM [Sample].[dbo].[tblEmployee] where Name=@Name", con);
cmd.Parameters.Add(new SqlParameter("@Name", txtid.Text));
con.Open();
GridView1.DataSource=cmd.ExecuteReader();
GridView1.DataBind();
con.Close();
}
```

***Stored Procedure**

Snippet code for Stored Procedure

```
protected void btnGetEmpbyName_click(object sender, EventArgs e
{
 String cs = ConfigurationManager.ConnectionStrings["DBCS"].ConnectionString;
SqlConnection con = new SqlConnection(cs);
```


```
SqlCommandcmd = new SqlCommand("sp_GetEmployeeByName", con);
cmd.CommandType = CommandType.StoredProcedure;
cmd.Parameters.Add(new SqlParameter("@Name", txtid.Text));
con.Open();
GridView1.DataSource = cmd.ExecuteReader();
GridView1.DataBind();
con.Close();
 }
```

File Inclusion Attack

- File Inclusion Attack means, where attacker will be able to access data which is sensitive or unauthorized which is obtainable on web server and it uses include functionality.[5]
- File Inclusion Attack can be categorized into:
  - Local File Inclusion: means where files can be obtained locally on server.
  - Remote File Inclusion -> means where it includes & executes the unauthorized code on remotely hosted file.

File Inclusion attack can be prevented by:

- The database can contain the file path and those file path can be assigned to ID. So, users can see their ID but they can't change or view path.
- The higher authority can restrict specific files.
- Instead of storing all the data which is related to files on web server it can be stored in database.

Cross-Site Scripting

- Cross-Site Scripting is executed in the client browser by editing JavaScript in web applications.[6]
- Cross-site scripting is classified as:
  - **Reflected XSS Attack**: where the current HTTP request will contain malicious script.
  - **Stored XSS Attack**: where the website database contains a malicious script.
  - **DOM Based XSS Attack**: where the malicious script present in client-side scripting.

Cross-Site Scripting can be prevented by:

- The data can be validated at the arrival of input.[7]
- The output of data should be encoded.
- Proper response headers should be used.
- Content Security Policy should be followed.

DNS Spoofing

- Computer hacking attack is known as DNS spoofing attack.
- The resolver DNS cache was introduced to the data which caused the name server to return an invalid IP address.
- DNS Spoofing can be avoided by:
  - Forged Responses
  - Weak passwords
  - Spam emails[8]

DoS (Denial of Service)

- DoS attack means where the network resource or server won't be available to the users.
- Generally, a lot of communication requests will be filled in the server.
- A denial of service will contain one system and one Internet connection where it can attack the server.
- Distributed Denial of Service (DDoS) will contain multiple systems and Internet connections for many requests will be present in the server and difficult to handle.[9]

Man-In-The-Middle Attack

- Man-In-The-Middle Attack refers to attacker seize the connection between client and server and accomplishes a bridge between them.
- An Attacker may perform operations like reading, insert and modify at the time of intercepted communication.
- Denial of Service and Man-In-The-Middle Attack can be prevented by:
  - **Security Extensions**: to deal with security threats against DNS the net Engineering Task Force(IETF) developed DNS Security Extensions(DNSSEC).
  - **DNS Updates**: The updated version of DNS will be having cryptographically secure transaction Identification and port randomization to save data against attackers.
  - **Password policies**: Avoid employing a weak countersign and implement countersign protection policies is of utmost importance.
  - We must avoid the WIFI which does not contain any password.
  - We should log out after using a secure application if we are not currently using it.
  - We should avoid using public networks while conducting a sensitive transaction.

Brute Force Attack

- Brute Force attack is a experimental & error method where it will be having a large number of data and it receives actual data. Actual data means password in general.

Dictionary Attack

- Dictionary Attack will be containing the most used passwords and verify to get the actual password.
- Prevention of Brute Force Attack and Dictionary Attack
  - We can limit the login when it is failed.
  - The root user can be made inaccessible through SSH by modifying asshd_config file.
  - We can use Captcha.
  - Two factor authentications can be used.
  - We can use distinctive URLs for login.

Session Hijacking

- Web-based applications or website, store state &it collects particulars of user sessions and uses cookies.
- If an attacker gets the cookies he will be able to access all the user data.
- Session Hijacking can be prevented by:
  - We can set an idle time for the application, so after a while, the account should be deactivated.
  - The session key should be regenerated after initial authentication. The session key will be changed immediately after authentication where it nullifies session fixation attacks.

Phishing

- Phishing is an attempt to acquire sensitive information.
- The main aim of phishing is to gain or steal sensitive information like login or credit card credentials.
- Phishing is classified into:
  - **Spear Phishing:** It is a form of phishing, where confidential data is collected from the targeted organization.
  - **Whaling:** It targets executives or others in powerful positions or job titles and high-ranking bankers.

Phishing can be prevented by:

- To recognize the phishing attacks, the organization or high authority must train employees that not to click the malicious link.
- The browsers can enable browser add-ons and extensions which prevents clicking on a malicious link.
- To prevent hackers who have compromised the user credentials from gaining access, two-factor authentication can be implemented.

CONCLUSION

Web-based Attacks have both advantages and disadvantages. Protects the data and information regarding any organization. Prevents from computer hackers and identity theft. Users have to ensure they have enabled pop-up blockers to overcome phishing, spam email, or malicious links. Users must maintain backup and protect it from strong passwords and use secure connection. People should know about laws against cybercrime or cyber law and actions which they can fight against crime.

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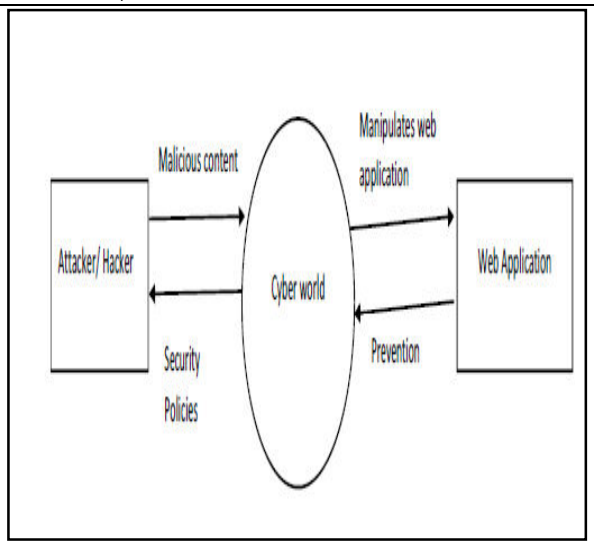

Fig.1 :Data Flow Diagram

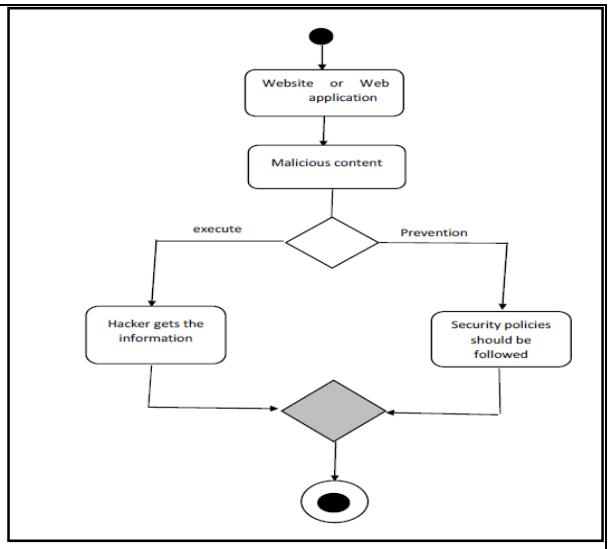

Fig.2 : Activity Diagram

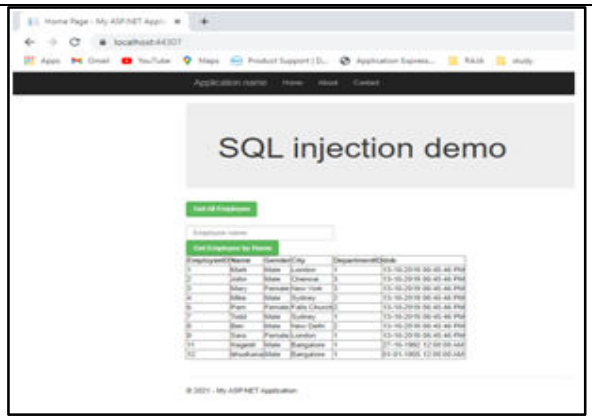

Fig.3 : Get All Employee Details

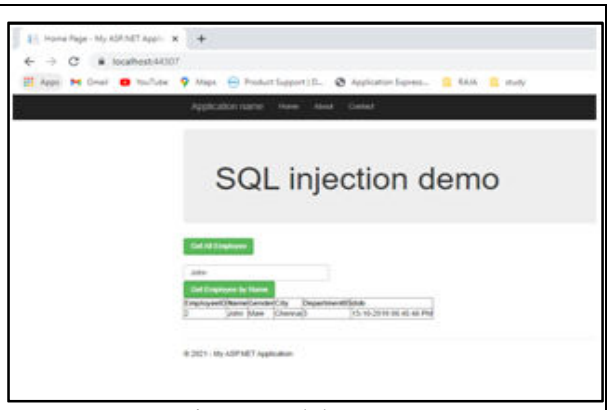

Fig.4: Search by Name

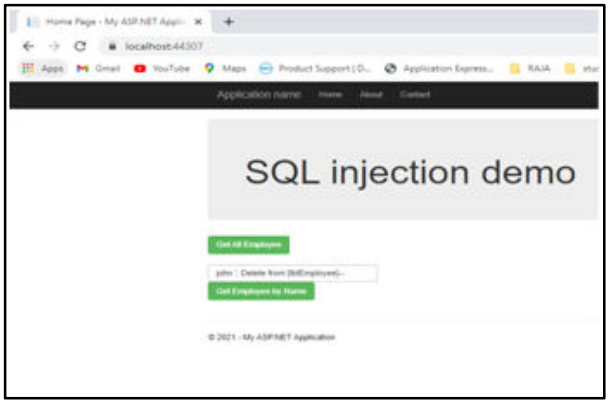

Fig.5: Data deleted from Employee table

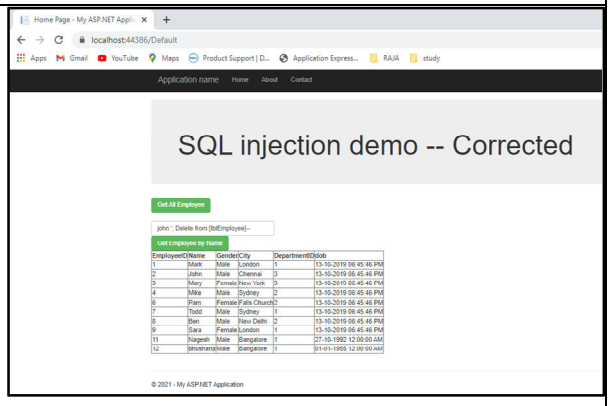

Fig.6: Attacker trying to delete the content from Employee table

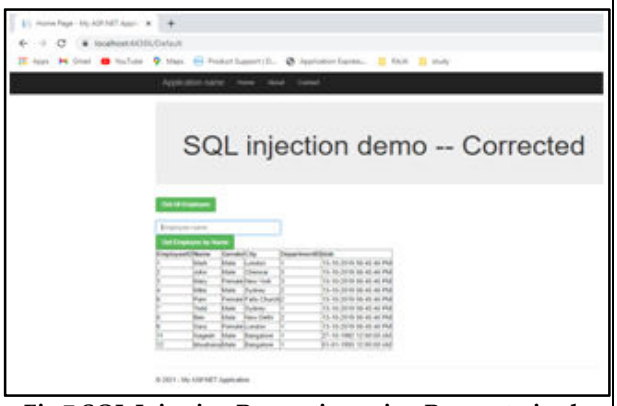

Fig.7:SQL Injection Prevention using Parameterized query and Stored Procedure

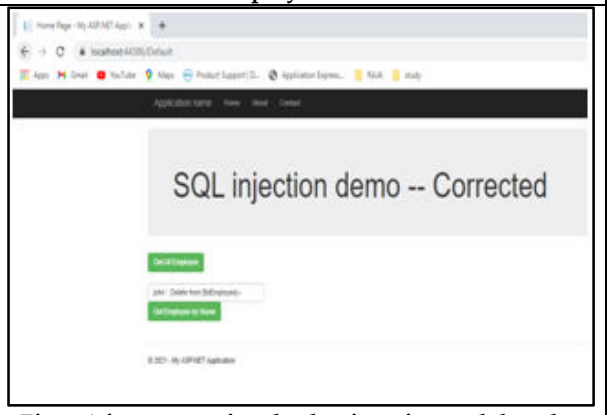

Fig.8: After prevention, hacker is trying to delete the details from table employee

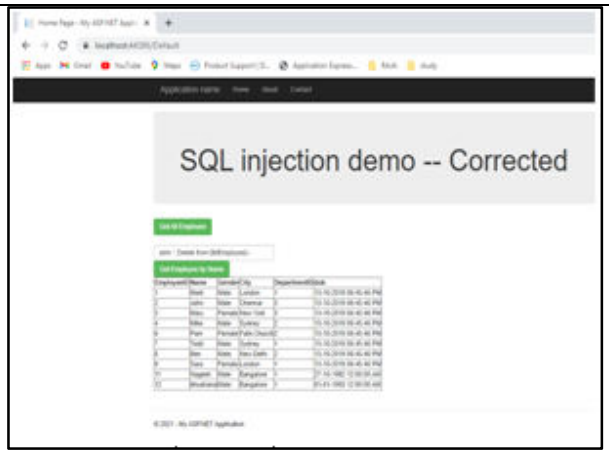

Fig. 9 : The details will be safe and secure after sql injection prevention using Stored Procedure and Parameterized query.

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RESEARCH ARTICLE

Analysis on Minimizing Energy Consumption in Cloud with Various Insights of Sharing of Workload

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ABSTRACT

Working with cloud data center with enormous amount of data has become emerging technology. Data center is a competence consisting of computers in a network and loading the data that various organizations like business use to organize, procedure, hoard and propagate with more segments of data. There are parameters to be considered for workload consolidation which is discussed. To consolidate the workload and power, there are many algorithms proposed for various data centers. This paper explains the clear view of various consolidation of workload for power reduction in various data centers of the cloud. This problem has become vital in research as nowadays, large segments of data sets required being stored in data centers at different fields. To have a positive impact on society and environment there is need to implement Green cloud by using energy efficiency. When data loaded in data center having more number of servers, sometimes few servers become underload/overload depending on the size of the data and this leads to resources of the cloud to consume more power than usual. Load balancing/sharing is one of the factors to consolidate workload. It can be examined at different layers of the network by using efficient algorithms.

Keywords: cloud data center, workload prediction, consolidation

INTRODUCTION

Individuals and group having group of tasks to be stored/ processed need to understand and learn with cloud and its features. The amount of energy consumed is estimated not only by the number of hardware resources but also

with the amount of workload on each server. In various IT companies, Servers are loaded with huge amount of data workload which needs to be harmonized. There are different methods used to categorize the techniques of server Consolidation. Besides, increase of power consumption has an effect on environment with lot of carbon emissions. It is necessary to apply workload consolidation technologies to implement Green Cloud by eliminating the footprints of carbon for imperishable growth. Many components of the prediction system analyses the workload in the future. Many algorithms are analyzed to share the workload on cloud servers using many methodologies[1][2]. To increase the performance of the servers, load has to be balanced by allocating and deal locating the resources. For effective cloud environment, many load balancing algorithms and techniques can be implemented. Many cloud data centres uses different metrics of energy for calculation. One of the most used metric called PUE (Power Usage Effectiveness) to measure the amount of energy consumed by data centre. Algorithms like assigning the task static and dynamic way are used to balance the workload.

PUE with the value 2.0 is that with the increase of number of different components of IT increased number of chilling is required[3]. In this paper, Metrics are analysed in different layers during data transmission using different components of the cloud. There are many resources which consumes lot of energy when working with physical components of the computer and other application programs. Workload consolidation means the use of combining two or more operations with the available setup and with the best use of the available resources. U.S data centres stated growth, where, 6000 data-centres disbursed 61 x 109 kilo watts per hour in the year of 2000, the consumption of power is more than 1% in United States, which leads to the expense in terms of billions [4]. In the later years if the problem is not considered very seriously, by using an method of enhancement then it will be great cause to environment contamination [5]. Genetic Algorithm (GA) analyses the workload based on number of tasks arrived in to the system. There are many factors which affects the system performance like throughput, time of response etc. [6]. Performance of a system can be evaluated with different software simulators like cloud sim, etc.

Balancing the Load in Servers

In Cloud data centers, load is not only the data traffic but also load of CPU, load in the network, etc. It is a method used to ensure that every server in the cloud have same amount of data is shared .The data has been shared by verifying whether the server node is free or not. Different companies use variety of algorithms based on the requirement of load. There are many benefits of using this technique like scalability will be increased, to handle rushing data traffics, etc. Each server is connected to power meter to track the consumption of power. Servers are considered as bins with each resource being one dimension of the bin. Many algorithms are implemented to use the resources efficiently. The algorithms for consolidation aim to minimize the energy efficiency consumed by the servers with relation to performance. Each server consumes power based on the application in execution. In few data centres, multiple clients share same hardware resources by using methods of virtualization. The state of the virtual machine that requires transferring to the other machine has memory, device state, cpu registers and storage.

Harmonizing the Load of Data in Servers

Many companies/Industries load huge amount of data and data centre requires energy for processing depends on the number of severs. Balancing /harmonizing load is one of the main considerations in the cloud where proper measures are taken to enhance the time taken for each server for completion in the data centre systems [17]. Maintaining the workload in data centre is usual to stabilize the data by checking the overload and under load which leads to minimization of energy, decreased cost, etc. Load balancer is designed for prediction of amount of data in each server and allocation can be done. Task management is handled by controller of the data centre. Virtualization is a technique used to distribute resources among the servers. Virtual manager manages the task of allocation and creation of virtual machines to physical machines [18].

Server Consolidation Techniques

There are different consolidation techniques necessary to divide workload on the server. The important feature of server consolidation is live migration. Virtual machine can be moved from one server host to another by considering many factors. The main focus of the consolidation is to limit the response time, reliability and resource utilization. Initially, workload has to be predicted. It may be based dynamically or statically. The techniques based on time taken to make decisions. Considering reliability can further be classified as hardware reliability and service reliability. There are different optimizations methods used to categorize the techniques which can be exact methods, heuristics or meta-heuristics. The other aspects of categorization are objective function and the mode they are evaluated. In this paper, survey on different views of consolidation of workload used depending on different considerations and their objectives. The above parameters of workload are used to achieve goals like usage of energy effectively [7].

Views of consolidations of Workload

Many techniques were used to reduce power in order to decrease the cost. When server is not in working stage, power is consumed. Hence shutting the system when not in use is the method where power can be reduced. The computer era of networks nowadays cannot be fulfilled without data centres. According to the study of Lawrence Berkeley National Laboratory in 2016,70 billion kilowatt hours of energy was disbursed by data centres in United States of America [8]. In different view, between 2015 and 2019 the traffic in internet is thrice. In the view of eco-friendly cloud, the co2 emissions should be reduced but global Internet traffic will be tripled by the year 2022 [9]. With the impact of number of resources of the system, [10] the aim is to predict workload dynamically where there is no overhead in migration. Scalability of the network is maximized in the paper by increasing the number of sever hosts of cloud data centre networks [11]. Hardware utilization is one of the consideration for server consolidation algorithms. Different algorithms considered variety of resources as the parameters. In the paper [12] [13], authors considered cpu and memory as the parameters. In [14], Xiaoqiao Meng et al. in says that algorithm which accounts network traffic configurations to increase the performance of the data centre. By considering obstacles in migration, server consolidation has become striking in migration [15]. Pakbaznia et al. in [16] Offered thermal power management in addition to reduced energy consumption.

Motivation and Challenges

Even many technologies emerged, cloud computing proved as an emerging model to solve many of the problems that occurred during huge data processing. Cloud computing is tangled with many other technologies. Examples are IOT, applications related to E-health with WBAN(Wireless Body Area Networks).Main inclination is to minimize the energy consumed at data centres in cloud with the usage of different methodologies. Server Consolidation is not only sufficient to achieve the motivation. Hence it's been combined with load balancing to get the comprehensive result. The current review gives importance to server consolidation techniques, various methods of load balancing, etc. There are various challenges in the review of server consolidation and load balancing in cloud computing. Some of the challenges are migrating the virtual machines, Algorithm dedicated to more than one node, easiness of the algorithm, achieving short response time, algorithm to reduce the energy consumption.

System Model

Data centre consists of many components like data centre controller, migration manager and monitoring engine. The other components include prediction system which predicts the workload of the future to help the manager for better formation of the system [19].

Refining the performance of the data center by balancing the load with efficient strategies:

To have an efficient working of the algorithm, with workload prediction, time taken to execute, there is need to plan about the method required for allocating the VM to each PM. To have an ideal elucidation for energy efficiency there is need for different methods like allocation of VM's to PM's. Load of data can be predicted using two standard methods called static and dynamic methods classified further into precise method, heuristics and Meta heuristics method, by considering the factors like resource usage, thresholds, and traffic in the network.

Precise Method of Allocation: To know the exact planning when to allocate VM to PM, it's required to design an optimum algorithm which has two methods:
a) Calculated method
b) Designing an algorithm
There are several methodologies to solve the problem like linear programming, stochastic programming, etc. The precise method is demonstrated in many areas [20].

Optimized solution to a problem process: It is used to explain the solution for issue dependent solution. This method is used to solve the problem with increased enhanced solution. NP hard problems are solved using the concept of heuristics with good performance. Sharing/loading of the Data/workload among the servers with different heuristics. Consolidation is done by selecting the members of the group based on workload stage.

Experiential Method
It is one of the optimized methods used to solve the problems. Meta-heuristics is contrary to heuristics which monitors the procedure in order to find the exact solutions. There are different Meta heuristics to solve the server consolidation problem. Genetic algorithms used by J.J. Prevost *et al [21]* Where Meta heuristics is used to balance the load and reduce the power. There are different algorithms used based on benefits and performance of the system. Many algorithms are also used to manage the resources effectively in the server and prediction system used to predict the workload in individual servers.

Parameters considered in consolidating servers in review of Literature
A. Exploitation of hardware in different servers:
One of the important factors in resource management is considering the hardware. Many resources of the hardware are considered in many algorithms of optimization. The resources include CPU, memory, hard disk, network, etc. There are many readings [22][23][24] where CPU is the major component and considered threshold of hardware to implement algorithms. Data centre load increasing with years and hence will impact of memory and Input / output resources on cloud. The algorithm in [25] says that load aware global aware resource. This algorithm consists of three constituents: physical resources, model for load detector, resource scheduler. In paper [26], the prospect of the function with an algorithm SAVES for arranging the data centres. With the use of simulation and test bed, achieved increased use of resources and with savings of energy by SAVE algorithm. [27] Projected a smart elastic algorithm which is about to list VM's which depends on CPU and thresholds in memory using the method of cooperation. The algorithm used has improved migration of virtual machines and fewer thresholds. With the use of standard deviation, mean it is possible to increase CPU utilization with workload. In [28][29], threshold for cpu and storage is used to balance and start migration in various physical machines. With the cloud data centre and its network, the performance of the server needs to be measured with various units which are called as metrics.

Handling traffic in the network
Many resources are used such as CPU, Memory to model the issue and set of PM's to decide the communication between VM's. Traffic flows between the machines and communication between them affect the performance of the data centre. In many systems where group of data is arranged as a batch, the time taken to process the jobs will impact the time taken to complete task. In [30], author says that the overall act of the network is enhanced by limiting the footprints of carbon. The step by step strategy is implemented Which has two approaches: algorithms for packing and communication in the network. The overall latency in the network should be reduced by using other attributes like throughput, response time, etc. Meng Wang *et al.* in [31] adopted the use of random variables to demonstrate the bandwidth. In paper [32], author proposes an algorithm with two main purposes and drawbacks which needs to be improved. The methods used are a) to turn off number of working PM's and integrate the workload. b) To design the network with arrays to recognize the traffic in various data centres.

Dependability of hardware

Depending on the number of hardware resources have more importance than facility provided. It handles the functions for some interval of time. It can affect parameters [33]:

1. Lifecycle of the system hosts.
2. As the use of servers increasing gradually, it also leads to increase the temperature of the server consequently.
3. Disaster of the hardware will lead to:[34]

Inability to use the service of the server, violation of SLA, low performance of the servers. Inability of the resources to perform hinders the performance of the servers. In [35], Deng at el proposed an algorithm for server consolidation where dependability of the hardware is considered as primary factor. It uses three parameters to check which Virtual machine matches the best physical machine. Availability of the service of the servers is a primary element in data centres whose quality will be affected.

Performance matrices which affects the load balancing/ Consolidation

Equalizing the load is very essential influence which has sufficient growth in the application of the server resources There is requirement for the scheduler to execute the "n" of tasks with "n" virtual machines. Each virtual machine has two stages: active and state of idle. The state of the host when not in working depletes 60% of the power than state of the host server when working. Many factors which affect the performance in cloud. They are:

1. Make span (ms) 2. Energy Consumption (EC).

Make span refers to time taken to execute the tasks assigned by the system, where time of execution is different [36].

2. **Time of response**: The time taken to the system to serve the request. [37][38].
3. **System usage:** It determines performance of the server by its efficiency later with balancing the load [38] [39].
4. **Throughput**: The degree of transferring the data to and from the System at given instant time. Better throughput is achieved through better performance.
5. **Energy Consumption:** It refers to energy consumed by the system hosts. With load balancing, reduces the number of active node which avoids nodes to consume unwanted energy.[40]
6. **Transmission of migration time:** The time required to VM to migrate from one server host to another [41].
7. **Tolerance of the system with continued execution:** The facility of the system to continue the procedure faultlessly even when one of the host fail to perform. [52].
8. Versatility of the system: The system can scale to N number of systems which increases the efficiency of the system with the proposed algorithm [43].
9. **Outflow of carbon di oxide from the data center:** The Intensity of carbon discharged from the resources of the cloud data centers. [44]
10. **Use of the variety resources of the host:** It refers to the Number of resources used by the system which is Balanced with the load consolidation.

Categories of Load Balancing Algorithm / Techniques: The mechanism for balancing the load which is beneficial to use resources efficiently within a stipulated time. There are varieties of algorithms like static and dynamic algorithms [45].

Assigning the task in static way: Traffic or tasks are partitioned among the servers in a uniform way. Initially the task is reached and routing the tasks to the destination hosts. Some of the static algorithms are: OLB, MET, Switching Algorithm ,etc.[46].

Assigning the task during execution time: The better way to assign tasks in data centre computing environment. The time of arrival is unpredictable and the method used to create the data centre based on the variety of tasks input. The inquisitive methods adapted for balancing the load has two strategies like offline and online approach. Batch or offline approach refers to execution of large number of tasks. Few batch approaches are Max-Min, Min-Min algorithm etc.

Hardware Load Balancer (HLD): It is one of the component which profuse traffic over multiple servers in the network.

Genetic Algorithm (GA): This concept is related to concept of biology of propagating population. It's getting familiarized in the area of Artificial Intelligence (AI) [47] [48]. Maximum of the research followers take up chromosome length as the sum of tasks arrived at the system. Fundamentals of GA are:

a)Inceptive Inhabitants is the collection of all the members that are allocated in Algorithm of genetics to fetch accurate result. Few individuals are chosen from the set of population and process is adapted to build the next generation [49].

b)Purpose of Fitness is the factor for generating an individual. The value of fitness demonstrates the achievement of each member in the residents.

c)Darwin's law: According to law of survival, the method of selection is used to select an individual for the next generation. There are different ways of chromosomes such as selection for the tournament, etc.

d)Traversing: The operation of traversing can be accomplished by selecting the two individuals and generating a tree which alters different fragments of the parents.

e) Alteration of gene values: The next step after traversing is altering the gene values. Gene values are altered by its state of inception which generates new gene values to the collection of genes. Genetic Algorithm is used to design for new genes.

Evaluation depletion of power and effect on the nature

With the effect of utilization of energy and its footprints of the carbon released from data centres, it is required to know the problems associated with it and measures to overcome. It's necessary to analyse different metrics at different levels of the cloud during data transmission using different components of the cloud [50]. Metrics used should also emulate the power efficiency and should inter relate between the various components of cloud computing. The structured layer of ecofriendly metrics contains:

1. Virtual machine Layer
2. Application Layer
3. Infrastructure Layer

The metrics create an impact not only on system performance but also observers the environmental impact [51].

1) **Infrastructure Layer:**

In Infrastructure layer, server hosts exist in particular site of the cloud and virtual machines installed on physical host machines. Infrastructure contains Metrics:

a) Utilization: it denotes the current utilization. It explains the proportion of available number of free hosts by total of servers under execution in the various servers of the cloud.

b) Usage of storage device: Percentage of each storage usage for the particular host.

c) Available host: At least one host should be available for servicing the request.

d) Usage of energy: It gives the measure of total power consumed by the host.

Virtual Machine Layer:

This layer emphases on the measures of metrics where the total number of energy used by individual hosts. The maximum usage of metrics required to determine the sum of energy consumed by working servers. The energy consumed depends on the total number of resources used. The metrics used are:

a) Consumption of CPU: The effect of power consumed / as by the virtual machine execution.

b) Energy consumption: The consumption of power at a particular time for the particular host by considering the circumstances like: when the system is idle, by running the physical hosts, etc. The more information related to the metrics and its usage explained in detail in the paper [52].

3) Application Layer: There are many applications running in the system over the very first layer of the system. The sum of the execution power of all the hosts will be estimated depending on the type of application under execution. The power consumed by the server is retrieved for execution time of the application. In this layer, there is a new

metric introduced which defines A-PUE which is initiated. The power consumed is proportional to the number of applications executed.

Eco metrics in Application layer are:
a) Power Consumption: Power consumed by the host by considering the parameter called "execution of an application".
b) PUE for Application (A-PUE): The power usage Effectiveness for the Application is the proportion between the powers disbursed by all the hosts to the power consumed by each application running on the system.

Performance evaluation environment
Cloud Computing Simulators:
Performance of a cloud is evaluated with a software simulator called Cloud Sim. It is an open source tool which provides to analyse the performance of different analysis techniques with the data centre environment. There are different elements to be considered to analyse the performance of different algorithms. They are server shutdowns, consumption of energy, violating SLA, etc. Network components such as switches, can be exhibited with Cloud Sim. There is another simulator called Network Cloud Sim [49] as an addition to the cloud simulator for executing the applications in the cloud environments through passing messages. Cloud Analyst [50] accomplishes accurate scheduling with the different groups of users data centres with current configuration. Green Cloud is an enhanced simulator over Cloud Sim [51] developed for simulation framework. It is used at packet level to reproduce the solutions to compound problems. Many different types of simulators are used with different usages in cloud. The different types of cloud simulators are summarized in the table below.

Cloud Net Sim++: Simulations for distant Cloud Data centres:- It is a simulator for distributed data centres which provisions different set of users, scheduling policies for power aware algorithms. Variety of communication protocols are maintained by cloud Net Sim++ which is an addition to OMNET++ which makes application of other frameworks. Further information related to architecture is not required for the research fellows to know about it. With reference to the architecture, more number of frames can be added and supports different transmission links. The primary objective of simulator is to predict the power consumed by different components of the cloud data centres. Power consumed by each instruction is calculated using MIPs (Million Instructions per second). It provides as intermediary between the servers of each rack. The data loaded contains different set of modules. Each module is executed based on the priority of the tasks assigned. This simulator supports different protocols of the network like UDP, TCP, HTTP, etc. for communication between the server hosts. There is a computation time for each task/job executed on the system. Hence the energy in total is calculated. The energy used by the server can be calculated as

P = PC + CPU f * f

Where PC refers to total power consumed which is not related to frequency. CPU f defines power consumed with frequency. Data centres which are different places can be connected using variety of network topologies. Network data traffic is measured using different parameters and different scenario like many to one traffic, random traffic, etc.

DISCUSSION

This segment reviews about different analysis done on energy management using consolidation of workload. Balancing the load and consolidation of workload related algorithms are analyzed in different researches for reducing the carbon emissions

Setting up the environment:
The work uses environment for performing experiments and to analyze different algorithms explained in [65].

Environment for Simulation

Various consolidation algorithms are evaluated with Cloud Sim [66].Cloud Sim is a type of toolkit originated in clouds lab in Melbourne University for supplying resources and exhibiting the environments for virtualization. It permits modelling of data centers with different data hosts and various virtual machines

Policies for managing the resources

The consumption of resources depends on type of task to be executed. Resources can be shifted to machines by stopping the machines which are not loaded properly or by transferring the resources from machines which are consumed to the full extent to other machines. consolidation of virtual machines include finding out machines which are burdened and which are not, choosing the machines for migration. Various algorithms are analyzed for finding the best machine for loading the workload.

CONCLUSION AND FUTURE WORK

This reviewed the study on literature on consolidation of workloads in cloud. There are many techniques/methods to manage the workload consolidation for energy efficiency. Various research works has been analyzed for monitoring the energy efficiency in cloud. This review of study encapsulates the various ways by using algorithms from many readings. The paper also reviews about various methods used for assigning virtual machines to the physical machine. Further, the review also directed to verify the various layers of power depletion. And with this, different simulators are used to evaluate the performance of cloud. In the further analysis, the analysis can be extended by extending the different concepts of task scheduling and balancing the load for efficient workload management using different methods.

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Table1.Comparison of various Cloud Simulators

Parameters	MDC Sim	Cloud Sim	Green Cloud
Platform	J2EE	Sim Java	NS2
Availability	Commercial	public code	public code
Time for Simulation	Seconds	Seconds	Tens of Minutes
EnergyModels	Rough	None	Precise
GraphicalSupport	NA	Limited	Limited
TCP network	NA	NA	Full
Power savingmodes	NA	NA	DVFS,DNS

Table 2.

2019		
Reference	Methodology/Algorithm	Aim of the method
Wenxia Guo	Self-Adaptive Consolidation	To non pre emptively process the Requests
Srimoyee Bhattacherjee	Advanced prediction based minimization of migration algorithm	Minimizing the energy consumption
Ashwin kumar and B Annappa	Context Adaptive self- managing VM Load balancing scheme	The focus is to facilitate the performance of the server with energy efficiency
Sonja Filiposka	Migration of hierarchical virtual machine management	Simulation is done using network Awareness

2018		
Enzobaccarelli	Minimization of energy using adaptive algorithm	Simulation used for attaining the migration of virtual machine overall wireless connections
Kurdi	Scheduling algorithm	It mainly aims at green cloud by reducingData energy.
Vivekanandan	Shuffled algorithm	Migration based on heuristics.
Zhihua	Consolidation using effiecient energy algorithm	To make up the consuption ofenergy.
Kamran Babar and Nazir	Virtual machineplacement using Quality of Service model	Decreases the violations of SLA
2017		
Dan Marinescu and Ashkan Paya	Energy aware load balancing and application scaling	Simulations were conducted on cloud by using migration
Sakthivel and Suresh	A novel performance constrained power management load balancing framework for cloud data-centers	To optimize energy , assured performance
Zhuihua Li et al	Bayesian network-based virtual machine consolidation	Prevent inefficient virtual machine migration
Tighe and Bauer	Topology and Application aware Dynamic VM management	To lessen latency between virtual Machines
2016		
JukkaKommeri	A prototype system for load-based management	Enhance the total energy efficiently
Huining	Cost efficient consolidating service for Aliyun's cloud- scale computing	To achieve the load balancing by using worst fit heuristic

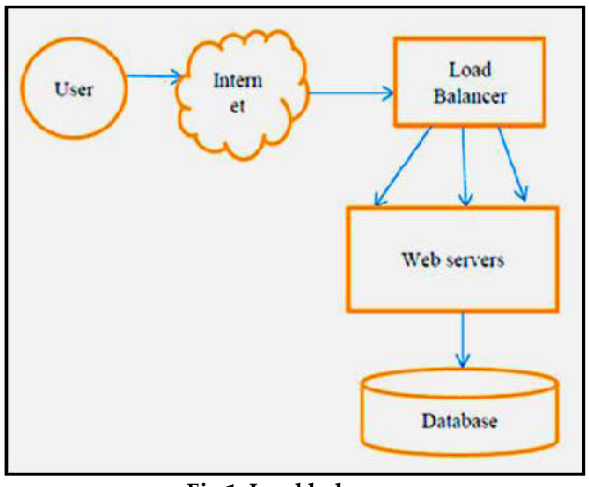

Fig 1. Load balancer

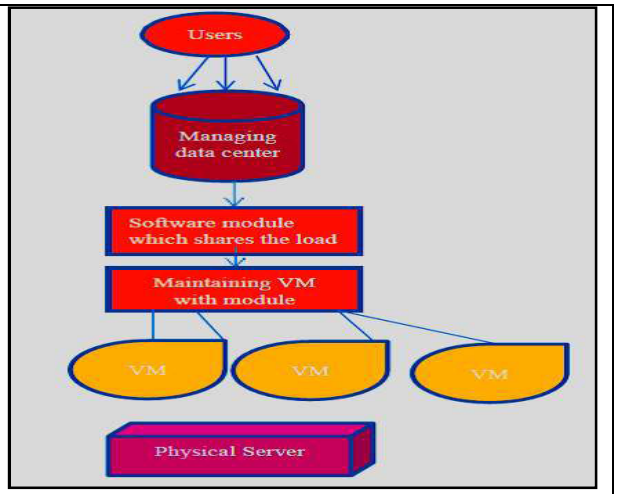

Fig 2. Load Consolidation in data centre

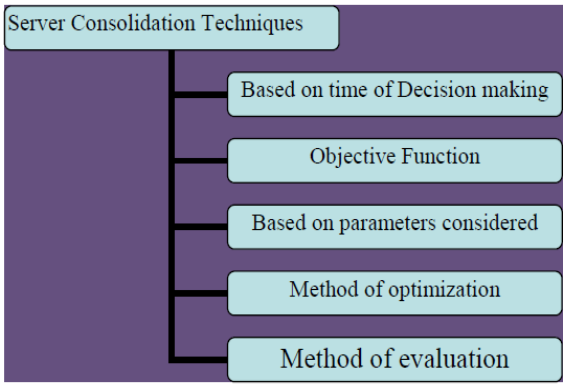

Fig 3. Parameters for consolidating the workload

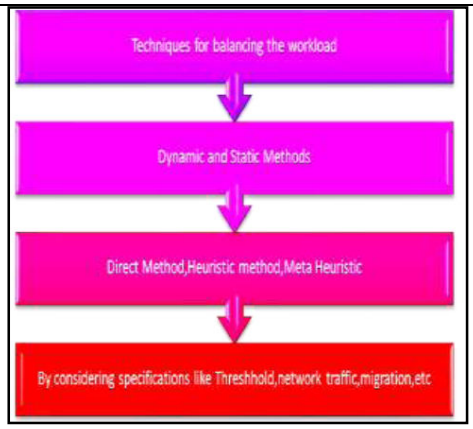

Fig 4. Classification of taxonomy.

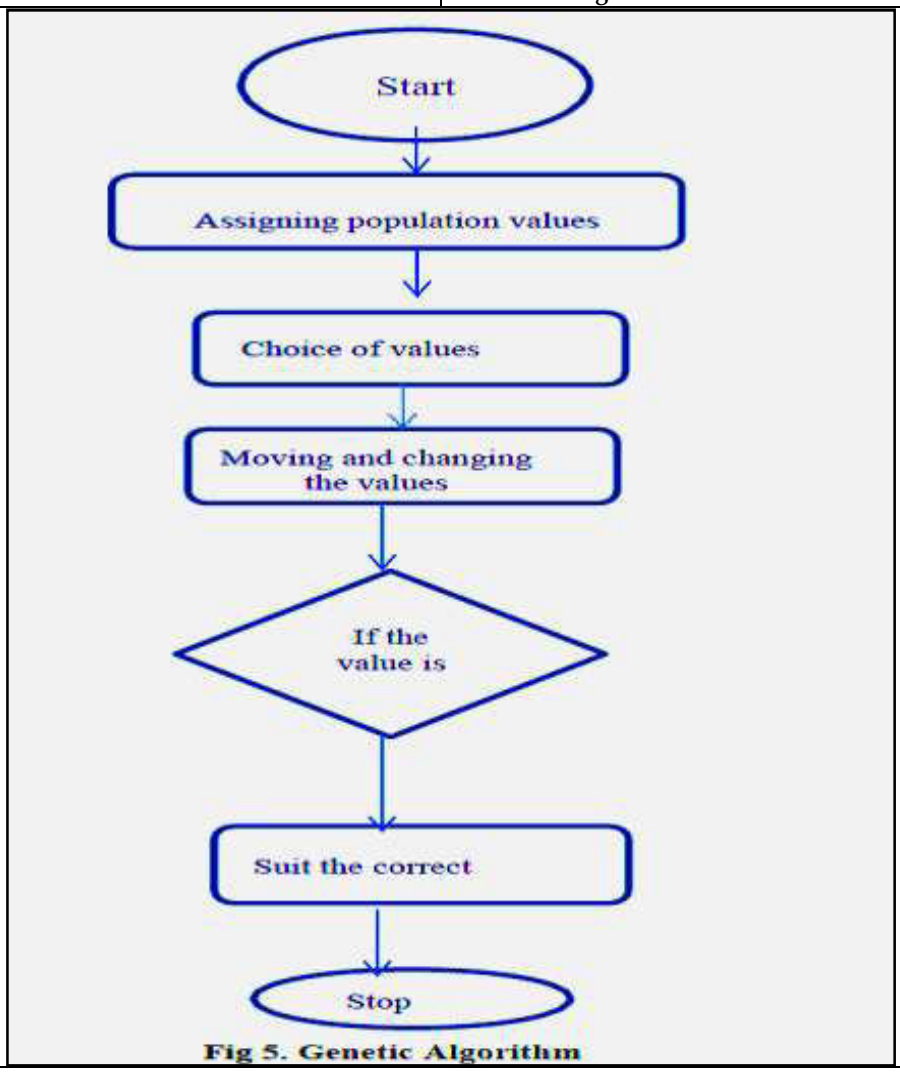

Fig 5. Genetic Algorithm

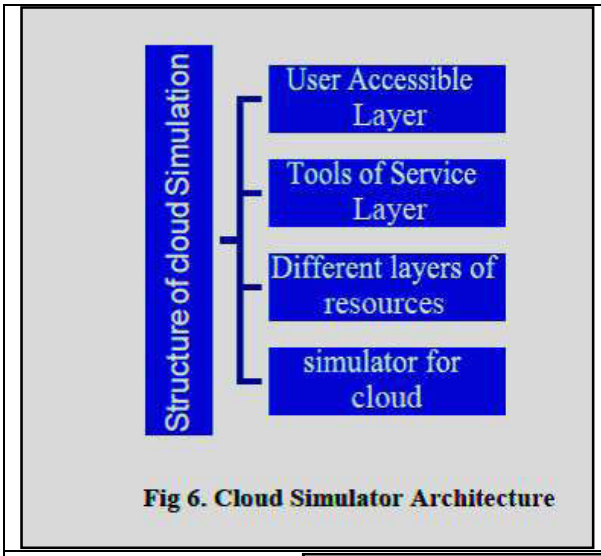

Fig 6. Cloud Simulator Architecture

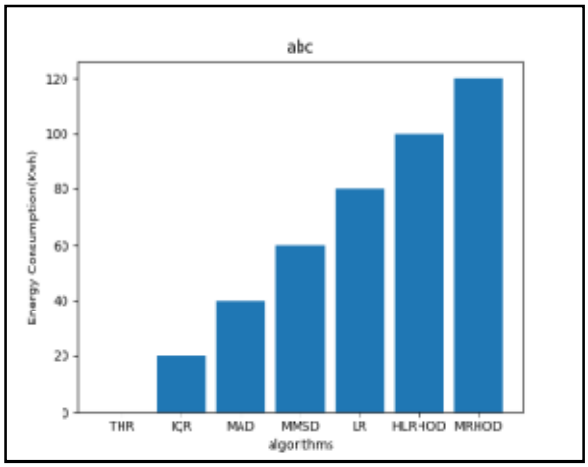

Fig.7 Use of power consumption with different algorithms

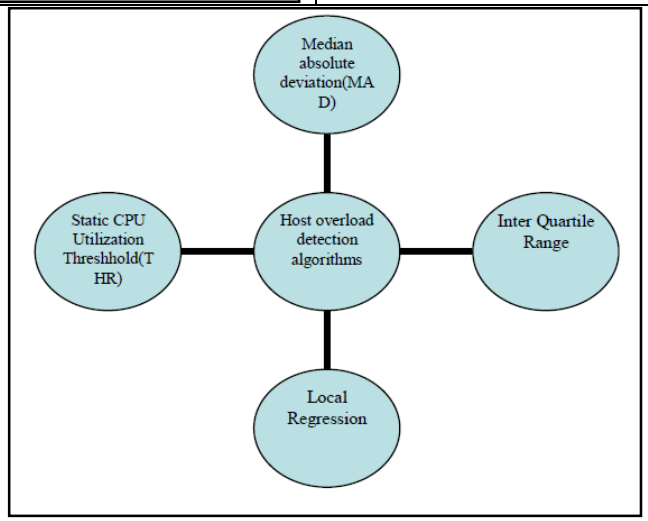

Fig.8 :Policies for managing the resources:

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RESEARCH ARTICLE

Effectiveness of Matrix Rhythm Therapy in Improving Range of Motion of Patients with Post- Traumatic Stiffness of Knee Following Anterior Cruciate Ligament Injury

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ABSTRACT

The objective of this study is to analyze the influence of Matrix Rhythm Therapy in improving the joint mobility of knee joint in patients with post traumatic stiffness following Anterior Cruciate Ligament injury. Twenty samples between 20-40 years of age with unilateral post traumatic stiffness following anterior cruciate ligament injury with grade 1 or grade 2 injury were randomly selected and divided equally into two groups randomly. Goniometer was used as a tool to measure active and passive knee flexion for both the groups before intervention and pre test assessment was recorded. After the pretest assessment, intervention with Matrix rhythm therapy and conventional physiotherapy treatment was given to Experimental Group and on the other hand Control group was exposed to conventional physiotherapy treatment alone for 15 days. Post test measurement of active and passive knee flexion was done on the 15th day similar to pretest measurement using goniometer. The results of the study showed better improvement of range of motion of patients with post traumatic stiffness of knee following Anterior Cruciate Ligament injuryin the Experimental group who were intervened with Matrix rhythm therapy and conventional physiotherapy.

Keywords: Matrix Rhythm Therapy, Anterior Cruciate Ligament Injury, Post traumatic stiffness, Range of motion, Knee

INTRODUCTION

The anterior cruciate ligament originates at the medial wall of the lateral femoral condyle and inserts into the middle of the intercondylar area. It contributes significantly to the stabilization and kinematics of the knee joint. [1]Anterior cruciate ligament injuries account for anywhere between 25 and 50% of ligamentous knee injuries [2]Anterior cruciate ligament injuries is the most common of all knee ligament injuries and 67 percent of Anterior cruciate ligament tears is sport related. The most common mode of injury is external rotation and abduction of the knee in flexion or hyperextension of knee joint in an internally rotated position. Anterior cruciate ligament injury disables the person and may lead to immediate collapse and pain of knee.[3]After ACL injury, regardless of whether surgery will take place or not, physiotherapy management focuses on regaining range of movement, strength, proprioception and stability.ACL insufficiency causes deterioration of the physiologic roll-glide mechanism culminating in increased anterior tibial translation as well as increased internal tibial rotation [4].

It is essential to regain the range of motion in the knee joint following Anterior cruciate ligament injury and many mobilization and strengthening exercises are being used to improve the passive and active range of motion in the knee joint.Matrix Rhythm Therapy works on the principle that normal physiologic function of the body is maintained in all tissues in the body by vibration/oscillation with a frequency of 8 to 12 Hz and interruption of rhythm by any disturbance such as injury, inflammation, trauma may lead to further loss of function and pain in the body [5, 6]A positive correlation exists between muscle pulsation frequencies which lie outside the 8-12 Hz and pain, muscle tension and other health problems. Changes in pulsation frequency are related to change in elasticity and plasticity of muscle and on the cellular level logistics of the living process. Matrix rhythm therapy activates the metabolism on the microscopic level and restores the elasticity of the muscle.[7] Hence it is essential to research the effect of matrix rhythm therapy in improving passive and active range of motion of knee in patients with post-traumatic stiffness of knee following anterior cruciate ligament injury.

MATERIALS AND METHODS

The study belongs to a randomized control trial design with two groupsi.e an experimental group and a control group. Twenty subjects with post traumatic stiffness (unilateral) following anterior cruciate ligament injury with grade 1 or grade 2 injuries between the age group of 20-40 years and managed conservatively were randomly selected. They were further divided equally and randomly into two equal groups. Subjects with other knee injuries were excluded from the study. Subjects meeting criteria for selection and registering at the outpatient physiotherapy department of VMKV Medical College and Hospital were only selected.

Clear instructions were given to both the groups about the purpose of the study and treatment procedure which they were going to receive and informed consent was obtained.The pre-test scores were taken for all the subjects by measuring the person's active range of knee flexion and passive range of knee flexion with the help of goniometry and were recorded. Subjects were positioned in supine lying with knee extension and initially hip was in 0 degree extension, abduction and adduction. Lateral epicondyl of femur was marked to place the fulcrum of the goniometer. The stable arm was fixed along the lateral midline of femur, referencing greater trochanter. The movable arm was fixed along the lateral midline of fibula, referencing lateral malleolus and fibular head. With the alignment of the goniometer, active range of knee flexion and passive range of knee flexion for both the groups were measured and recorded.

After the pre-test assessment of active and passive knee range of motion, the subjects of Group I (Control group) were subjected to Conventional therapy.Conventional therapy included the following exercises based on the individual needs and progression was made based on the patient tolerance and requirement everyday for 15 consecutive days.

- Patellar mobilization
- Isometric & Isotonic hamstring strengthening exercises
- Heel slides in supine lying
- Knee mobilization using Continuous passive mobilization apparatus
- Mobilization using Hold relax technique
- Active assisted knee mobilization in high sitting
- Active mobilization using reeducation board in side lying
- Partial squats against wall
- Static cycling with tolerable range and resistance

Subjects of Group II (Experimental group) were subjected to Matrix rhythm therapy along with Conventional therapy for a period of 15 days.Matrix rhythm therapy was given to all the subjects of the experimental group. The subjects were treated with the coherent vibrations of 8-12 Hz frequency. Subjects were instructed to take three liters of water per day during the treatment period .The following areas were treated with Matrix rhythm therapy:

- Para spinal regions to balance the sympathetic and parasympathetic system
- Thoracic regions & Pelvic regions to improve lymphatic drainage
- Anterior hip and thigh regions to improve flexibility and elasticity
- Posterior hip and thigh regions to improve their activation and performance
- In and around the knee to reduce pain, swelling and improve mobility.

The total treatment was fixed as 60 minutes per session for three days in a week, in which during initial treatment more time was spent in the trunk and proximal areas and later more time was allotted to the leg of concern. It was followed by conventional therapy in a similar fashion as that of Control group.Post-test measurements were taken on the 15th day in the similar fashion as that pretest measurement for both a groups and were recorded. A pilot study with 6 subjects to understand the feasibility of the study was done 3 months before the main study.Normality of the data was ensured using Shapiro-Wilk test and hence't' test was used to analyse the data.

RESULTS

Paired t test and independent t test were used to obtain the results of the study. The outcomes of statistical analysis are presented in the list of tables.Active and passive range of knee flexion was found to have significantly improved in both the Experimental group and Control group through paired t test. (Table I & II)Improvement of Active and passive range of knee flexion was significantly better in Experimental group (Group I) which received Matrix rhythm therapy additionally than the Control group (Group II) who received Conventional physiotherapy alone. (Table III).

The following results were obtained from the study

- Conventional therapy is significantly effective in improving active and passive range of knee flexion.
- Matrix rhythm therapy and conventional therapy is significantly effective in improving active and passive range of knee flexion.
- The combination of Matrix rhythm therapy with Conventional therapy is significantly more effective in improving active and passive range of knee flexion than conventional therapy alone.

DISCUSSION

The outcome of the study supports matrix rhythm therapy as an effective modality in improving active and passive range of motion in subjects with post traumatic stiffness following anterior cruciate ligament injuryThe following studies represent the improvement of range of motion caused by Matrix rhythm in various clinical situations.Dr. Neha Pelapkar (PT) in her case report concluded that intervention by Matrix Rhythm Therapy with Matrixmobil on post-operative knee arthrofibrosis patients showed improvement in range of motion of knee, reduction of pain, improvement in gait and overall lower limb function.[8]

VarunNaik*et al.* concluded that Matrix rhythm therapy reduced 30% of pain and increased Shoulder range of motion and is a effective modality for pain and range of motion in the management of frozen shoulder [9]T.V.Gnanasekar (PT) in his case report stated that Matrix rhythm therapy along with a Complete Decongestive Therapy was helpful in improving range of motion of shoulder, pain, arm volume and Quality of life in breast cancer related lymphedema condition.[10]Vijay *et al.* in their study showed that both Matrix rhythm therapy & Therapeutic exercises improved range of motion, physical health, functional status, and patient satisfaction in a significantly effective manner [11].

Matrix rhythm therapy brings about mechanical and magnetic vibrations according to the body's own characteristic micro-vibrations. Asymmetrical pressure on the tissue thereby leads to simultaneous stimulation of plumb-suction effect and a physiological stimulation of neuroreceptors. The body self oscillation and that of nervous system is stimulated and restored. Thus essential metabolic processes occurring between the cell and the extracellular matrix proceeds. Within a short period of time, the metabolism in the affected region is restored back to normal. Matrix rhythm therapy affects cytological level, thus causing a time for rearrangement of cellular micro processes and this forms the basis for cyto-regeneration and healing in general.The result is that the affected tissues becomes permeable and flexible and can again take a part in body recovery and thereby increasing the range of motion.

CONCLUSION

The result of the study make us conclude that Conventional therapy with Matrix rhythm therapy is more effective in improving active and passive range of knee flexion of patients with post-traumatic stiffness following anterior cruciate ligament injury than Conventional therapy alone.

ACKNOWLEDGEMENT

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Table . 1 Descriptive statistics - Experimental Group

Experimental Group					
Variable	**Group**	**Range**	**Mean ± SD**	**t**	**P value**
ACTIVE KNEE FLEXION IN DEGREES	Pre	61 – 75	68.40 ± 4.93	-17.088	0.0001
	Post	70 – 86	78.20 ± 6.01		
PASSIVE KNEE FLEXION IN DEGREES	Pre	61 – 72	66.40 ± 4.43	-11.112	0.0001
	Post	76 – 91	81.40 ± 5.15		

Table . 2 Descriptive statistics - Control Group

Control Group					
Variable	**Group**	**Range**	**Mean ± SD**	**t**	**P value**
ACTIVE KNEE FLEXION IN DEGREES	Pre	62 – 74	67.80 ± 4.10	-8.748	0.0001
	Post	64 – 77	71.50 ± 4.58		
PASSIVE KNEE FLEXION IN DEGREES	Pre	59 – 74	65.70 ± 5.54	-15.652	0.0001
	Post	67 – 80	72.70 ± 5.98		

Table . 3 Descriptive statistics Pre and Post Group

Variable	**Group**	**Mean ± SD**	**t**	**P value**
ACTIVE KNEE FLEXION IN DEGREES	Experimental Pre	68.40 ± 4.93	0.286	0.781
	Control Pre	67.80 ± 4.10		
	Experimental Post	78.20 ± 6.01	2.644	0.027
	Control Post	71.50 ± 4.58		
PASSIVE KNEE FLEXION IN DEGREES	Experimental Pre	66.40 ± 4.43	0.299	0.772
	Control Pre	65.70 ± 5.54		
	Experimental Post	81.40 ± 5.15	3.513	0.007
	Control Post	72.70 ± 5.98		

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REVIEW ARTICLE

Literature Review of Age and Gender Determination using Facial Feature

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ABSTRACT

Human face is a very complex object, it can be used to predict and estimate a lot of information about the person including age and gender. Age and gender information can be very useful in wide variety of applications. This paper discusses about the evolution of age and gender determination system by taking very old proposed methods into account to the most recent ones. We've studied total of 9 proposed architectures which were found promising and included brief analysis of each of them. The paper discusses overall progress of Age and gender determination.

Keywords: Age estimation, gender classification, Age and gender determination

INTRODUCTION

Human face is one the most important human biometric character and it consists of a lot of information including age, gender, emotional state, race, etc. and since work of Darwin[1] a lot of researchers have devoted to extract such information. Though as a human we can identify some of this information like gender, expressions very easily from a single picture but human face is very complex object as little variation in shading, shape, texture etc. can change the perception of the face[2]. Age and gender are one such piece of information that can help to know a lot about a person. We while addressing anyone address them according to these two criteria like vocabulary would change according to the gender and we tend to address more formally to older ones than the person younger to us. When it comes to gender classification it is found that humans were able to identify gender for adult with 95% accuracy whereas this accuracy reduced while considering child faces[3]. It is also found that humans consider very few key

points while determining the gender which includes shape of face, hair length, eyes etc. Images without hair were shown to people and it was found that people were not able to predict gender that accurately. Gender information helps a lot while profiling a person as with this information ideas about likes dislikes, behavior, etc. can be build. Age is another information that can be extracted from a facial image but unlike gender it is not that simple to estimate the age of person just by looking at the picture a study suggests that even doctors estimate it inaccurately by 10 years[4]. Age estimation using facial image is complex subject as it involves analysis of multiple data points including size of wrinkles, distances between various fiducial points and analyzing that with bare eyes is not possible.

Though people can predict these information but automatic extraction of this information is being extensively studied[5]. As to estimate this information a lot of analysis and data has to be taken in account. This automatic extraction helps in various applications one such example of it is automatic beautification adjustment in camera apps on the basis of gender. Recently advertising industry is developing a lot of interest for age and gender determination to do more target based advertisements and this is why more researchers are attracted to the problem of age and gender determination in field of computer vision[6]. Not only it helps them to run target based advertisement but also it helps them to understand consumer needs and behavior. Although a lot of research has been done for automatic age estimation but it still remains a challenging problem as face is not just defined by intrinsic factors such as genetics but also is dependent on extrinsic factors such as lifestyle, expression etc.[7] The important sections of this paper are as follows: Section 2 comprises of selection criteria for literature and its analysis. Section 3 consists of Overview of literature where we've summarized the literature. Section 4 discusses about the gender classification and various gender classification methods. In Section 5 we've discussed about the age estimation and various age estimation methods. Section 6 discusses about the review of various studied methods and evolution of them. In Section 7 we brief about the limitations of this review. Finally a conclusion is drawn and future scope for research is discussed.

LITERATURE REVIEW METHODOLOGY

In this section, we would discuss about the approach followed to select the literature as well the criteria laid out for same.

Criteria for Method Selection

The research papers which are utilized for this review are based on below mentioned criteria:

Title and year of publication of paper:
The papers were chosen in range of oldest paper to the recent ones to understand the evolution of the methods.
abstract of the paper
Abstracts of various papers were analyzed to get an overview of then paper. This helped to filter out the relevant papers
Reported results of the paper:
Papers were selected on the basis of method followed and the results obtained.

Analysis of Literature

The literature reviewed can be analyzed on basis of:
Objective of research*:* Primary objective should be either gender classification or age estimation or both.
Methodology used: identifying what kind of architecture was used to determine age and gender.
Evaluation metrics: performance reported for the proposed method.

Overview of Literature

In this review, 9 papers were identified and used. Table 1 shows distribution based on year range.

The following section will analyze the type of problem they solve (age determination or gender determination or both), Table 2 shows the distribution for the same.Table 3 shows the datasets used in the papers to train and test their models.

Gender Classification

This section discussed about the various methodologies review for gender classification. Some of the below methodologies are mentioned in Section 5 as well, as they are used to determine gender and age both.

Classification using fiducial points

This approach has been discussed in paper [2], this is one of the oldest approach where 40 points were extracted from a frontal facial image these facial loci are referred as "fiducial points". The vertical and horizontal distances (fiducial distances) were calculated and on the basis of these distances classifier function was able to determine the gender of person in the image. The accuracy of the method was recorded as 93.1% for the males whereas 96.2% for females.

Using SVM classifiers

As discussed in paper [8], initially images were taken from FERET database and pre-processed using face alignment system where first a head was searched and scaled followed by feature search. Then this data was passed to classifier with 5-fold cross validation and the split for training data and testing data was kept at 80-20 split where 80% was training data and 20% was testing data. It was found that SVM classifiers gave the most accurate results with error rate of 3.4% for low resolution images and 6.5% for high resolution images. This error rate could have been minimized if hair information would have been taken in account.

Determining gender with help of wrinkle texture and color of facial image

The approach discussed in paper [9] makes use of very less information to deliver the output. Initially skin region is extracted using color table and color transform system then the skin color is determined after that wrinkles are enhanced which helps in formation of density histogram. Then these wrinkles are enhanced and by using DTHT (Digital Template Hough Transform) shorter and longer wrinkles are extracted. Since it is difficult to extract wrinkles from female's face ranging in age from 20 to 30 years so first age is estimated with the help of above data which would be discussed in further section of the paper. Then with use of this estimated age and wrinkle information the gender is classified. The accuracy of discussed method was found to be very less but can be improved by making use of the multiple datasets.

Using BIF and CCA to determine the gender

The method in this paper [10] uses biologically-inspired-feature(BIF) to extract the features which uses Garbor filters and MAX pooling to perform basic operations like translation, rotation and scaling. Canonical correlation analysis (CCA) is used on features extracted by BIF to establish linear relationship between multidimensional variables. This approach helps to determine gender and estimate age with the help of single model. Accuracy of the method is reported at 95.2% for gender determination.

Using LBP for gender determination

This approach described in paper [6] uses Local Binary Pattern(LBP) descriptor which is a very powerful text encoding descriptor based on set of local binary patterns. Here seven most informative features are selected with the help of LBP and using that gender is classified.

Age Estimation

This section comprises of methodologies review to estimate the age though some of methods might have been named in above section but are used for age estimation as well.

Estimating age with the help of wrinkle texture and color of facial image

Feature extraction and selection which includes extracting skin region, enhancing and extracting wrinkles has been explained Section 4.3. Once wrinkle information is present it is referenced with look up table (LUT) to estimate the age. This LUT is created by extracting wrinkles from dataset images and by integrating the obtained wrinkle distribution information.

AGES algorithm

This approach has been discussed in this paper [5], where authors have proposed AGES (AGingpattErn Subspace) algorithm. In this algorithm authors have created a model where aging pattern in determined by taking facial image at different age which are labelled in sorted manner. For estimation features are extracted and proper aging pattern is identified then the reconstruction is done where reconstruction error is calculated, the age with minimum reconstruction error is selected.

Manifold learning and regression

In paper [11]authors applied manifold learning to reduce the dimensions using various techniques including LPP[12], PCA[13], NPP[14], OLPP[15] and CEA[16] followed by the regression to estimate the age, the authors found results of LPP + regression and OLPP + regression outperformed PCA + regression and NPP + regression whereas they found CEA + regression performed the best with mean age error of around 5 years.

Using CNN

The authors in paper [17] used deep convolutional model to estimate the age of person in facial image where they used two convolutional layers and two sample layers to produce feature maps. Now the authors extracted deep convolutional activation features of all images in the dataset to train the model and then SVM classifier is used to estimate the age. The model created by authors can be improved if it would be trained on the larger dataset. Similar approach has been seen in paper [18] where CNN with VGG-16 architecture has been trained on multiple datasets to create a model which gives out more accurate result in comparison to the former one.

DISCUSSION

We've seen that there has been tremendous developments in field of Age and Gender determination using facial image. As applications of this problem are continuously increasing the better methodologies are being developed which can determine age and gender more efficiently and are easy to use. In multiple papers authors have mentioned about complexity of age estimation as age is not only dependent on intrinsic factors but also on extrinsic factors which makes it challenging aspect but we can see that with more and more work going on in the subject the mean age error is being reduced with evolution of new models.

Limitations

While conducting this review we faced some of limitations which are mentioned below:

i. There was very limited access to paid journals and subscriber access journals and papers so we had to refer to papers which were available in open access journals.
ii. There are very few datasets which are available publically so it limits the possibility of fair comparison of all discussed methods.

CONCLUSION AND FUTURE WORK

We've seen development in the field of age and gender determination from the use of single feature to estimate age and classify gender to using of multiple features simultaneously to give more accurate results. For age estimation we saw that some researchers identify it as problem of classification where others as problem of regression as age in continuous value. We present this review to identify available methods for age and gender determination and hope it will help researchers to develop new methodologies by understanding already established methods to contribute to field of image processing.

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Table 1. Paper by publication year

Year range	#
1997-2004	3
2005-2009	2
2010-2014	3
2015-2020	1

Table 2. Paper by objective

Objective	#
Age determination	4
Gender determination	2
Both	3

Table 3. Most used Datasets

Dataset	# of uses
FERET	2
FG-NET	2
MORPH	2
Gallagher's database	2
Others	2

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RESEARCH ARTICLE

A Novel Approach to Detect SQL Injection Attack using Machine Learning Algorithm

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ABSTRACT

Web application is playing a very significant role in today's day to day life. As the usage is increasing Web security is a major concern. Web application takes inputs which are susceptible to SQL injection attack. Data in the databases are central to modern websites as they contain critical information such as user id, password, bank account details, business statistics etc. These databases are vulnerable to treats. The websites are continuously monitored and targeted by malicious users in order to acquire these data. Structured query language (SQL) injection attack (SQLIA) is one of the common and dangerous attack used by the malicious user on the websites in order to manipulate the query to delete or steal confidential data from databases. It falls under the top ten vulnerabilities when it comes to web application. In this paper we have proposed a methodology Injected code detector to detect the SQLIA using SVM machine learning classification algorithm. Preprocessing of query is done using word tokenization algorithm to extract features. Feature vectors are created using TF-IDF. The aim of our proposed methodology is to achieve better detection accuracy and reduction of false positive.

Keywords: SQLIA, unauthorized access, Machine learning, SVM, TF-IDF

INTRODUCTION

The development of web application and usage has increased. According to statista [1] the global usageof internet is estimated to 2.65 billion by 2021[1]. Web application attack has increased by 800 percentage by 2020 [2]. 392 attacks which was directed towards websites [1]. These attacks is a global problem that is dominating the new cycle. These applications uses database such as Oracle, My SQL, MS- Access for storing data and poses the threat to individuals data, Large International companies, Banks and Government sectors. The advancement in technologies and web applications has changed the way business are done, and access and share information. This has attracted hacker to steal the data. According to Open Web Application Security project (OWASP) SQL injection attack is the top 10 vulnerabilities in 2020 [3]. [4] 65% of Web attacks is SQL injection attack. It was reported that 8.3 Million users credentialwas hacked by 2020 using SQL injection [5]. Approaches to over come web attacks which is specific to SQL injection attack should focus on structure of SQL queries which are dynamically created and detect malicious queries.

Over view of SQLIA

SQL in a language which is designed to manipulate and manage data from databases. A regular queryfetches data from databases or modify's data through web application interface.

Original Query

Select * from users where name ='xyz' AND id='1' ;

SQL injection attack is a code injection technique used to execute malicious SQL statements. The malicious SQL query consists input forms which get access to database and then add, delete or modify database. The attacker get unauthorized access to sensitive information such as account credentials. It is a type of cyber security attack that targets the databases and crack's the query and tricks the system to do unexpected things. Figure 1 depicts SQLIA

Injected Query

Select * from users where name='xyz' AND '- - 'id ='1'

Causes for SQLIA

Insufficient input validation, syntax validation and no proper secure coding framework for web designing leads to malicious code injection. SQL injection occurs when SQL is dynamically generated within front end application. When user inputs are received through web application, attacker injects untrusted inputs as a part of database query. When an application fails to sanitize user inputs and incomplete validation of user input the attacker changes the input and gets access to database. The attacker will alter the working of query that is executed. Poor coding practices and within the database stored procedures are the reason behind SQLinjection attack [5].

Example :

A simple dynamically created SQL statements by retrieving acc_num from the URL designed in ASP.NET . http://www.Bank.com/customer /login.aspx?acc_num=101

When the customer login's Banks website by providing credentials the input supplied to acc_num is taken from URL and concatenated with SQL query.

Select * from Account details where acc_num = 101

The above query retrieves account details. Any value put at the end of the query in .NET is passed to thedatabase at the end of the select statement. If the attacker changes the query string to something like this : http://www.Bank.com/customer/loging.aspx?login.aspx?acc_num=101;delete from accounts;

Then SQL query sent to the database will be more vulnerable. The SQL query with concatenated string is:
Select * from Account details where acc_num = 101; delete from accounts; The SQL database understands that statement ending with ";' means there is next statements which has to beexecuted and execution of delete leads to vulnerability.

Background and Related WorkMachine Learning (Ml)

Machine learning is a branch of Artificial Intelligence. It provides computers with an ability to learn by experience. Machine Learning algorithms learns from patterns. ML algorithms are trained to find patterns and features from massive amount of data in order to make predictions and decisions based on test data. Using ML algorithms, model can be built to identify keywords in the SQL that are malicious and Sql injection can be detected. Many research's have already proposed techniques to detect SQLIA using ML.

In [6] the author has developed 10 layer neural network(NN) model for detection of SQL injection attack.A URL generator is developed which develops benign and malicious URL'S from top 500 websites of UK, A URL classifier is developed which classifies the URL as malicious and benign. A NN model is developed which is trained, validated and tested to detect malicious URL's. A good performance in accuracy are obtained. In [7] the author proposed model using decision tree to prevent SQL injection attack. In this model URL request from client sent to server is filtered using decision tree, and classifies the SQL query into attack class and non attack class based on the created SQL injection database. The model first acquires data of SQL injection attack from sources and then uses class rules for classification of queries to attack class and non attacks. In [8] the authors's have used SVM classification algorithm to predict SQL injection attackand achieved an accuracy of 96.47%. In [9] the authors have detected SQL injection attack using neural network. Firstly authentic user URL is acquired from log data of DPI ISP data provider and then statistical research is done on the normal data and SQL injected data. Based on this features are designed to train MLPModel. The accuracy obtained was 99.5%.The author [10] has used regular expression for tokenization on sql queries an then Navie Bayes and Gradient Boosting classification algorithms are applied to classify the incoming traffic as malicious code or non malicious. Navie Bayes has generated accuracy of 92.8% and Gradient Boosting has generated accuracy of 97.4%.The author[11] has shown that decision tree and rule based have improved performance over neural networks. The author has simulated data set by capturing data from traffic generation server , web app server , remote database server. After capturing data preprocessing is done where string data is preprocessed to word vectors. To reduce features feature selection is done using correlation. Subsets of features are generated and tested for correlation using Genetic search algorithm. The authors[12] have used Query tree and SVM to detect SQL injection. The query entered bythe user is compared with the user is compared with the trained dataset using SVM linear kernel along with Query tree. If the entered query is injected query it is marked as malicious. Fisher Score is used for Feature selection to reduce redundant features. Accuracy of classification is 94.1%. Efficient extraction of features vectors is important for malicious code detection. N-Gram based malicious code extraction is proposed [13] which efficiently extracts feature vectors from malicious code and classifies to malicious code using SVM Linear kernel with accuracy of 98.0%.

PROPOSED METHODOLOGY

In this section we have proposed a methodology to detect SQL injection using machine learning algorithm. Machine learning model provides high accuracy on test data. They also work on high dataset which is a major factor for web vulnerabilities and also there are different types of SQLI attacks. The work focuses on proposing efficient ML model to detect SQLI attack with feature extraction for detection.The framework is designed for detecting malicious SQL query is shown in the figure 2. The dynamic query will be sent to the Injected code detector (ICD) – a machine learning model for detection of SQLI and report the attack. The non injected sql query will access database. The proposed approach consists of an Injected code detector between web browser and database. In this approach all the query between database and web browser is exchanged through the Injected code detector to check for possible

attacks in the dynamic sql query. Injected code detector which is ML model, is used to find malicious sql query tokens. Features are extracted from dynamic query is fed into machine learning classification which is trained for decision of the injected and non injected sql query. If the sql query is injected then it will bereported. The process of detection of sql injection is done in steps as shown in figure 3. At the first step web browsersends a request to web server using URL. Data preprocessing is done on the generated dynamic sql query for tokenization. The tokens are string number, keyword or punctuation. These tokens cannot be broken further.

Data Collection

Acquiring data for SQLIA detection from enterprise is not easy. Checking the dataset for quality of realismis very important before deploying it to the system. We will be using synthesized data to train and test our model and promising to achieve good performance . Some of the sample queries of SQLI and its types forData preprocessing are

Tautology SQLI attack
Select * from users where username='xyz' or 'a'='a'- - and password='pass'
Union based SQLI attack
Select * from login union select 1,2,3
Boolean based SQLI attack
Select name, description from items where id=2 and 1=1
Time based SQLI attack
Select * from product where id=1; if system_user='xyz' wait for delay '00:00:30'

Data Preprocessing

Data preprocessing is very important step in machine learning. Data consists of queries which has to be classified. The ML model has to be trained for classification. Tokenization is a common task in text analysis , Natural language processing (NLP) [16]. Tokenization is a process of separating text into smallerunit. These units are non separable and called as tokens. The queries are broken down to small tokens.
Tokenizing is done on the queries as the malicious query contains certain tokens which describes it. Some of the tokens of SQLI are shown in the Table 1.
Word tokenization algorithm is used for generating tokens. It works by splitting text which is query intotokens using a certain delimiters. The tokens are allocated with weights.
For example:
' AND '- - 'id ='1'; (1)
Now when tokenizing is done on (1) the number of each terms is used for calculation of weights as shown inTable 2.

Feature Extraction

Feature extraction is to find features from the dataset. The tokens are the features which describe the query to be malicious. At first, it can speed up the detection process that is, finding what features are really important. A feature vector is an abstraction of features of SQL query which is a collection of tokens. Feature vector is described as
(w1,w2,w3… wn)

Where wi is the weight of each term. In our proposed method the weights of these tokens in the entire queryare calculated using Term Frequency- Inverse Document Frequency (TF-IDF) method as it has generated good results[15]. TF-IDF is deployed for vectorization of query. TF-IDF includes two factors Firstly, Term frequency i.e. total number of times a given term appears in the text document alongside by the total number of words in the text and secondly, the inverse document frequency measures the information word provides. In our proposed methodology term and word refers to token and document refers to entire query. IDF show how uniquely or rarely a given word is in entire documents. TF-IDF can be computed as TF * IDF where

$$TF(t1) = \frac{ci,j}{\sum k\ Ci,j}$$

Ci,j – is the count of token t1 in a query

∑k ci,j – is the overall count of tokens in the entire query

$$IDF = \log\left(\frac{N}{dft}\right)$$

N – total queries taken

dft – total queries that have t1

Classifier

The out put from feature vector is given to classifier which classifies queries as injected and non injected query. SQLI attack detection is a binary classification problem. The queries are subjected to the binary classification where the class label of the queries is detected and actions are performed dependent on the detection, either by reporting a malicious query or allowing query to access the backend database. In our proposed methodology we are using SVM model for classification and detection. From figure 4 analysis of the other research work SVM has given a good detection rate compared with other classification models . The detection is performed by the identification of discovered patterns along with a set of training data.

SVM

Support Vector machine is a supervised machine learning algorithm. Finding Hyperplane of N dimensional space is the objective of SVM where N is the number of features that distinctly classifies the data points andby maximizing the margin to separate the classes.

The algorithm to detect SQLI using SVM is as shown below:

Algorithm: injected code detector

Step1: select training dataset Step2: input the SQL query string

Step3: Feed the training set into the SVM training to generate modelStep4: now use test data set to make detection

Step5: classify the model on test data using SVM classification. Labeled output gives the accuracy

Step6: repeat the step 2 to step 5 till correct classification is achieved

Analysis of Existing Methodology

A study of various methodologies for SQLI attack is done in Related work and the performance analysis of these existing work is shown in the Table3

The above performance analysis table focuses on different ML algorithms for detection of SQLI and our proposed work expects to give promising results in terms of accuracy detection and false positive alarms. In an aim to increase the accuracy of detection and reduce false positive alarms in SQLI attack we have used SVM in our proposed model for classification which will show a very high accuracy rate comparing with the above mentioned models in table 3.

In order to evaluate the performance of our proposed work Injected code detector, TF-IDF for feature vectorand SVM for classification is used. From the above graph it is clear that SVM algorithm in proposed work will classify the queries and yield better accuracy among all other algorithms.

CONCLUSION

Among the different types of threat to web application SQL injection attack is the highest. Taking the advantage of this the attacker can steal confidential data, delete the data from database. The hacker can perform all the operations for which he is not authorized. The proposed work Injected code detector uses word tokenization algorithm for data preprocessing, TF-IDF for feature vector generation and SVM classification algorithm for detection of SQLIA with high detection accuracy and reduction of false positive. Many techniques are available to detect SQLIA but still

SQLIA is the highly vulnerable so it is necessary toprovide security efficiently. We extend our work by applying this proposed methodology on dataset and promising to achieve high detection accuracy

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Table 1: Tokens of SQLI

Name	Corresponding Token
Keywords	SELECT, UPDATE, INSERT, CREATE, DROP, ALTER, DELETE, UNION
One linecomment	# --
Multiple line comment	/* */
Operators	< > <= >= == != << >> | & - + % ^
Logical operators	NOT AND OR && ||
Punctuations	[ ] ( ) , ; ' "
Numeral	Numeral included in +, - , e and R
Literal	"any string"

Table2: Tokenization

Name	Token	Weights
Punctuation	' ;	6
Logical operator	AND	1
Line comment	- -	1
Literal	id 1	2
Operator	==	1

Table 3: Performance Analysis

Author name and year published	Dataset	Classifiers	Performance
Naghmeh Maradpoor 2014[6]	Top 500 popular website address in the UK from alexa.com	Neural network	Good performance in accuracy, true positive rate and false positive rate.
B.Hanumathu *et al* 2015 [7]	Synthetic data	Decision tree classification	Accuracy-82%
Romil Rawat *et al* 2012 [8]	Dummy dataset	SVM	Accuracy – 96.4%
Peng Tang *et al* 2020 [9]	DPI –ISP	Neural Network	Accuracy-99.5%
Sonali Mishra2019 [10]	Libinjection-opensource	Gradient boosting, Navie Bayes	Accuracy-Gradient boosting-97.4%, Navie Bayes- 92.8%
Kevin Ross 2018 [11]	Simulated Data set	Random Forest(RF), SVM, ANN, Decision tree	Acurracy for webapp - RF-96.5%, SVM-94.0%, ANN-96.7%, Decision tree- 95.6% .
Aniruddh Ladole, D.A Phalke 2016[12]	Sample dataset	SVM Linear Kernel	Accuracy-94.1%
Junho Choi *et al* 2011 [13]	Sample dataset from web content	SVM Linear Kernel	Accuracy – 98.0%
Gustavo Betarte *et al* 2018 [14]	DRUPAL	KNN-(k=3)	Accuracy-97%

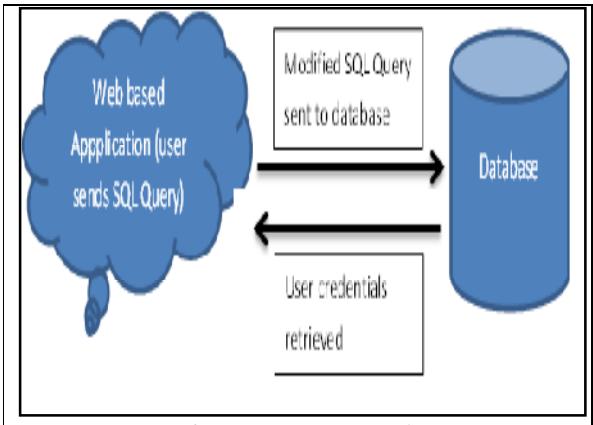

Figure1: SQLI attack

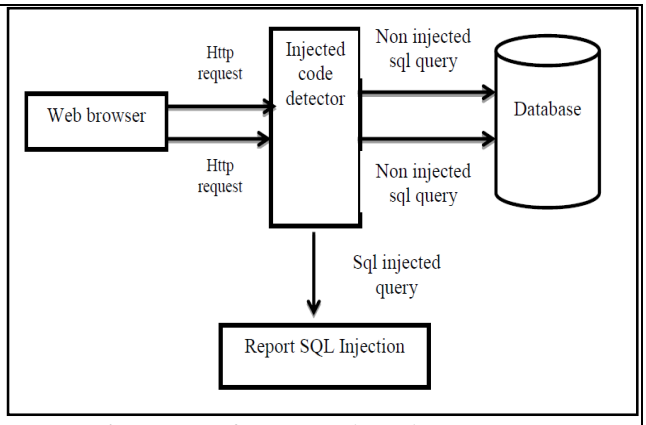

Figure 2: A frame work to detect SQLI

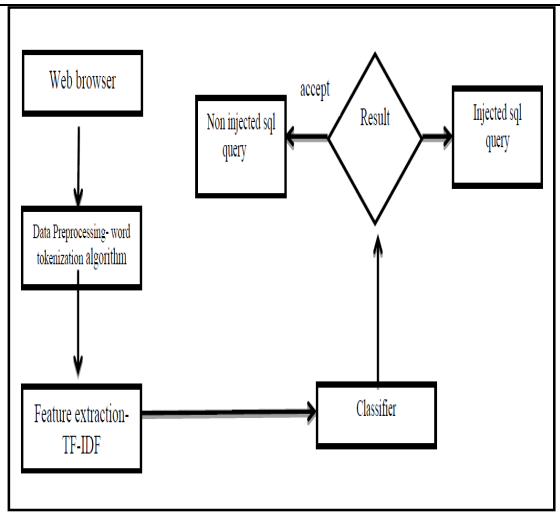

Figure 3: ICD(Injected code detector) Frame work

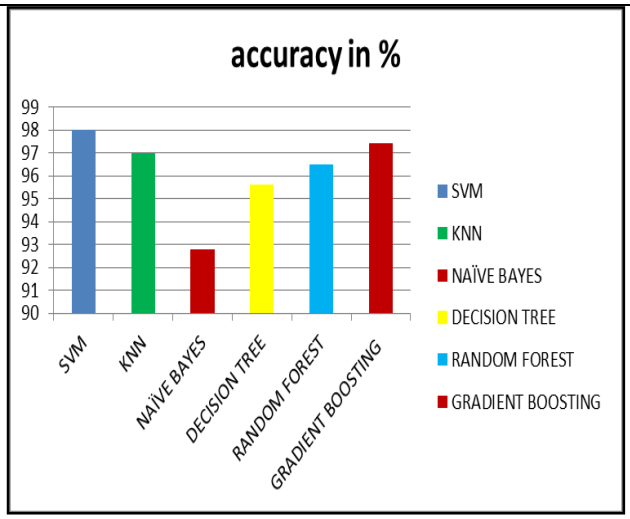

Figure 4: ML algorithms performance analysis for SQLI

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RESEARCH ARTICLE

Significance of Mapreduce Tools in Bioinformatics

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ABSTRACT

Bioinformatics domain is an exponential contributor to the big data store which has a massive collection of heterogeneous data captured from various sensors and experimental results. Handling, managing, storing, and processing this big data of biology needs well equipped tools and softwares. Since this vast data is stored at different repositories in various geographical locations the Distributed Computing plays a vital role in optimum utilisation of these big data stores. Map Reduce-the software framework which is a sub-project of Hadoop the hoard of open source softwares for distributed computing is a key-player in the development of various applications that is capable of handling in parallel the rapid changes in the volume and processing methodologies. An exhaustive list of Big Data tools in particular the tools based on Map Reduce, its purpose and applications for Bioinformatics are presented with a brief study on the challenges, applications, and opportunities of Big data.

Keywords: Bioinformatics, Big data, MapReduce, Distributed Computing, tools.

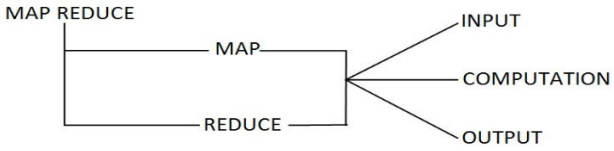
INTRODUCTION

The Demand-Supply model is the best explained and suited model in the context of Bio and Big data. Bioinformatics being interdisciplinary in nature, which combines the data and methods from different fields posing a bunch of challenges for the development of enormous tools and techniques. On the other hand, Big Data being the peaks of large data volumes with heterogeneity allows the analysis of data to get the trends and insights from the existing data. The technology progression has given a huge scope for extraordinary quantity outlining of biological systems in a very cost-effective manner. Big data is the result of this low-cost data generation with a high impacting result. Big data analytics has proven to be the best way of processing of huge data with the nature of data being structured,

unstructured sometimes simi and poly structured [1]. The real time biological data flowing out of research laboratories has given additional trials on the time bound techniques that need to be adapted in deriving the meaningful insights from the data. The data being distributed across the repositories it puts more emphasis on the Distributed Computing environment. Hadoop being one such distributed computing framework, it has gained popularity by giving promising results with the voluminous variety and velocity data sets. A subset of Hadoop is the Map Reduce framework which is a processing and programing model which functions based on the technique of Map and then Reduce. It mainly uses the concept of Key-Value pair to break the data into small chunks to reduce the computation steps and the processing time. This paper presents a comprehensive study on the sources and types of Big data tools that are available for handling the data in bioinformatics [2]. Also, a gist on various challenges and opportunities of Big data to Bio domain is discussed. The paper is organized as follows, in Sect. II, a brief on Hadoop and Map Reduce framework is presented. Sect. III details about the challenges of Big data with respect to Bioinformatics. Sect. IV gives the exhaustive list of tools for biological data using Map Reduce. The conclusion on the study is presented in Sect. V.

Hadoop/MapReduce Framework

Apache Hadoop is a distributed computing framework software which handles large data sets across clusters of computers. Its high scalability nature makes it more adaptable as it can grow form single server to many machines, with computation and storage capabilities at each node. It works efficiently at the application layer of ISO-OSI model by handling failures and delivering universally available service across the cluster of computers. Map Reduce is a Google developed parallel architecture. The framework operates on master/slave concept i.e., one master node handles the configuration and control throughout the problem execution time, whereas the other slave nodes generally called as worker nodes does the actual computation on the data sets [3]. Master node is responsible for splitting the data and assigning them on to worker nodes and places them on to the global memory as key-value pairs. Map Reduce is a general-purpose parallel programing model best suited for large data sets requires the users to work on two functions map and reduce as below:



The Map Reduce framework is capable enough to handle scheduling, splitting, load balancing, failure management, and communication between worker nodes.

Confronts of Big data and Bioinformatics

Though the Big data has adopted to the newer challenges and demands, the exponentially growing field of Bio has made its mark in throwing challenges incessantly to the big data domain. As the biological data out of research and experiments are voluminous and variety being the point the development of new software tools and constant up gradation of existing tools with adequate hardware support is the biggest challenge. As the technology changes the programming knowledge is also a factor which demands a good correlation between the bio knowledge and programming skills [4]. Biological sequences are generated and stored in various repositories in different formats, a thorough knowledge of newly created formats is essential as it is an important input for the software tools development. According to the CISCO global internet report on the accelerating speeds of mobile internet is going to increase from 13.2 Mbps as in 2018 to 43.9 Mbps by 2023. Though this is a revolutionary change in terms of transmission the actual challenge lies with the data Input speed. Although distributed computing has taken care of computing process the slow input rates can affect the overall computational throughput. The heterogeneity of the bio related data needs a quick attention in terms of unifying them into useable formats so that the visualization of these data sequences becomes easy to give meaningful biological insights out of them. Biological data interpretation is the

key for finding the trends and patterns of the data, so there is a developmental need for efficient visualization tools [5] [6]. The solutions to storage, security, and exchange of the bio big data are a treasure-trove to researchers and solution providers [7][8].

Big data Tools for Bioinformatics based on Map Reduce

Huge amount of organic information is produced with quick advancements in genomics and proteomics. To get actual insights on these data requires refined computational tools. To this end Hadoop's Map Reduce has played a vital role. The data flow from various biological sources like Health informatics, next-gen sequencing[9], Cancer Genome Atlas, mRNA expression, Protein expression etc., are the motivation for development of bio enriched tools[10].Table 1 describes in detail the list of tools exclusive for handling big data of bioinformatics before the cloud era.

Year 2013 and onwards the Cloud technology played a revolutionary role in the field of Bioinformatics as the Cloud Technology took over to address the major challenges of Big data in terms of newer tool and storage issues. Many experimental tools were created using Map Reduce, which gave a promising output. Rainbow [11], was a successful tool on the cloud as it was capable of analyzing around 500 varied whole genome sequences. The Map Reduce framework was well utilized to develop many tools viz., PaPFR for the study of Alzheimer's disease, SNP selection algorithm was composed to analyze the Hap Map YRI data, particle swarm optimization technique was devised on Map Reduce platform and was employed in various clod computing clusters. The growth of Big data field was enormously loaded with the exabytes of data from health care and clinical trials, which lead to the development of cloud-based systems. As a result, "Hadoop Geographical System" framework was developed to handle the medical imaging data [12]. Further the Hadoop/Map Reduce was vastly used in development of many cloud-based tools exclusively for Health Informatics [13].

CONCLUSION

The well proven standard which acts as a prime solution to handle the massive voluminous varied data is the distributed computing. Hadoop/ MapReduce framework is one such single roof solution to design, architect and develop various applications to bioinformatics domain. The ever-growing field of bio is creating bunch of challenges to researchers and developers with its bigdata. To this end newer technologies, tools, and techniques have been and are being developed. The current issue being the storage solutions of these bigdata. There is a huge scope for research in the field of data storage.

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Tool Name	Reference	Significance	Source
Cloudburst (Hadoop architecture)	Schatz, 2009	The SNPs (Single Nucleotide Polymorphism) were discovered by mapping the reference genome to short read sequence data.	http://sourceforge.net/projects/cloudburst-bio/
Crossbow (Hadoop architecture)	Langmead, B et al., 2009	Resequncing of whole geneome was possible with shot reads along with SNP genotyping analysis	https://github.com/BenLangmead/crossbow
Myrna (Hadoop architecture)	Langmead, B et al., 2010	Was developed for computing the short read alignment for RNA	http://sourceforge.net/projects/bowtie-bio/files/myrna
Genome Analysis Toolkit (MapReduce)	McKenna et al., 2010	The toolkit is useful in the analysis of next generation DNA sequencing data. It also contains a variety of tools for discovering and genotyping of genomes	https://www.broadinstitute.org/gatk/
CloudAligner (MapReduce)	Nguyen, T et al., 2011	It was intended to map the short read sequences generated by nextgeneration sequencing protocols. It accomplished high performance due to partitioning and parallelism	http://cloudaligner.sourceforge.net/
Nephele (MapReduce)	Marc, E et al., 2011	Tools was developed based on complete composition vector algorithm for genotyping. The tool also helped in reducing the processing time for generating trees.	http://code.google.com/p/nephele/
Cloudgene (MapReduce)	Anita, Kloss-Brandstatter et al., 2012	It is a graphical user interface to support processing and analysis culsters of data sets. This application empasises on employing private and public clouds for customer data and also supports the assimilation of available MapReduce based bioinformatics applications which encompasses HadoopBam, Seal, Crossbow, and Myrna into Cloudgene	http://cloudgene.uibk.ac.at/
Genome sequence alignments (MapReduce)	Jonas, Almeida et al., 2012	devised to develop an 'alignment-free' solution to sequence and analyse genomes	https://github.com/usm/usm.github.com/wiki
BioPig (Hadoop/MapReduce)	Nordberg, H et al., 2013	It is an analytical tool particularly for parallel applications in bioinformatics, it also effective because of its scalbility ability for hadling genome sequence data.	https://sites.google.com/a/lbl.gov/biopig/
BlueSNP (R / Hadoop)	Huang, H et al., 2013	The tool supports distributed data processing, it helpsto determine the empirical p-value and finds the quantitative expression trait loci of several genes.	https://github.com/ibm-bioinformatics/bluesnp

Table 1. List of Bioinformatics tools using Hadoop/MapReduce

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RESEARCH ARTICLE

Post Isometric Relaxation and Reciprocal Inhibition Techniques in Improving Hamstring Flexibility in Middle Aged Women – A Quasi Experimental Study.

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ABSTRACT

To compare the effects of Post isometric relaxation (PIR) and reciprocal inhibition (RI) techniques in increasing the hamstring flexibility among the middle aged women. A quasi experimental study of 48 subjects who had hamstring tightness were selected and randomised into two groups namely PIR and RI. The subjects were selected from selected places of Salem district of Tamil Nadu, India. Thre were three outcome measures used for the study namely passive knee extention (PKE), sit and reach test and stand and reach test. The outcome measures were assessed before, after 2 weeks and after 4 weeks of intervention. The study results showed that there was a significant improvement in the hamstring length in PKE in both the groups right from the 2 weeks but not for the other two outcomes which showed improvement only after the 4 weeks of intervention. There was significant difference between the two groups after 2 weeks and 4 weeks of intervention in all the three outcomes which favoured PIR. This study concludes that both the intervention are effective in showing improvement in the hamstring length in middle aged women, but PIR have superior effects than the RI in both immediately (2 weeks) and short term effect (4 weeks).

Keywords: Post Isometric Relaxation, reciprocal inhibition techniques, muscle energy technique, MET and hamstring

INTRODUCTION

Hamstring strain is very commonly encountered by the sporting professionals. These injuries apart from being common are also challenging and frustrating for both the patient and also to the treating doctor or physiotherapist

because of its high recurrence rate. In the past century the concentration that was given for quadriceps strengthening was not provided to hamstring which was looked from flexibility point of view only. Hamstring strains account for 12–16 percent of all muscle injuries with a reoccurrence rate as high as 22–34%. Adding to this, recurrent hamstring strains have been proved to result in marked time loss than first time hamstring strains. [1, 2]There are several risk factors being identified for hamstring strains in the past literature which includes: diminished flexibility is the major concern,[3] strength deficits have been also correlated to hamstring injuries that too when they are occurring along with lack of flexibility [4] history of muscle fatigue, poor core stability, [5] apart from this lack of proper warm-up before games, [6] improper lumbar posture, [7] and history of prior hamstring injury [8] are all predisposing factors for a recurrence of hamstring injury. In contrast to the prevalence of hamstring injuries among athletes, the prevalence of such injuries in recreational-sporting and non-sporting general population is not defined properly. This lack of data is especially high among women and older individuals, who are attend to general clinics, physiotherapist and orthopaedic clinics with hamstring tears. Most often they are wrongly diagnosed or treated with analgesics and rest so that they are often under diagnosed. Patients suffering a hamstring injury in sport are mainly presenting in the 2nd and 3rd decade of their life.[9, 10] In contrast, the age range of non athletic patients with hamstring injury is much greater with an age range of 60 years and over [11, 12].

There are various intervention that are available for management of hamstring injury that includes passive and active stretching, strengthening plyometric and so on. There are many manual techniques that were adopted in the management of hamstring injuries out of which muscle energy technique (MET) is a unique intervention. MET uses a muscle's own energy generated by gentle isometric contractions in relaxing the muscles through autogenic or reciprocal inhibition there by lengthening the muscle. When compared to contemporary static stretching, MET is an active technique where the patient offers an active participant. The principles of MET is Autogenic Inhibition and Reciprocal Inhibition. If a sub-maximal muscle contraction is followed by a passive stretching of the muscle it is described as Autogenic Inhibition or post isometric relaxation (PIR) and when submaximal contraction of a muscle is followed by passive stretching of the antagonistic muscle group Reciprocal Inhibition results (RI) [13]. Comparison between these two manoeveur on hamstring flexibility was analysed among young healthy Indian adults, where both found to be effective in improving flexibility of hamstring but, PIR had shown superior therapeutic effects [14]. In the current study the main objective was to compare these two interventions among middle aged Indian women

METHODOLOGY

We adopted a quasi-experimental study in testing the study hypothesis. A 1:1 allocation ratio was adopted. The subjects were selected from seven locations in the Salem district, Tamil Nadu, India. The selected women had a history of hamstring tightness and are medically and psychologically fit and between the age of 35 and 45 years. The parameter for hamstring tightness was kept as passive knee extension angle above 19.2 degrees. The subjects were excluded from the study if they had sustained any injury to hamstring before, history of lower limb and back surgery and any degenerative disease of the lower limb. The subjects were also excluded if they were involved in any sports in the past as professional player. Every participant was explained about the study and duration and level of participation required for the study and then were requested to sign the informed consent form. The subjects were assessed initially at the community. Informed consent was obtained from the subjects and then only they were included for the study. visit at patients home or in the community screening hall. For later management, the treatment location was decided based on the number of patients from a given area. Subjects were invited to the Department if the numbers were less and if there were 4 or more patients a therapist travelled for treatment to the patient place, but treatment was given individually.

The subjects were selected conveniently from the population after screening 166 subjects from selected parts of Salem district. 48 subjects were selected who fulfilled the selection criteria. The selected subjects were randomly assigned into two groups namely PIR group and RI group. A random table was generated using computer software, and

concealment method was done usinga opaque cover method to conceal the sequence until interventions were assigned.

The subjects in PIR group were given warm up exercise for 10 to 12 mins with rest periods in between. The warm up exercises included a) Marching in the standing position itself with upper limb reaching outwards b) moving back and front from the standing position one step ahead with upper limb reaching forwards c) moving one step side wards from the standing position and coming back to normal with both upper limbs reaching sideward. After the Warm up exercises Post Isometric Relaxation Technique for hamstring muscle was given. The treatment technique was given to both the legs. The subjects were made to lie in supine lying with contra lateral hip and knee supported by a pillow below the knee. The therapist stood on the side of the leg to which post isometric relaxation need to be given. The hip is flexed to 90 degrees and knee is fully flexed. Then the knee was extended until the restriction barrier was identified. Then the leg was placed on the shoulder of the therapist and the patients was asked to contract the muscle sub maximally by pushing downwards on the shoulders of the therapists whereas the therapists give a submaximal resistance (a counter force). The contraction is kept held for 7-10 counts and then it is relaxed for 10 counts. After that again the limb was passively moved by the therapists and new barrier was identified. Then the procedure was repeated from the new barrier. The technique was given 6 times. The same protocol was repeated for the other leg. Treatment technique was given once daily for 6 days a week for four weeks consecutively for both the sides [15].

The subjects in RI group were given warm up exercise for 10 to 12 mins similar to the PIR group. After the Warm up exercises Reciprocal inhibition was provided for hamstring muscle. The treatment technique was given to both the legs. The subjects were made to lie in supine lying with contralateral hip and knee supported by a pillow below the knee. The therapist stood on the side of the leg to which post isometric relaxation need to be given. The hip is flexed to 90 degrees and knee is fully flexed. Then the knee was extended until the restriction barrier was identified. Then the leg was placed on the shoulder of the therapist and the patients was asked to contract the muscle sub maximally by pushing upwards away from the shoulders of the therapists whereas the therapists give a submaximal resistance (a counter force). This made the knee extensors and the hip flexars to cointract which are the antagonists for the hamstring muscle. The contraction is kept held for 7-10 counts and then it is relaxed for 10 counts. After that again the limb was passively moved by the therapists and new barrier was identified. Then the procedure was repeated from the new barrier. The technique was given 6 times. The same protocol was repeated for the other leg. Treatment technique was given once daily for 6 days a week for four weeks consecutively for both the sides [15]. The outcome measures used for the study were passive knee extension in lying measuring the range of motion – knee extension which can reflect the hamstring flexibility, sit and reach test and stand and reach test for measuring the functional range of motion of knee extension hamstring flexibility. The outcome measures were used before the intervention after two weeks of intervention and at the end of fourth week of intervention.

Statistical Methods

SPSS version 25 was used for the statistical calculations for the study. The baseline homogeneity was found using the chi square test for demographical data. Indipendent t-test was used to find the between group difference and Repeated measures ANOVA was used to find the withing group difference and a Bonferroni test was used for post HOC analysis if there was a statistical difference found in ANOVA. The significance level for the study was kept at 0.05 with a confidence interval of 95%.

RESULTS

The process of subject recruitment is presented in figure 1. A total number of 166 subjects were screened for the study and 48 eligible subjects were selected for the study and recruited into two groups using a random allocation method. The basic demographic data of the participants in both the groups are displayed in table 1.

The chi square analysis that was done among the demographic data did not show any significant difference between the two groups for age (categorised into two groups 35-40 years and 41-45 years) (chi-square value 0.6. and p-value is 0.438), height (chi-square value of 0.68, p value of 0.401), weight (chi-square value of 0.76. and p-value of 0.228) and BMI (chi-square value of 0.59 p value of 0.799). In the baseline assessment of the pre-test value there was no significant difference among the two groups for all the three outcome measures. (PKE –F value of 0.111 and p value of 0.740, Sit and reach test - F value of 0.215 and p value of 0.645, Stand and reach test - F value of 0.156 and p value of 0.694). In the post-test analysis of the three outcome measures PKE showed a significant difference between the two groups (PKE –F value of 10.645 and p value of 0.002), but there was no significant difference between the two groups in sit and reach test and stand and reach test (Sit and reach test - F value of 1.533 and p value of 0.222, Stand and reach test - F value of 1.278 and p value of 0.264). In the post-test 2 analysis, there was a significant difference in all the outcome measures. (PKE –F value of 22.125 and p value of 0.001, Sit and reach test - F value of 5.180 and p value of 0.028, Stand and reach test - F value of 12.277 and p value of 0.001). In the within group analysis of PKE there was a significant difference between the three test in both the group (PIR group f= 199.741, p value = .000, RI group f= 163.642, p value = 0.000). the post Hoc analysis using Bonferroni test revealed that there was a significant difference between all the three tests with a p-value of 0.001. The descriptive statistic of PKE of both the groups is presented in table 2.

In the within group analysis of sit and reach test the same trend was seen in both the groups (PIR group f= 517.317, p value = .000, RI group f= 107.682, p value = 0.000). The post Hoc analysis using Bonferroni test revealed that there was a significant difference between all the three tests with a p-value of 0.001. The descriptive statistic of sit and reach test of both the groups is presented in table 3. In the within group analysis of stand and reach test the same trend was seen in both the groups (PIR group f= 331.478, p value = .000, RI group f= 45.848, p value = 0.000). The post Hoc analysis using Bonferroni test revealed that there was a significant difference between all the three tests with a p-value of 0.001. The descriptive statistic of sit and reach test of both the groups is presented in table 4**.**

DISCUSSION

In the current study the hypothesis was to find the difference between the edffects of two MET techniques employed commonly namely the PIR and RI. A total 48 subjects participated in the study with 24 patients were recruited into each group. As the subjects were selected conveniently from the population the design is quasi experimental. To avoid bias the subjects were allotted using a random sampling technique. The base line analysis of the demographic data and the outcome measures showed that there was no significant difference among the groups which clearly states that the group were similar at the time of commencement of the intervention and explains that the changes that have happened in the variables are all due to the intervention and thereby limiting the confounding variables.

There were three outcome measures that were selected for the study, in which the PKE is a direct measure of the hamstring length and the remaining two are considered to be the functional measure of the hamstring length. In the analysis of the outcome measures it is obviously seen that the actual length of the hamstrings improved in the first two weeks of intervention but the functional range took 4 weeks to improve which was a unique findings of the study. The results shows the results were superior previous results of [16] and [17].

The major limitation of the study was the less sample size and lack of women from all walks of life with a varied age group. As there was a limited participation from the elderly women the researcher had to limit the sample age to 35-45 years. The functional range measured in the study using the sit and stand reach test may have a confounding influence from the lumbar spine stiffness which can also influence the performance. [18]

CONCLUSION

This study concludes that both the intervention are effective in showing improvement in the hamstring length in middle aged women, but PIR have superior effects than the RI in both immediately (2 weeks) and short term effect (4 weeks). The sustainability of these effects for a long term after cessation of the intervention need to be studied in the future, with more number of samples.

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Table 1 - Basic demographic data of the participants in both the group

Criterias	PIR group	RI group
Age	41 (1.2)Years	39 (2.1) years
Height	158 (4.2) cms	1.57 (3.3) cms
Weight	78 (8.4) Kgs	80.2 (7.5) Kgs
BMI	29.2 (1.4)	30.9 (1.1)
Work	House wife - 18	House wife – 13
	Employed - 6	Employed - 11

Table 2 - Descriptive statistic of PKE scores of PIR and RI groups

		N	Mean	SD	SE	95% CI	
						Lower Bound	Upper Bound
PIR-PKE	PRE TEST	24	56.50	1.142	.23313	56.0177	56.9823
	POST TEST	24	60.87	2.070	.42269	60.0006	61.7494
	POST TEST 2	24	71.00	3.787	.77319	69.4005	72.5995
	Total	72	62.79	6.622	.78047	61.2355	64.3479
RI-PKE	PRE TEST	24	56.75	1.326	.27087	56.1897	57.3103
	POST TEST 1	24	59.87	1.392	.28433	59.2868	60.4632
	POST TEST 2	24	64.25	1.594	.32554	63.5766	64.9234
	Total	72	60.29	3.408	.40170	59.4907	61.0926

Table 3 - Descriptive statistic of sit & reach test scores of PIR and RI groups

		N	Mean	SD	SE	95% CI	
						Lower Bound	Upper Bound
PIR-SIT & REACH	PRE TEST	24	12.00	.722	.14744	11.6950	12.3050
	POST TEST 1	24	14.00	.510	.10426	13.7843	14.2157
	POST TEST 2	24	17.37	.494	.10095	17.1662	17.5838
	Total	72	14.45	2.30	.27188	13.9162	15.0004
RI-SIT & REACH	PRE TEST	24	11.87	.612	.12500	11.6164	12.1336
	POST TEST 1	24	12.75	.442	.09029	12.5632	12.9368
	POST TEST 2	24	14.37	.710	.14512	14.0748	14.6752
	Total	72	13.00	1.19	.14126	12.7183	13.2817

Table 4 - Descriptive statistic of stand & reach test scores of PIR and RI groups

		N	Mean	SD	SE	95% CI	
						Lower Bound	Upper Bound
PIR-STAND & REACH	PRE TEST	24	1.0625	.473	.09665	.8626	1.2624
	POST TEST 1	24	2.2500	.44	.09029	2.0632	2.4368
	POST TEST 2	24	4.6875	.56	.11583	4.4479	4.9271
	Total	72	2.6667	1.59	.18817	2.2915	3.0419
RI-STAND & REACH	PRE TEST	24	1.0000	.44	.09029	.8132	1.1868
	POST TEST 1	24	1.5625	.47	.09665	1.3626	1.7624
	POST TEST 2	24	2.2500	.44	.09029	2.0632	2.4368
	Total	72	1.6042	.68	.08031	1.4440	1.7643

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REVIEW ARTICLE

A Comprehensive Review of Security Issues in Big Data using Cloud Computing

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ABSTRACT

Data being one of the major possessions in this generation, Big data is making an impact on the world economic and social changes. Data is continuously generated, resulting in a massive volume of data that cannot be handled by a traditional relational database management system (RDBMS).The world's data collection is bringing insightful solutions in decision making, managing our health, cities, finance and education. From sharing the hardware and software resources physically to virtually cloud computing has made a huge impact in IT industry. In an instance anyone can access the resources being provided through networking. Bringing such two technologies together makes the data and storage more powerful.

Keywords: Big data, Big data types, Cloud Computing, Service Models, Security Issues

INTRODUCTION

Big Data and Cloud Computing are two of the most common buzzwords in the IT industry today. Big data is concerned with dealing with massive amounts of data, while Cloud computing is concerned with infrastructure. The convergence of big data and cloud computing results in better outcome for enterprises. Furthermore, both technologies are in the process of evolving, resulting in a cost-effective and scalable outcome. Basically, Cloud computing growth is also fuelled by Big Data. Without Big Data, there would be very few cloud-based applications,

since there would be no requirement for them. This is because Big Data is often collected by cloud-based applications. Services of cloud computing are existing only because of Big Data. Similarly, the only reason that we collect Big Data is because we have services that are capable of encoding and decoding. Hence, we can say that both are reliable on one another.

Overview of Cloud Computing

Just like the real clouds in the sky formed by water molecules, similarly we have cloud in cloud computing formed by networks [1]. The Cloud is basically used to signify the internet. And, Cloud computing is a technology used to provide the software, infrastructure and storage services over the internet. It is a booming technology that has recognized itself in the upcoming peer group of IT industry and organizations. With cloud computing, the resources are paying, the customer has to pay as they use the service. shared and costs too. Users has the privilege of paying only for what services they use. There is no system of pre-

Characteristics

The following are some of the major characteristics:

On-Demand Self-Services

All the resources in cloud computing can be obtained virtually from the service provider without person-to-person interaction. The services include virtual machine, storage space, database instances, etc.

Broad Network Access

Resources are accessible through the network and can be retrieved from various platforms. Some of the various service providers are sales force, Amazon (AWS), etc.

Multi-Tenant

This model allows several users to share the similar applications or the physical infrastructure while protecting privacy and security over their data. For example, people working in a building and sharing their building infrastructure but they still have their own working spaces and cabins and floors and privacy provided with the infrastructure.

Resource Pooling

It means that various users are provided services from the same existing physical resources. Providers should have a large and flexible resource pool which is capable to provide several users necessities.

Rapid Elasticity and Scalability

Some of the benefits about the cloud computing is that it is capable of providing resources quickly as the organizations need them and then to eliminate them when not required. This is the role of Elasticity. With scalability, there is minimal investment as a customer. This is more organized. This means that when the customer requires extra computing services, they can just buy them as required which are available at an instant.

Measured Service

The usage of the resources is measured and users pay only for what they have used. This means that the resources used by the consumers is being monitored, measured and reported by the service provider so that they can remind the user to scale up their resources or scale down when not in use. These resources are totally based onpay for what you use.

Deployment Models

Cloud deployment models are basically defined as: private, public, hybrid and community clouds. It is basically defined as to where the infrastructure for the deployment exists in and who has control over that infrastructure. Each cloud computing deployment model satisfies different needs, the organization must choose for which satisfies their needs.

Private Cloud

As the name says the services are maintained and operated by a single organization. This model is more expensive than the public cloud due to the high maintenance. Although they are expensive, private clouds are better in the security and privacy concerns of organizations [2].

Public Cloud

Here the resources such as hardware (OS, storage, CPU) and software (application server, database) are provided to the public as the name suggests. It is basically used for development and testing the applications etc.

Hybrid Cloud

The term "hybrid cloud" refers to a combination of public and private clouds that are used and connected by the same company. This type of cloud is mainly used when the organization needs to scale up their resources. A shopping website, for example, may use public cloud to communicate with customers while using private cloud to store data.

Community Cloud

It is a model which is equally shared between organizations that belong to a particular community. Community cloud is basically accomplished and held internally or by a third-party service provider. This model is deployed typically at banks, government applications, or trading firms.

Service Models

Cloud computing service models are divided into three categories, each of which meets the needs of various organisations. The three models are Infrastructure as a Service (IaaS), Platform as a Service (PaaS) and Software as a Service (SaaS).

Infrastructure as a Service (IaaS)

The main essential computing resources are provided virtually by the IaaS such as network, storage, hardware, operating system etc. [3]. IaaS is the combination of private and public cloud deployment models. Some of the service providers who prove IaaS are Amazon's EC2 and Flexiscale [4].

Platform as a Service (PaaS)

This platform provides the resources to the users in such a way that the users can implement their own software or an application in the cloud. For example, Application server (Java) and Database server (MySQL) where consumer will use it to develop their own applications so that their requirement meets by the needs [5].

Software as a Service (SaaS)

This platform is easily accessible for users through internet and browsers. There is no necessity for the users to purchase, manage, or upgrade software or hardware. Some of the SaaS providers are: Microsoft Office 365, Google Apps etc.

Overview of Big Data

Before the emergence of computers, accumulating and recording the information was a tedious job. Now that there are inventions of computers, digitization and internet – the situation has changed remarkably. Information can be collected with less amount of efforts and at a prominent speed, and also the cost of storage is efficiently economical. This has brought the world to the emergence of big-data era. The cloud provides not only already-available infrastructure, but also the capability to scale this infrastructure quickly so we can control large spikes in traffic or usage."Big data" can be referred as the data being gathered on a much larger scale than formerly or previously possible. It is a pile of data which is enormous in volume, and yet growing tremendously in parallel to time[6].In contemporary research, big data has been distinguished by 5 Vs:

Volume - The extensive data size that cannot be easily captured, stored, manipulated, analysed or managed by conventional data storage and computing automations.

Variety- The variegation of sources and formats of data. The data formats comprise of texts, structures, sounds, videos, images, or a composition of all these.

Velocity- The pace of data emergence, analysis, conception, and the storage based on progressive growth of collection of methods.

Veracity - The differing reliability or quality of data sources

Value- The data needs to be transformed into something that is valuable in order to draw out the information. Just the raw data holds no value and is of no use [7].Social media can be taken as an example of Big data where the statistics depicts that five hundred plusterabytes of fresh data gets consumed in the social media site's databases like Facebook or Instagram every single day.

Big Data Types

Big data can be classified into:
1.Structured
2.Unstructured
3.Semi-structured

Structured Data Any data which can be handled, retrieved and stored in a fixed format is said to be a 'structured' data. Over the period of time, strength in computer science and technology has gained accomplishment in coming up with techniques to work with the type of data where the format of the data is previously known. For the sake of clarity, we can say that the term "structured data" typically refers to information that is present in a traditional row-column database [8].

Unstructured Data Any data whose form is unknown or unspecified is said to be an unstructured data. The process of retrieving value out of unstructured data gives multiple challenges as the data here is enormous in behaviour. A heterogeneous data source containing simple text files, videos, images, etc. can be shown as the classic example of an unstructured data.

Semi-Structured Data Any data containing or representing both the forms of data (structured and unstructured data) is said to be known as semi-structured data. We can see a particular data in an undefined form but with a structured mannerism. The data determines the amount of structure used. A table definition in relational database management system can be considered as an example for semi-structured data.

Security Issues

Distributed Denial of Service Attack

Big data DDoS defence is the utilisation of big data technology for determining and reducing Distributed Denial of Service (DDoS) attack. Cloud-scale techniques and storage mechanisms can be considered useful in analysing and collecting huge volumes of network flow data by also making simultaneous use of Big data DDoS defence. This results in significant accuracy in putting a stop to DDoS attacks than it is possible with the traditional, limited-data DDoS defence appliances. The objective of a DDoS attack is to restrict access to either an application or a service network by denying the access for illegitimate users [9]. Identification and mitigation of attacks can be done by Cloud-Based DDoS defence services without the necessity of network under attack for the deployment of on-premises resources.

Man in The Middle Attack

Man in the Middle attacks existed prior to the appearance of computers. To present the basics of MITM attacks it can be used an example of a postman who looks into the letters of people and may even change its content [10].A Man in the Middle attack is a form of cyber eavesdropping or overhearing in which malicious hackers involve themselves into a conversation between two parties and interrupt data through a compromised but reliable system. The targets are often conceptual property or important information. MITM initiators will also use malware to open the communications channel with the hopes of building extensive networks of comprehended systems. Man-in-the-Middle Attacks can be used as path into systems in order to carry out an advanced persistent threat (APT).In various cases organizations are unsuspecting their data that has been tampered with until it is much too late.

SQL Injection Attack

One of the most expected threat to a SaaS application is the SQL injection attack. This might lead to lose important and subtle data such as financial or personal data. Data-driven websites are likely vulnerable to SQL Injection attacks. The hackerim plants harmful data with the SQL code. Hence, some unidentified user makes devious actions in the system by getting access to the server. Often with the assistance of malicious code, the device misinterprets an unidentified user's input as authorised, granting the hacker access to the server's and website's configuration. [11].

Data Breach

Basically, cyber criminals distribute data whether it is transferred physically or virtually. Similarly, in the era of cloud, the safety of data cannot be compromised within the cloud too and this leads to Data Breach. It is an attack that is capable of unveiling sensitive data to some anonymous third party illegally [12]. If an unauthorized user can access through all sensitive data, then they could wish to sell it or distribute it to organizations. A person's health records, Identity of a person are often being targeted for data breaching and need the highest levels of safety in cloud computing. Some of the companies which were targeted to data breach were Yahoo, Microsoft, Amazon Web Services etc.

CONCLUSION

The paper reviews the ukase of Cloud computing for hosting Big data as well as the security challenges that these technologies face. We may infer from though Big data and Cloud computing are two distinct technologies that depend on one another.

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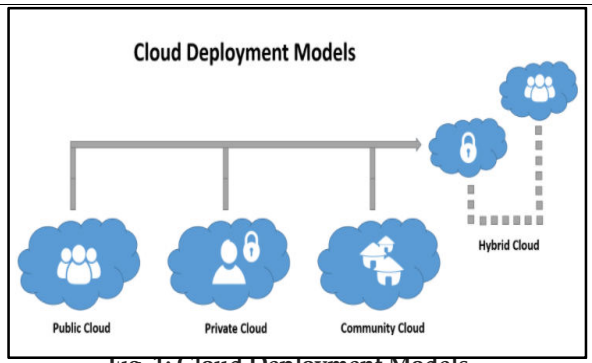

Fig. 1: Cloud Deployment Models

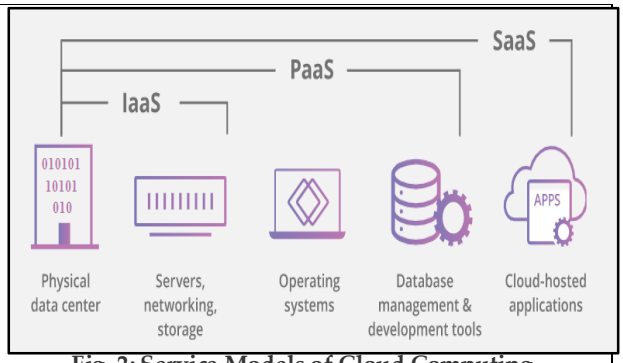

Fig. 2: Service Models of Cloud Computing

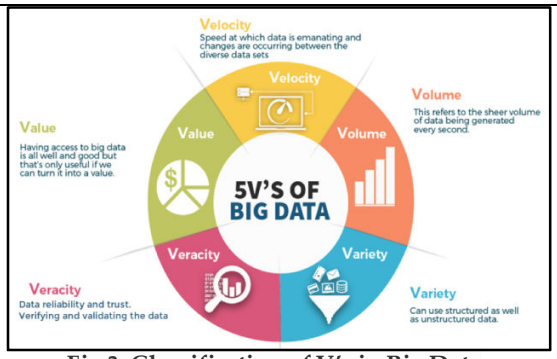

Fig.3: Classification of V's in Big Data

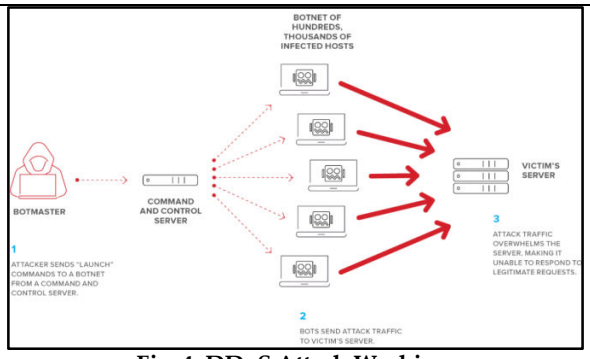

Fig. 4: DDoS Attack Working

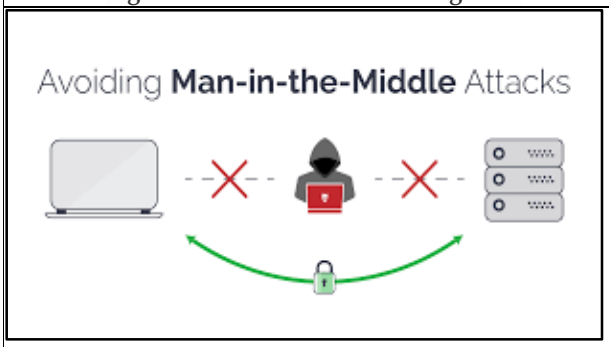

Fig. 5: Man-in-the-Middle Attack

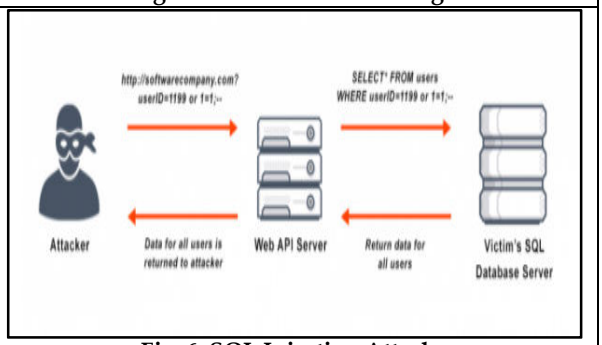

Fig. 6: SQL Injection Attack

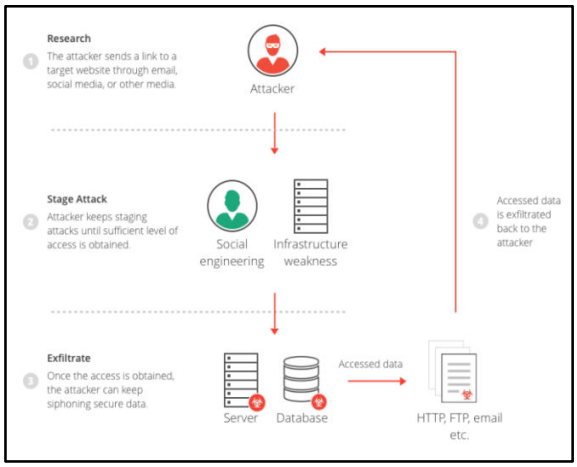

Fig. 7: Data Breach

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RESEARCH ARTICLE

Machine Learning methods in Autism Spectrum Disorder: A Taxonomy and a Comparative Study

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ABSTRACT

Autism is a lifelong, neurological disorder typically appearing before the age of three years. It is a kind of developmental disability affecting verbal and non-verbal communication and social interaction. Sensory disorders, such as oversensitivity or under sensitivity to noises, smells, or contact, are often associated with Autism Spectrum Disorder (ASD), a neuro developmental disorder. Although the primary cause of autism is hereditary, early diagnosis and treatment will help to improve the situation. Machine learning based diagnosis has emerged in recent years to supplement conventional clinical approaches, which can be time-consuming and costly. The use of machine learning methods in ASD is an active area of research. Although several surveys are existing in the field of ASD, the literature lacks comparative study and taxonomy of ML based methods. In the paper, we first discussed various machine learning algorithms for ASD in detail and introduces a taxonomy of machine learning algorithms with respect to autism disorder. Then we consider supervised machine learning algorithms for ASD and evaluated the performance of algorithms. Our study indicates that Random Forest outperforms well than the other ML algorithms in terms of performance metrics. We hope that our work will be beneficial for future research directions in the ASD domain.

Keywords: Autism spectrum disorder (ASD), KNN Algorithm, ANN Algorithm, Supervised Learning Style

INTRODUCTION

Autism spectrum disorder (ASD) is a form of developmental disorder characterized by a wide range of symptoms. It has an effect on how people communicate and connect with one another, as well as how they live and learn. When a child is very young, the symptoms and signs emerge. It is a chronic illness that cannot be healed. Conventional clinical approaches, on the other hand, have a hard time detecting and diagnosing ASD. ASD is most often diagnosed at the age of two, although it can be detected later also depending on the symptoms[1]. Although clinical methods are available to diagnose ASD, these include time-consuming diagnostic procedures that are used unless there is a high risk of ASD growth. For diagonising, a check list can be used for patients such as toddlers, children, adolescents and young adults [2].ASD can be diagnosed with ML tools and mechanisms with a highly improved output.ML is a branch of AI that learns from experience and predicts the targeted output based on the learned experience.

Machine learning has shown its effectiveness in prediction and classification tasks by learning past data. Furthermore, machine learning is a time consuming approach in the ASD domain by learning directly from the training data. Unsupervised and Supervised learning are the two broad types of machine learning. In this literature, we have covered a few machine learning techniques (both supervised and unsupervised) for autism identification and collected a list of them. Currently, researchers are focused mainly on ML based autism detection and several works have been published in the field of Autism Spectrum Disorder. In the literature, we have summarized several studies which cover various facets of utilizing ML in ASD. The paper extends with a taxonomy of machine learning that has been adopted in the domain of ASD. Furthermore, the paper analyses and compares different supervised ML approaches that were published previously. The paper concludes with the challenges and provides a bird's eye view for future researchers.
The main contributions of the paper are the following

- We reviewed several ASD methodologies utilizing machine learning strategy
- We proposed a novel taxonomy that classifies ML based Autism Spectrum Disorder based on the learning style.
- We provided a comparative study of supervised ML based ASD with respect to different facets like accuracy, sensitivity, specificity and AUC curve in a tabular form.

The paper is summarized as follows, the 'Materials and Methods 'section provides an overview of ML based ASD approaches. Furthermore, the section provides a novel taxonomy of ML based approaches and a comparative analysis of supervised ML based ASD approaches. In 'Results and Discussion', comparative study of various supervised ML based ASD are plotted. Finally, the section named 'Conclusion' concludes the paper with challenges and future research approaches.

MATERIALS AND METHODS

ML Based Taxonomy for Autism detection

[3] presented here highlighted the applications of ML algorithms for autism detection. The taxonomy we have considered as a systematic framework for autism detection with respect to the learning style. We have classified the techniques into two types 1). Supervised Learning Style 2).Unsupervised Learning style. The taxonomy highlighted here focuses on the state of the art of ML based autism detection mechanism with respect to the performance evaluation aspect. However, there has been a limited number of works that utilized ML methods for autism detection. The taxonomy presented in this review is presented in Fig.1.We have covered several machine learning methods for autism detection and compiled a summary of autism detection methods. Finally, all the network models are analyzed with respect to performance metrics and tabulated. The next section provides a detailed overview of widely used ML algorithms for autism detection.

Supervised Learning Style

The supervised learning styles reviewed in this paper covers widely used ML algorithms for autism detection by identifying the patterns. This subsection contributes to the understanding of currently available supervised learning methodology in ASD research and it is hoped that this section will be beneficial to the new researchers in this domain

Support Vector Machine (SVM)

SVM is a supervised machine learning approach which is used for the task of classification and regression. As SVM is an effective maximal margin classifier that can categorize the data with +1 and – 1 values. SVM maps the inputs into high dimensional feature space and fits the hyperplane to classify the dataset to predict the target result [4].In order to provide accurate diagnostic result SVM are especially useful particularly in ASD research areas. As described in [5] the proposed methodology trained and cross validated the SVM based model to categorize ASD disorder from other disorders. In addition to that SVM can provide high accuracy by providing deeper insight into all the behavioural characteristics namely eye movement data, neuroimaging data etc.

Logistic Regression (LR)

Logistic regression is an ML tool used for binary classification purposes. With the goal of developing an efficient technology to determine the impact of parental age, the study [6] collected and analyzed the individuals in California between 1982 and 2002. The Logistic regression model can be used as open source autism detection classifierwhich can determine the association between the target variable and binary dependent variable employing sigmoid function. In addition to that LR model is easy to implement and can be used as a benchmark model for prediction with high performance.

Naive Bayes

It is the simplest supervised classification approach that predicts the outcome by calculating the posterior probability distribution. The increasing number of works has been published based on the application of Naïve Bayes algorithm for prediction and classification. The prediction approach calculates the posterior probability using the likelihood table [7]. However, a limited number of works based on Naïve Bayes have been published on the application of autism detection.

Random Forest (RF)

RF is a supervised machine learning model that utilizes ensemble based learning approach for classification and regression task. The classifier contains a subset of decision trees to obtain the prediction based on the majority voting. With the predictability point, the Random Forest model leads to better performance because of the greater number of decision trees. The model outperforms the existing models by reducing the likely hood of over fitting the training dataset. To avoid over fitting the bootstrapping methodologies are utilized that give rise to built in training and validation for the RF model [8]. used ML models to analyzed and classify the neuroim aging data into ASD and TD(Typically Developing).Out of 252 brain imaging datasets,126 is for TD and 126 for ASD participants. For the classification task, the authors conducted experiments using a matrix of functional consecutiveness between regions. Out of 220 regions, the top most 100 regions show a high 91% accuracy, a sensitivity of 89% and a 93% specificity.

KNN Algorithm

KNN algorithm is an ML model which follows a supervised learning approach is used for classification and regression tasks. This is one of the simplest models that assumes the similarity between the existing cases and new cases. The model is basically a classification algorithm which is based on data vectors into a different number of several categories and tries to predict the classification of the new sample. Thus the model was able to predict based on the closeness which is expressed in terms of Euclidian distance [9]. Deployed a KNN model to build an open source classifier that predicts autism disorder with improved accuracy of 90%.

ANN Algorithm

An Artificial neural network is the connection of perceptron's, which mimics the human brain power. The main objective of the model is to predict the outcome for the newly inputted data. The neural network has to be trained by means of error rate. [10] Uses ANN technique to diagnose the ABIDE dataset which comprises brain structural images. Here neural networks set out a classification task to classify the brain imaging data into HCS (Healthy Control subjects) and AS (Autism Spectrum).

Unsupervised Learning Style

A diverse array of ML methods have been applied and adapted in the domain of Autism spectrum disorder. Many research studies provided a primer with respect to supervised learning and covered some recent applications of supervised learning in ASD. However, there is a limited number of research studies have been conducted for unsupervised learning strategies. Although no studies could be found for the detection of autism detection using unsupervised way of ML algorithms. Then the subsection articulates the recent developments and applications of ML based studies in Autism Spectrum Disorder.

K-Means Clustering Algorithm

K-means clustering algorithm is the simplest of all and widely used unsupervised algorithm. K-means clustering separates the data sets into K clusters and each data is connected to the centroid of each cluster [11] analyses the challenging behaviors in Autism Spectrum Disorder of 2116 patients. This clustering algorithm has been proposed to identify the behavior and in all the clusters a single dominant behavior is present.

Gaussian Mixture Model

The Gaussian mixture model is the most powerful unsupervised clustering algorithm. Like K-means clustering, the Gaussian model also involves the clustering process. The major benefit of leveraging the Gaussian model considers the probability value for distributing the new data in different clusters.[12] set out to identify autism in adults aging 18 to 35 years from ABIDE dataset which comprises brain images. In an attempt to accelerate the prediction process, the proposed model uses the Gaussian Mixture model that clusters the regions of the brain and the SVM classifier classifies the data into Autism data and control patients data.

Comparative Study of Supervised ML in ASD

Many supervised ML frameworks have been found in the diagnosis of ASD. The supervised ML algorithm reviewed in this paper helps to identify the patterns in the given dataset for the diagnosis of autism disorder. For empirical comparison, six supervised learning classifiers were selected for analysis is however, each of these ML based methods has strengths and weaknesses. SVM and Random Forest is the most used algorithm in the field of ASD and also give the best overall performance among ML algorithms. Table 1 lists the research papers on supervised models for autism detection. These methodologies are selected for the empirical comparison and it may shed a light for future researchers in the autism detection domain.

RESULTS AND DISCUSSION

The purpose of the paper is to study the machine learning algorithms in ASD domain. The capability of the ML model to learn and to predict the output based on the training data has opened the door for the supervised ML models to get into a remarkable position in the field of autism detection. The accuracy, sensitivity, specificity and ROC of each model are illustrated in Table 1.The above table illustrates that all the above models are capable of predicting Autism Spectrum Disorder in a better way. The below figures indicate the results of this comparison based on the performance of various ML models. The aim of this study is to study the performance metrics of the models for autism detection. The results indicate that Random Forest and Naïve Bayes outperform well in terms of accuracy.

The general comparison of the above ML models indicates the evaluation metrics for autism detection. Out of all the models, Random Forest and Naïve Bayes show outstanding performance in terms of accuracy. Both the models are easy to implement and train and the new researchers can consider this model for autism detection. In fig 3 SVM gives better sensitivity measure in comparison with other models. Considering Fig 4, Random Forest gives good specificity. The results in Fig 5 shows that LR performs well based on the AUC curve. All the six supervised ML models can be considered in the future for Autism detection. Considering the performance, the Random Forest model acts as a capable model in the benchmark for autism detection. Unsupervised model shows better performance for analyzing challenging behavior of ASD individuals however, the models do not perform better than supervised models for autism detection.

CONCLUSION

This paper presents a taxonomy of ML algorithms in ASD and a comparative study of supervised ML algorithms in autism detection. ML algorithms especially supervised ML algorithms have become a viable option in the field of detecting ASD. The results show that Random Forest performs well across the metric accuracy and specificity. One of the major weakness in the current literature are for autism detection unsupervised algorithm cannot perform well for autism detection and there a limited research works exist in the ASD domain. However, there a limited works exist in the ASD utilizing machine learning because of resource constraints. This study aims to provide a view of the only supervised way of autism prediction mechanism. In the future, it is hoped to add unsupervised machine learning methods also in the repository of autism detection.

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Table 1: Supervised ML Comparison

PAPER	MODEL TYPE	ACCURACY	SENSITIVITY	SPECIFICITY	AUC
Liu *et al.*, [13]	SVM	89	93	86	0.90
Chen *et al.*, [14]	RF	91	89	93	___
Surya et al.[9]	KNN	90	___	___	___
Florio *et al.*, [15]	ANN	80	92	70	0.88
Grether *et al.*, [16]	LR	___	___	___	0.962
V.JalajaJayalakshmi et al.[17]	NB	95	____	____	___
Nakai et al.[18]	SVM	76	81	73	––
Zhou *et al.*, [19]	RF	93	75	94	0.88

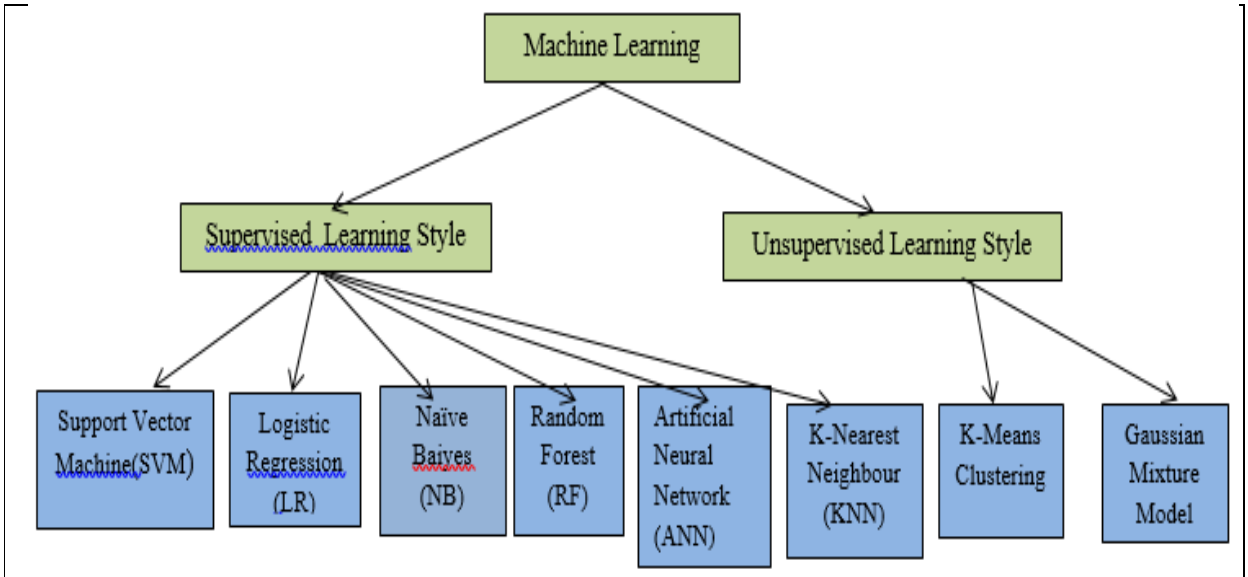
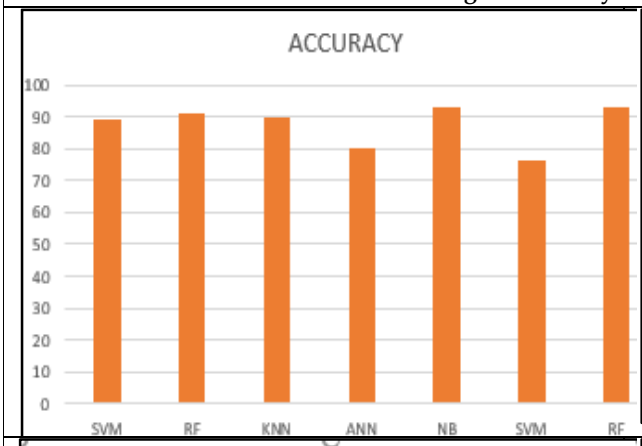
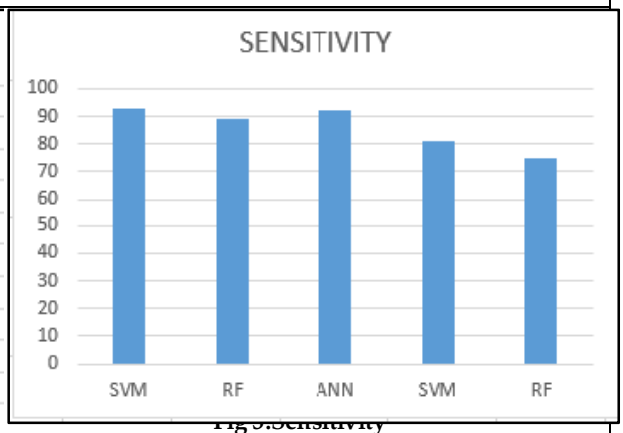
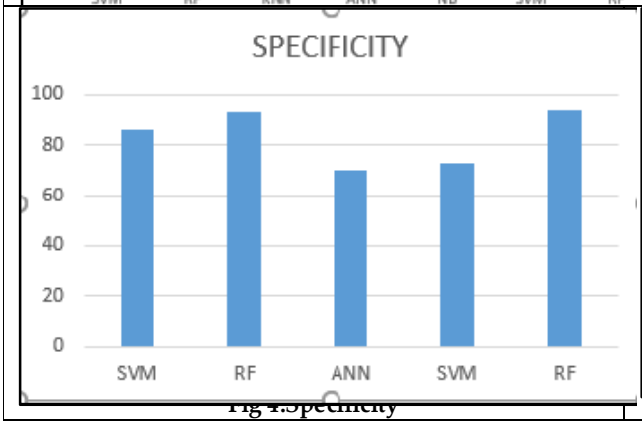


Fig 1:Taxonomy of ML based ASD







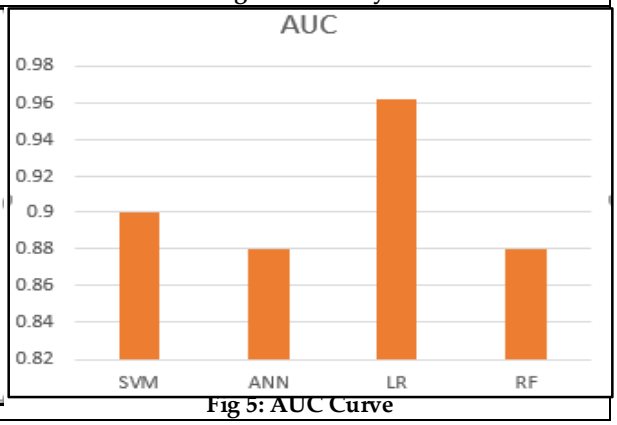


Fig 5: AUC Curve

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RESEARCH ARTICLE

Simulation of Hybrid System (Involving Solar, Wind and Biodiesel) using Multilevel Inverters for Smart Grid Communication Systems

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ABSTRACT

The demand for electricity is constantly increasing for various applications due to its flexibility and efficiency. Non conventional sources are becoming popular as generating power is not practical in conventional ways. Here, we combine solar, wind and biodiesel as an alternative to thermal and hydraulic generation. The article discusses the task involved in simulating, designing and integrating renewable energy sources. Multi- level inverters (MLI) are used to achieve the harmonic level in IEEE standards. Smart Grid consists in improvising the transmission and distribution system to make it reliable and of good energy quality. Therefore smart grid when combined with hybrid system with advanced levels of electric data from one node to other node considering the authentication and security as the primary and essential need to make the system intelligently. A software simulation model is developed in MATLAB/simulink.

Keywords: Hybrid, solar, wind, biodiesel, Multilevel Inverter, THD.

INTRODUCTION

Electricity is the most necessary for our daily life. There are two ways to generate electricity using standard energy resources. Current demand will increase in word therefore to meet demand we have got to get current. The standard energy resources are depleting ay by day. Presently it will be utterly vanishes from the earth therefore we have a tendency to have to notice another means to get electricity. There are several non conventional energy resources like geothermal, tidal, wind, solar, wind, biodiesel etc[1]. There are many renewable energy sources such as solar, wind, hydro and tidal. Among these renewable sources, solar and wind are the fastest growing energy sources in the world.

A hybrid system of wind and PV power sources and biodiesel provide a stable form of power generation. Hybrid energy systems are cost effective solutions with high reliability and power quality. As the demand from the customer is fulfilled by levels of the inverters switching in the design if the inverter is improved. The inverter is designed as a MLI by its levels of switching. Based on these background, the paper gives us the information of modern topology for 3 phase 7 levels of MLI [2].

Communication : The main goal of the SG system to provide the authentication and security and to do this means to digitalize the system, so to achieve this it becomes very important to provide the communication or link between the various nodes at the sender as well as receiving end. The speeds the work of identifying the errors, inspects the system, secure the system against cyber attacks and so on.

METHODOLOGY

A hybrid renewable generation system comprises of wind turbines, PV panels, biodiesel, storage batteries to collect wind energy, we are using wind turbines [3]. The output of wind will be in form of AC and continuously varying, so for a constant power we rectify it using wind controller comprising of a rectifier and a boost converter, boost converter is used to boost up the voltage. The output from the wind controller is fed to the inverter and finally supplied to the AC loads.

Solar Energy

The huge amount of solar energy available makes it a very attractive source of electricity. 30% (approximately) of the solar radiation returns to space while the rest is absorbed by the oceans, clouds and land masses. When sunlight is radiated, a photovoltaic cell generates current and the pair of electronic holes is generated, while the photovoltaic cell equipment absorbs photons with an energy that exceeds the band gap of the material. These produce photons, are carriers that eliminate the internal electric fields of this cell as shown in figure below. Figure1. Shows the Internal reaction of solar energy.

Wind Energy

The actual power will depend upon several factors such as the type of machine and rotor used, losses in friction and pump and other equipments connected to the machine. There are also physical limits to the amount of energy that can realistically be extracted from the wind. However, important areas of the world have annual average wind speeds of over 4-5 m / s (meters per second), making small-scale wind power generation an attractive option.

Biodiesel Energy

The Biodiesel production is shown with a block diagram in Figure2. Bioenergy can be produced from many sources of biological material.

There are three common thermo chemical processes:

(1) Combustion, which requires sufficient oxygen for oxidation

(2) gasification, which requires insufficient oxygen to prevent complete oxidation

(3) Pyrolysis, which occurs in the absence of oxygen.

Hybrid System

In this work 3 sources are integrated to form hybrid grid to which load is connected[4]. The sources when operated independently will provide variable power but by integration it becomes feasible to get fairly reasonable sustainable power [5].

Simulation of Solar PV Plant

Figure3. Shows the Simulation of a solar PV model and Figure 4.and Figure 5. Gives the output waveform of the solar panel model and battery [6].

Simulation of Wind Power Plant

Figure 6.Shows the Simulation of wind model and Figure 7. shows the output waveform of wind [7].

Simulation of Biodiesel Plant

Figure 8.Shows the Simulation model of Biodiesel and Figure 9.shows the output waveform of the plant.

Simulation of Multilevel Inverters

Figure 10. Shows the Simulation model of Seven level MLI using five Switches and Figure 11. shows the output waveform of the MLI[8]. Table 1.describes the switching sequences for the single phase seven-level topology using five switches with the help of circuit breaker reduction.

RESULTS AND DISCUSSIONS

Using hybrid renewable sources (solar, wind and biodiesel) the proposed model is designed to illuminate a load. we designed complete model for 5kw for that we got output as 4.7kw.[9]The requirement can be met by independent power generation making use of locally available resources. But simulation and installation of individual sources reveals that power is variable when operated independently. Therefore the integration of sources leads to sustainable which is clear from the results obtained from the simulation. In this work, seven level MLI show that the THD obtained is 3.85% which falls within the IEEE standards (0-5%) as seen in Figure 12, so that work made is proceeded by eliminating the switches for same level using MLI and results in THD improvement[10]. Therefore the combination of this advanced inverter with the hybrid system helps in the communication of electric data from one node to other node with the security.

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Table 1 . Switch Scheme for reduce level topology

	a	b	c	d	E
0	0	0	0	0	0
Vdc	1	0	0	1	0
2Vdc	0	1	0	1	0
3Vdc	0	0	1	1	0
2Vdc	0	1	0	1	0
Vdc	1	0	0	1	0
0	0	0	0	0	0
- Vdc	0	0	1	0	1
-2Vdc	0	1	0	0	1
-3Vdc	1	0	0	0	1
-2Vdc	0	1	0	0	1
-Vdc	0	0	1	0	1
0	0	0	0	0	0

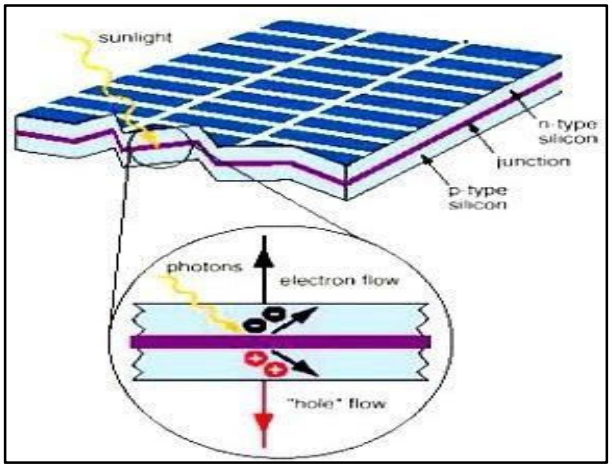

Figure 1. Internal reaction of solar energy

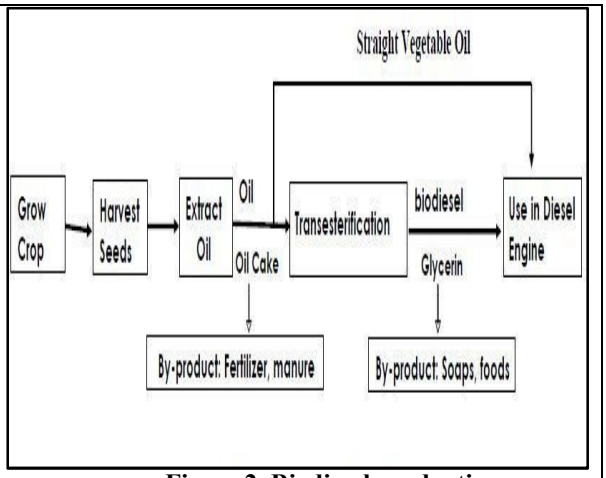

Figure 2. Biodiesel production

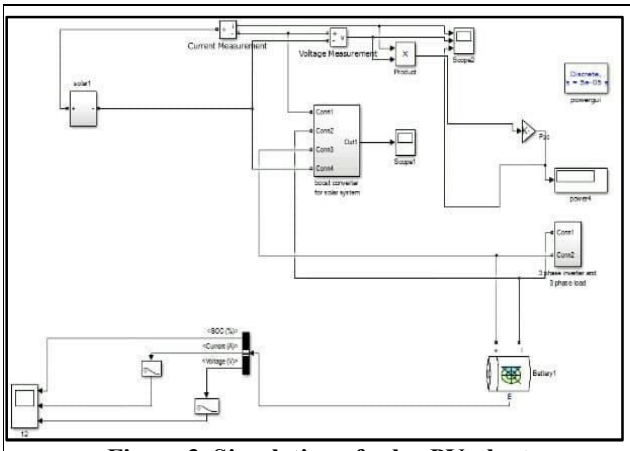

Figure 3. Simulation of solar PV plant

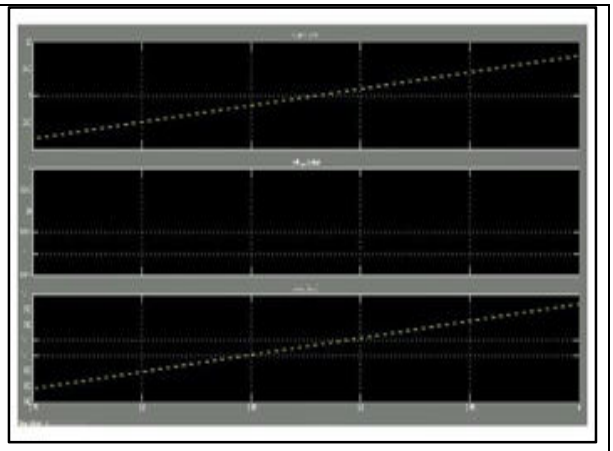

Figure 4. Output waveform of solar panel model

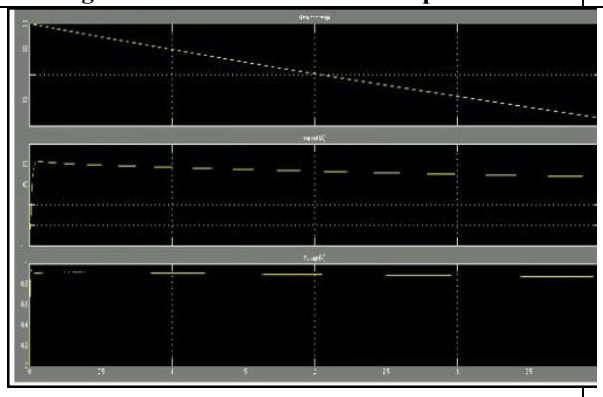

Figure 5. Battery output waveform

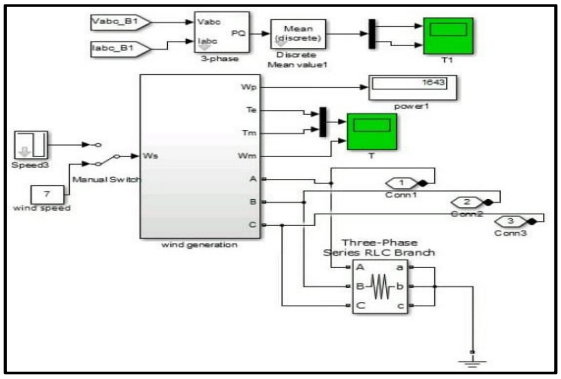

Figure 6. Simulation of wind model

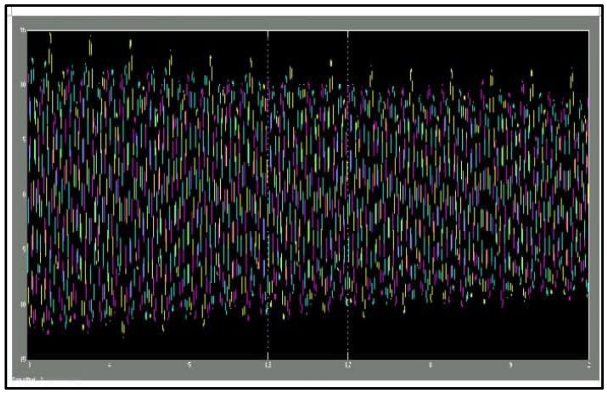

Figure 7. Wind output waveform

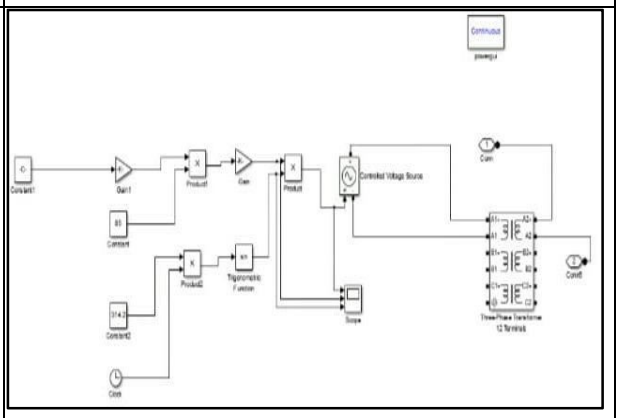

Figure 8.simulation model of biodiesel plant

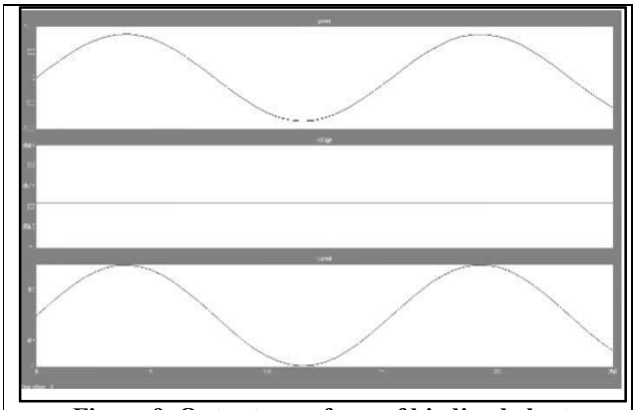

Figure 9. Output waveform of biodiesel plant

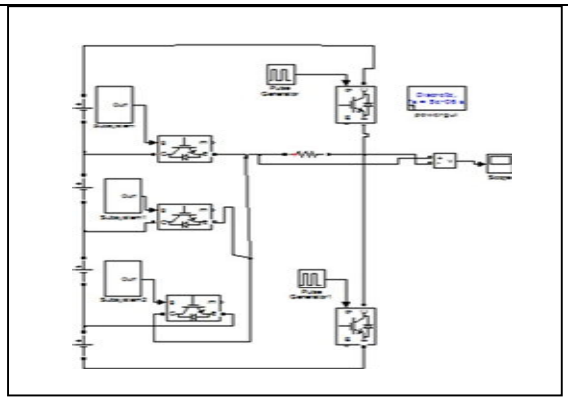

Fig.10 Simulink using five Switches

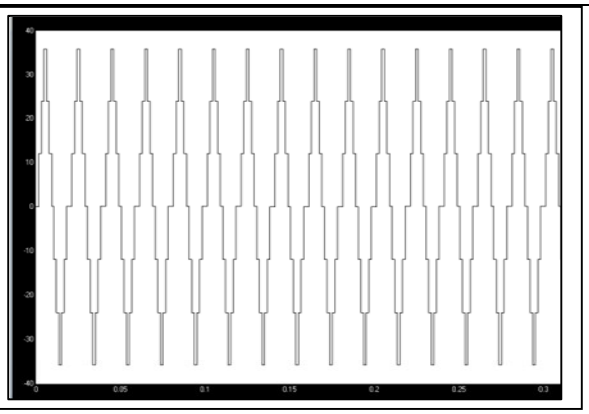

Fig.11 Output of MLI waveform

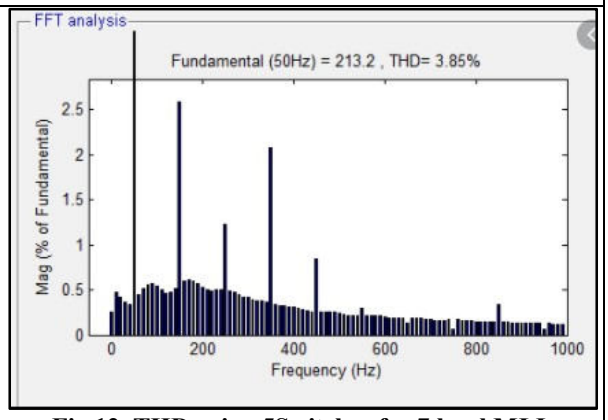

Fig 12. THD using 5Switches for 7 level MLI

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RESEARCH ARTICLE

Effect of Proprioceptive Neuromuscular Facilitation on Flexibility

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ABSTRACT

The purpose of the study is to evaluate the effect of Proprioceptive Neuromuscular Facilitation on flexibility. Twenty college-level athletes between the age group of 18 and 22 yrs at Vinayaka Missions Research Foundation – Deemed to be University, Salem who had below-average joint range-of-motion (specifically a sit and reach the score of 13.5 inches [34.3 cm] or less were selected using simple random sampling technique and were further divided into two equal groups randomly. Pretest measurements of flexibility were collected using sit and reach tests. After the pretest assessment, the experimental group received Proprioceptive Neuromuscular Facilitation along with their warm-up exercises and the Control group received warm-up alone for 2 weeks and on the 14th day, post-test measurements of flexibility were collected similarly to that of pretest measurement. The results were in the favor of the Experimental group who received Proprioceptive Neuromuscular Facilitation additionally along with the warm-up exercises in improving the flexibility of the athletes.

Keywords: Proprioceptive Neuromuscular Facilitation, Warm-up exercises, Flexibility.

INTRODUCTION

"Flexibility" is just the ability to move muscles and joints through their complete range. It's an ability we're born with, but that most of us lose. Flexibility plays a major role in one's ability to engage in various types of physical activity; and while a significant factor in human function, it often receives modest attention in many exercise programs. Major

benefits associated with superior flexibility include a reduction in the rate of functional decline; increased training capabilities; improved postural symmetry and muscle relaxation; reduced tension in muscles, joints, and connective tissues; a reduction in the risk for injury; potential relief of pain; and improved quality of life (QOL). Maintaining a level of flexibility over one's lifespan is associated with a decrease in functional decline and greater independence, whereas a reduction in flexibility can ultimately lead to the restriction, chronic pain, dysfunction, and reduced QOL.

Proprioceptive Neuromuscular Facilitation can be employed to make an immediate increase in flexibility and to help athletes enhance their performance [1].The proprioceptive Neuromuscular Facilitation (PNF) technique improves muscle elasticity and demonstrates a positive effect on active and passive range of motion [2]. PNF stretching is positioned in the literature as the most effective stretching technique when the aim is to increase passive range of motion [3]. Passive range of motion (PROM), active range of motion (AROM), peak torque, and muscular strength are some outcome measures being adopted in the latest research contributions to measuring the efficacy of the intervention. The significance of PNF in therapeutic and athletic settings can be demonstrated by the habit of practicing PNF to adapt to injuries by gaining AROM and PROM or improving performance. In clinical settings, therapists apply PNF to rebuild functional range of motion (ROM) and increase strength in patients who have undergone invasive surgeries and in patients with soft tissue damage. Studies show a lot of evidence to prove that PNF techniques do enhance ROM [4,5].

Warm-up prior to the start of physical activities are common and lauded by health professionals, coaches, and landmark textsfor its potential for both performance enhancement and injury prevention. Warm-up (WU) can be referred to as a physical and/or mental activity performed to prepare an individual for a higher muscle demand, usually before a high-intensity competitive or recreational event like a sport or exercise takes place, traditionally involving a universal and a specific WU activity. The general WU usually comprises low-intensity aerobic components (e.g. walking, submaximal running) and stretching exercises. The specific WU comprises of specific-skill exercises, which includes activity that reflect upon the type of movement required for the sport or event. WU also aims to improve performance by increasing the muscle temperature and smoothening the contractions (i.e. reducing the muscle's viscous resistance) or increasing the pace of nerve transmission

METHODOLOGY

Study Design

Randomized control trial with an experimental group and a control group.

Inclusion Criteria

- All the college level athletes of both genders belonging to the constituent colleges of Vinayaka Mission's Research Foundation – Deemed to be University, Salem
- Subjects who had a below-average joint range of motion (specifically a sit and reach a score of 13.5 inches [34.3 cm] or less were only included.
- Subjects between the age group of 18 and 22 years were only included.
- Subjects with Medical fitness for participation in sports from a recognized Government doctor were only included.

Exclusion Criteria

- Athletes belonging to the off-campus of Vinayaka Mission's Research Foundation – Deemed to be University, Salem were excluded.
- Athletes with recent injuries were excluded.

Study Population
All the college level athletes between the age group of 18 and 22 years at Vinayaka Missions Research Foundation – Deemed to be University, Salem who had below-average joint range-of-motion (specifically a sit and reach a score of 13.5 inches [34.3 cm] or less will form the population of this study). All the psychologically and medically fit athletes belonging to both genders without any other associated problem were taken as the population of the study.

Number of Samples and Method of Selection
20 samples were selected using Simple Random Sampling and were further divided into two equal groups.

Type of Sample
Human Volunteers (Athletes)

Materials Used for the Study
1. Sit and Reach Box

Procedure
The control group performed the FIFA 11 Plus warm-up practices. This programme had three stages and has a total of 15 exercises (Table No. 1). The first stage consisted of running exercises with low displacement speed (i.e., trotting and slow running 8–10 $km.h^{-1}$), combined with active stretching for lower limbs. The second stage consisted of six exercises (with three levels of difficulty each) to the muscle groups of the legs and focus on balance, strength, agility, and plyometric exercises (i.e., involving high-speed stretch-shortening cycle exercises, such as jumping and acceleration-deceleration). The third stage consisted of running exercises at moderate and high speed, combined with a change of direction

The experimental group performed the FIFA 11 Plus warm-up practices similar to that of the control group and then received contract-relax Technique (PNF) . The contract-relax technique began with a passive pre-stretch of the hamstrings. It was held at the point of mild discomfort for 10 seconds. The athletes were then directed to extend the hip against resistance from the researcher. This was done so that a concentric muscle action occurs. The athletes were asked to relax. Following this, a passive hip flexion stretch was applied and held for 30 seconds. The stretches were repeated 4 times in both legs in an alternative manner with 3 seconds of rest after each stretching.

Data Analysis
The collected data from both the groups in the sit and reach test were analyzed using a paired 't' test and independent 't' test (Table No. 2).

RESULTS AND DISCUSSION

20 samples were selected using simple random sampling and they were allotted into two equal groups randomly. The first group received warm-up exercises and the second group received Proprioceptive Neuro-Muscular Facilitation along with the warm-up exercises. The analysis of the collected data using paired "t" test for 9 degrees of freedom at 95% confident level have revealed that both Warmup and Proprioceptive Neuro-Muscular Facilitation with warm-up was significantly effective in improving the flexibility of the athletes. The analysis of the collected data using independent "t" test for 18 degrees of freedom at 95% confident level have revealed that Proprioceptive Neuro-Muscular Facilitation with warm-up was significantly more effective than warmup exercises alone in improving the flexibility in athletes.

The increase in flexibility due to Proprioceptive Neuro-Muscular Facilitation may be due to the Golgi tendon organ relaxes a muscle after a sustained contraction has been applied to it for longer than 6 seconds.Isometric contractions

(the hold phase) and concentric contractions (the contract phase) used immediately before the passive stretch (the relax phase) facilitate autogenic inhibition. Autogenic inhibition is a reflex relaxation that occurs in the same muscle where the Golgi tendon organ is stimulated [3]. PNF increases the Range of motion and improves the strength of muscles thereby enhancing performance [6].

Dynamic warm-up exercises raise your body temperature by heating up your muscles. They also boost your metabolism and accelerate the supply of energy to your muscles. As your muscle temperature rises, your muscle viscosity (or resistance) decreases. It increases tissue and muscle flexibility and prepares your body to perform fast and explosive movements. For a warm-up, stretching is commonly performed following a short aerobic workout, which hoists the internal heat level, diminishes muscle solidness, and builds flexibility [7].

CONCLUSION

The results of the study make us conclude that Proprioceptive Neuromuscular Facilitation with warmup is significantly more effective than warmup exercises alone in improving flexibility in athletes.

ACKNOWLEDGMENT

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Table No. 1. FIFA 11 plus warm-up protocol

S.No	Exercise	Duration
	Part 1: Running	8 minutes
1	Straight ahead	2 sets over 30 meter each exercise
2	Hip out	
3	Hip in	

4	Circling partner	
5	Shoulder contact	
6	Quick forward and backward	
	Part 2: Strength- plyometric- balance	10 minutes
7	The bench: alternate legs	3 sets x 40 seconds
8	Sideways bench: raise and lower hips	3 sets x 20 repetitions on each side
9	Hamstrings: intermediate	1 set x 7 repetitions
10	Single leg stands: throwing ball with a partner	2 sets x 30 seconds each leg
11	Squats: walking lunges	2 sets x 10 repetitions each leg
12	Jumping: lateral jumps	2 sets x 15 jumps
	Part 3: Running exercises	2 minutes
13	Across the pitch	2 sets x 30 meters (70 – 80% maximum pace)
14	Bounding	2 sets x 30 meters
15	Plant and cut	2 sets x 5 repetitions (80-90% maximum pace)

Table No. 2. Sit and reach test data with paired'ť' test and independent'ť' test

Test	Variable	"ť" calculated value	"ť" table value
Paired "ť" test Warm-up exercises	Flexibility	4.52	2.26
Paired "ť" test Warm-up exercises with Proprioceptive Neuro-Muscular Facilitation	Flexibility	11.30	2.26
Independent "ť" test	Flexibility	5.90	2.09

"ť" calculated value > than "ť" table value Significant at 5% level

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RESEARCH ARTICLE

DevSecOps on Cloud Storage Security

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ABSTRACT

Software Progress is closely connected with technology. Now the stage of development is that the relationship between human and technology is so high. As our technology is growing the chances of data theft has also grown. Therefore, the security for any applications is the first priority. Considering all these current problems in the data security department, DevSecOps is one of the new innovative concepts that suits to come out the difficulties. This paper is to inform IT Professionals why security is important and approaches to improve safekeeping of cloud storage through a new concept DevSecOps. Here it takes more focuses on the transformation of the data through more security measures. And by following this method, one can have faster response and more secure from the data theft and attacks. Where it leads to a complete protected system. Without the proper practice of the security, the nonstop delivery of services by DevSecOps is risky. But if we see another side, they give the best possible security to reduce risk and threat.

Keywords: Software as a Service, Platform as a Service, Infrastructure as a Service, DevOps, DevSecOps

INTRODUCTION

Overview of Cloud Computing

Cloud computing is the natural candidate to support the exponential magnification of data. Cloud is nothing but the group of water molecules. But in cloud computing the word 'cloud' refers to networks. In simple words the cloud computing is the assembly of networks. Here it can be used by the user at anytime from anywhere. Here the user can

access his data from the cloud by just using his simple browser or an application in order to access his data with proper security. In older times the physical infrastructure was implemented and it was very difficult to maintain, to overcome from that situation the cloud was introduced and here the user can just select a good moderator provider for the services of the cloud computing. The user can use limited cloud data for free and for additional he has to pay for the additional data he used. The entire security of the data is handled by the cloud team [1]. Lot of network is handled by cloud which forms a cloud area where the load on personal computer is too less. As a PC has a normal web browser and user can access his data from the cloud through a mode of networks. From this cloud server we can reduce the hardware and software requirements from the user end [2]. And Some of the best examples for cloud computing are YouTube, Gmail, Facebook, Instagram etc. In cloud computing mainly there are three service providers

Software as a Service (SaaS)

SaaS is a friendly service model for applications that are extremely interoperable, utilized by various clients internally and externally, and for temporary projects. SaaS models are preferred by small and medium-sized organizations that don't wish to invest in IT maintenance. Example: Sisco WebEx, DropBox

Platform as a Service (PaaS)

PaaS is deeply accessible and extremely useful, and it enables associations to construct and make new services and solutions without the requirement of talented engineers in the programming support. PaaS is liked by IT in crossover cloud environments.

Examples: AWS and Google App Engine (GAE).

Infrastructure as a Service (IaaS)

Infrastructure as a Service (IaaS) IaaS is the use of APIs to deal with the most minimal degrees of organization foundation, including organizing, capacity, workers, and virtualization

IaaS is the most adjustable service model for cloud computing, so it is particularly feasible for new businesses and associations searching for agile scaling. It is additionally liked by organizations that look for more prominent power over their assets.

Examples: Cisco Metapod and Google compute engine (GCE).

DevOps

DevOps One of the latest things in present day programming advancement is the DevOps technique. This well-known philosophy plans to welcome turn of events and operational movement on one table. The DevOps practice is frequently associated with deft undertaking the executive's techniques as the two systems have quick and effective conveyances in centre. DevOps is a culture that attempts to take out the absence of corresponding effort among advancement and tasks by joining them up to advance participation, co-operation and correspondence DevOps is an advancement system pointed to overcoming any wall between Development (Dev) and Operations, underlining correspondence and coordinated effort, consistent incorporation, quality confirmation and conveyance with mechanized sending using a bunch of progress. From the above definition, it would be able to be separated that the fundamental target of the DevOps practice is to improve the connection between the turn of events and the tasks office and for those offices to turn out cooperatively for the achievement of a product item Since this methodology is like the handy procedure, in which the various partners of a undertaking are firmly associated. Example: Amazon Web Services (AWS) which has the greatest part in cloud foundation and created huge DevOps skill.

DevSecOps

DevSecOps is the Combination of security into IT and DevOps development. Preferably, this is managed without decreasing the self-confidence or speed of designers or expecting them to leave their development toolchain climate.

If you want a simple DevSecOps definition, "it is short for development, security and operations. Its mantra is to make everyone accountable for security with the objective of implementing security decisions and actions at the same scale and speed as development and operations decisions and actions". With the growth of the Sec(security) to DevOps, a consideration on the coordination of safety is made. The somewhat clear objective of the presentation of greater security centre in DevOps measures is to guarantee the security of any product or data that is handled in its turn of events and activity.

DevSecOps is tied using the DevOps philosophy for security. Giving that information to the various groups, and guaranteeing that security is carried out at the perfect level and at the perfect time. DevSecOps puts security at the edge of necessities to stay away from the expensive errors that come from regarding security as an early idea. Normal security has consistently been about rejection and utilizing the security strategy to keep individuals from opening insider facts. This is the place where the idea DevSecOps becomes an essential feature. It represents Development, Security and Operations. This is fundamentally a rule for how to mesh security into DevOps – a training organizations have effectively began utilizing. To completely understand DevSecOps, we need to ensure we understand DevOps.

LITERATURE REVIEW

While beginning with the literature evaluation an initial look for applicable literature that makes a speciality of the studies place became taken. It was given clean pretty fast that the place itself is alternatively unrepresented in educational literature and maximum already present literature opinions had been conducted with a greater open angle, including "grey" literature like blogs, articles, and white-papers that had been applicable with inside the evaluation process. Going with that choice, the literature evaluation a part of this thesis is essentially grounded at the maximum current literature opinions with inside the place from Myrbakken & Colomo-Palacios from 2017 in addition to the maximum current one in every of Prates et al. from the summer time season of 2019. Initially, the plan became to behaviour a literature evaluation that specialize in reviews that typically 2728 Research Method talk the sensible implementation of DevOps/ DevSecOps techniques and the connected metrics and methods. The concept became to then behaviour studies primarily based totally at the coat hanger version supplied. This version lets in to alternatively acquire an information in-exercise software program-engineering strategies in preference to undeniable concept" which could be especially thrilling for the subject at hand. However[3], at the same time as beginning the studies and after first feedback-rounds with fellow college students and the supervisor, an opportunity technique became selected instead. Just like it's miles the case with of the formerly mentioned literature opinions the choice fell to apply a Multivocal Literature Review (MLR) technique for the concept acquisition and present-day evaluation of this thesis. The MLR technique is described as utilizing all available literature applicable to a selected subject matter in preference to cognizance most effective on educational literature. It consists of the usage of blogs, articles, and white-papers in the evaluation process. Thus now no longer most effective educational or researcher's angle however also evaluations of practitioners and improvement firms are included[5]. The lift of relevant grey literature for the conduction of this thesis is supplied later at some point of this part

Principles of DevSecOps

- Construct Security in Instead of Bolting it On.
- Lean in Over Always Saying No.
- Depend on Continuous Learning Instead of Security Gates.
- Empower Open Collaboration Over Security Requirements.
- Offer Threat Intelligence Over Keeping Information to Ourselves.

Advantages of DevSecOps

- More distinguished speed and quickness for security teams.
- A capability to react to alter and wishes quickly.
- Better coordinated effort and correspondence among teams. •Earlier identification and correction of code vulnerabilities
- Early ID of weaknesses in code.
- DevSecOps lets you do a lot of work quickly.

Disadvantages of DevSecOps

- DevSecOps cannot show exactly where the error is in the source code, so developers need to find errors themselves[4]
- DevSecOps May Not Solve Your Problem
- For each and every small issues companies should depend on DevSecOps.

Implementations of DevSecOps

1.Planning: Planning is the primary way to deal with any main job and the important point of DevSecOps security starts from here.
2.Developing: Developers should move toward DevSecOps with a "how to do it" approach, instead of a "what to do" approach[3].
3.Building: Automated form devices can inspire the entire DevSecOps execution measure hugely.
4.Testing:Automated testing in DevSecOps must use solid testing works including front-end, back-end, API, data set and inactive security testing [3].
5.Security:Traditional testing techniques consistently stay set up in DevSecOps to work out.
6.Deploying:Automated provisioning and arrangement can quick track the advancement interaction while making it a more reliable one.
7.Operating: regular monitoring and upgrades are the Operations team's important tasks [3].
8.Monitoring:Frequently watching for inconsistencies in security can save an association from a break.
9.Scaling:Gone are the days when associations spent valuable hours and cash on the upkeep of enormous server farms.
10.Adapting:Continuous improvement is essential for the growth of any organisation. Only by evolving in its practises, including DevSecOps practices—security, functionality, and performance—will an organisation be able to achieve the desired growth [3].

Future Enchancement

Devops is being adopted by all organisations in order to improve their performance. There is no traditional work strategy without devops. Devops' future is dependent on security, best practises, continuous integration, continuous deployment, continuous testing, and continuous monitoring for the benefit of organisations and customers. Devops trends are influenced by various automation tools such as ansible, puppet, terraform, and others. Devops Engineers play a critical role in the organisation.Continuous integration of specific services and applications is now a part of the Devops culture. As a result, the customer or organisation will benefit from project scalability. Devops culture was created to bridge the gap between developers and administrators. Devops engineer is the best position in the organisation for a high-paying job role. So, if you want job security, good pay, and knowledge, this is the position for you.

CONCLUSION

DevSecOps can be well-defined as how DevSecOps affects an association with respect to what standards and practices they must follow to, the advantages. If it's complete effectively and in what way, it is innovative from the necessity to execute security in DevOps. We discovered that many people define DevSecOps as the addition of security processes and practises into DevOps atmospheres. We recognized a number of tasks and benefits associated with executing DevSecOps[6]. The difficulties we found should not be viewed as impediments to applying DevSecOps, but rather as a indication of its infancy. Better processes, procedures, tools, and so on would most likely solve them as DevSecOps matures. It is maturing, as shown by the benefits we found.

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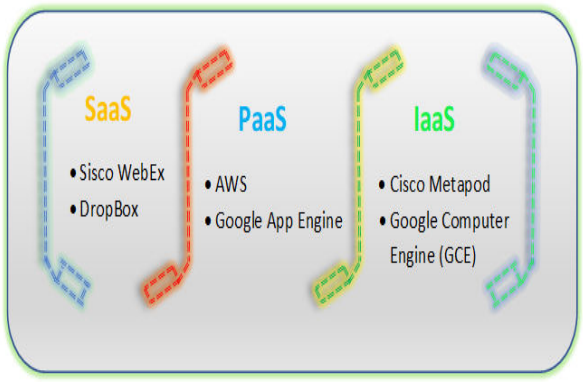

Fig.1 Examples for SaaS, PaaS and IaaS

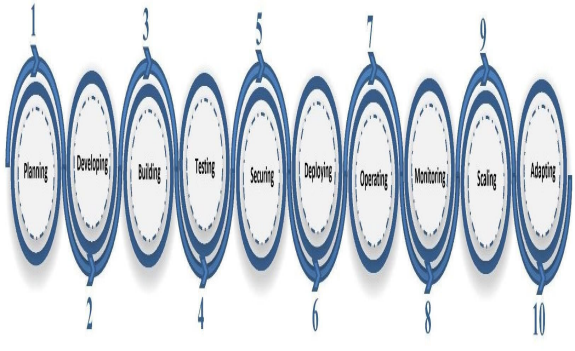

Fig.2 Implementation of DevSecOps

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RESEARCH ARTICLE

COVID 19 Vaccine Implementation Stages, Exploratory Data Analysis and Daily Vaccination Prediction using Machine Learning Algorithms

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ABSTRACT

Vaccine is a product that induce immune system against infection. Basically three different types of approaches are used for creating the vaccines. Covid19 vaccines also produced using these three kind of approaches. In this paper explained about different kind of approaches used for covid19 vaccination process, comparing the types of vaccine candidate used for covid19 vaccination by different countries. The exploratory data analysis of countrywide daily vaccination growth and trends. Machine learning regression algorithms like linear regression, Bayesian, boosted and decision tree are used for predicting the daily vaccination growth. Comparative analysis of different algorithms are used for measuring the best performance. Boosted regression tree algorithm is performing good and it is giving the 98% accuracy. next to that linear and Bayesian algorithms are performing equally good with 96% of accuracy and. Decision forest regression model have 94 % of accuracy.

Keywords: Inactivated vaccine, Live-attenuated vaccine, Viral vector vaccine, linear regression ,Bayesian, boosted Gradient, decision tree

INTRODUCTION

Vaccine: A product that motivates a individual's immune system to produce protection to a exact syndrome, protecting the individual from the particular disease. Vaccination is the process of introducing a vaccine into the body to generate immunity against a particular disease. Vaccination is a injection of a killed virus to stimulate the immune system fight against the microorganism to preventing from syndrome. The work of Vaccination is thought-provoking the immune system the natural disease-fighting system of the body. Vaccination is safe, and effective way of shielding people against harmful diseases, before they come into contact with them. In general most of the Vaccines are produced in the form of Injection

Working of Vaccine.

Vaccines decreases the threats of getting a infection by functioning through your body's regular defences to form the protection

1. small amount of disease is given in the form of injection to human body
2. 2.Human body generates antibodies to fight against the disease.
3. If the microbe enters in your body, antibodies works a against the microbe and it will not permit the person's sick
4. you are immune against the disease

The vaccine as a result, it is a harmless and smart method to create an immune response in the body, without triggering disease. The human immune systems are structured to remember. Once open to one or more dosages of a injection, we naturally continue to shielded against a syndrome for years together or even a time of lifespan

Ingredients of the Vaccine

Vaccines consist of tiny piece of the disease-causing organism for constructing the tiny fragments. They also contain other ingredients to preserve the vaccine safe and operational. These essentials are involved in all type of vaccines and have been used for long time in billions of dosages of vaccine. Each vaccine element helps a specific purpose, and each item is verified in the manufacturing process. All elements are verified for safety.

Antigen

All vaccines contain Antigen, substance that is capable of stimulating an immune reaction, precisely triggering lymphocytes, which are responsible for fighting against body's infection ,called as white blood cells

Preservatives

Preservatives are compounds that stop the development of microorganisms, predominantly bacteria and fungi. It is added in vaccines to stop microbial development and prevents from contamination. If once the vial is opened,it will be used for immunizing more than one person. 2-phenoxyethanol is the most used preservative in vaccines.

Stabilizers

Stabilizers are used to help the vaccine maintain its efficiency during storage.

Different types of vaccines for Covid19

The three commonly used methods to forming a vaccine.

- The whole-microbe approach
- The subunit approach
- The genetic approach (nucleic acid vaccine)

The Whole-Microbe Approach (Fig.2.)

Inactivated Vaccine

The method to create a vaccine is to consider the disease affected virus or bacterium and deactivate or destroy with the help of chemicals or radiation. This type of method is already in practice for example flu and polio vaccine are fall under this category. The production cost of this method is also relatively low. But it need distinct lab to develop the virus or bacterium in secured manner and it will consume stretched time for production. This type of vaccines are given by two to three times.

Live-Attenuated Vaccine

A live-attenuated vaccine is produced using a living and weakened form of the virus The MMR vaccine and the chickenpox and shingles vaccine are examples of this kind of vaccine. This also can be manufactured for larger scale. But it may not advisable for those who have immune system's defences are low.

Viral Vector Vaccine

This form of vaccine is generated using secured virus to uses a safe virus to distribute exact sub parts are termed as proteins of the germ of interest so that it can activate an immune reaction without triggering disease. To perform this process, specific parts of the pathogen a reimplanted into a secured virus. These cured virus it works as a vector to supply the protein into the body. The protein generates the immune reaction. Ebola vaccine is one of the example for a viral vector vaccine and this type vaccines can be generated quickly.

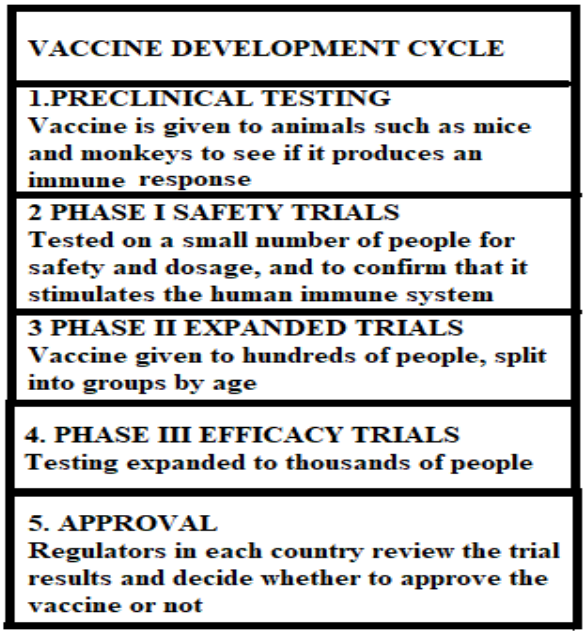
The Subunit Approach

A subunit vaccine is generated using the specific parts or subunit of a virus or bacterium that activate the immune response system. It is not consist of whole virus or Vector. The subunits are usually proteins. Majority of the vaccines available for children's are subunit vaccines.

The Genetic Approach (Nucleic Acid Vaccine)

This is not like the vaccine methods that use either a weakened whole virus or parts of one, a nucleic acid vaccine it uses a unit of genomic substantial that delivers the commands for particular proteins, not the full microbe. DNA and RNA, both are the instructions to our cells, use to create proteins. In our cells, DNA is first turned into communicator RNA, and it is used as structure to create particular proteins.

Vaccination Development Process



All the vaccinations are developed using this five stages (fig). Each stage response is recorded carefully before going to next step. The outcome of four stages are successful then it will be passed to final stage and the vaccine is approved.

Exploratory Data analysis of Covid19 vaccine

Different types covid19 Vaccine Candidates –Worldwide

In this figure (5) shows that the different types of Covid 19 vaccine candidates present in the market and the usage statistics of different candidates. The graphs shows that the most used vaccine candidates are Jhonson and jhonson, Moderna, Pfizer/BioNtech, next to that is Sinopharm, sinovac and the third is Covaxin, oxford/AstraZeneca.

Country wise vaccine candidates are listed below

- Moderna, Pfizer/BioNTech - USA;
- CNBG, Sinovac - China;
- Oxford/AstraZeneca, Pfizer/BioNTech', 'Pfizer/BioNTech - UK;
- Pfizer/BioNTech - mostly EU;
- Pfizer/BioNTech, Sinopharm - UAE;
- Sinovac - Turkey;
- Covaxin, Covishield - India;

Countrywide Vaccination Trends

The graphical presentation (fig 6) shows that the countrywide daily vaccination growth in upgrade direction. The observations shows that the vaccination progress is increasing order that means people are vaccinating more on daily basis. We have given the growth rate of few countries like India, USA, Australia and Italy.

Daily Vaccinations Prediction Model using Machine Learning Algorithms.

The actual value Vs Predicted value of the regression is given below.

The above graphs shows that the difference between the actual vaccination rate and the predicted value, it shows the accuracy of the predicted algorithm.

Root Mean Squared Error (RMSE)

A good model should have Less RMSE value .Experimental results shows in fig. 9. that Boosted regression tree algorithm is performing good ,next to that Decision forest algorithm is good ,Linear regression and Bayesian algorithms have less performance in terms of RMSE Value.

Mean Absolute Error (MAE)

The lower values of fig .10. MAE indicates the high accuracy. In this case Boosted Decision tree algorism model giving good accuracy compare to other algorithms, next to that Decision forest regression algorithm is also good. Next to that Linear regression and Bayesian regression are the worst performers in this comparison model.

Relative Absolute Error (RAE)

The above fig.11.shows that Linear regression, Bayesian and boosted decision models are performing well compare to Decision forest regression model.

Relative Squared Error (RSE)

Experimental results in fig.12. shows that Boosted Decision tree algorithm is performing good, next to that linear Bayesian and Linear regression algorithms are performing equally good and decision forest is not performing well.

Co-efficient of determination (COD)

The significant of coefficient of determination is to measure fitting of observed data. Higher coefficient indicates a good fit for the model. Experimental results in fig. 13. Shows that Boosted regression tree algorithm is performing

good and it is giving the 98% accuracy. Next to that linear and Bayesian algorithms are performing equally good with 96% of accuracy and. Decision forest regression model have 94 % of accuracy..

CONCLUSION

In this paper we have studied the structure of different vaccines and types of vaccination candidates and exploratory analysis of vaccination status of different countries. We have used different machine learning algorithms to predict the vaccination status. Four different machine learning algorithms are used for prediction of vaccination status and results are measured using different metrics. The experimental observation shows that people vaccination rate is higher compare to previous months. Using the Machine Learning algorithms we can predict the daily vaccination rate. We have used four different machine learning algorithms to predict and compare the accuracy ratio .Experimental results says that all the algorithms are comparatively good and all are giving the above 94% rate of coefficient of determination.

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Table 1. The comparative analysis of different ML algorithms

Algorithm	Mean Absolute Error	Root Mean Squared Error	Relative Absolute Error	Relative Squared Error	Coefficient of Determination
Linear Regression	27800.25558	61910.08	0.179974	0.035453	0.964547387
Bayesian Linear Regression	27528.93612	61840.17	0.178218	0.035373	0.964627411
Boosted Decision Tree Regression	9455.272868	36843.75	0.061212	0.012556	0.987443948
Decision forest Regression	12316.51012	52960.74	0.140659	0.054397	0.945603044

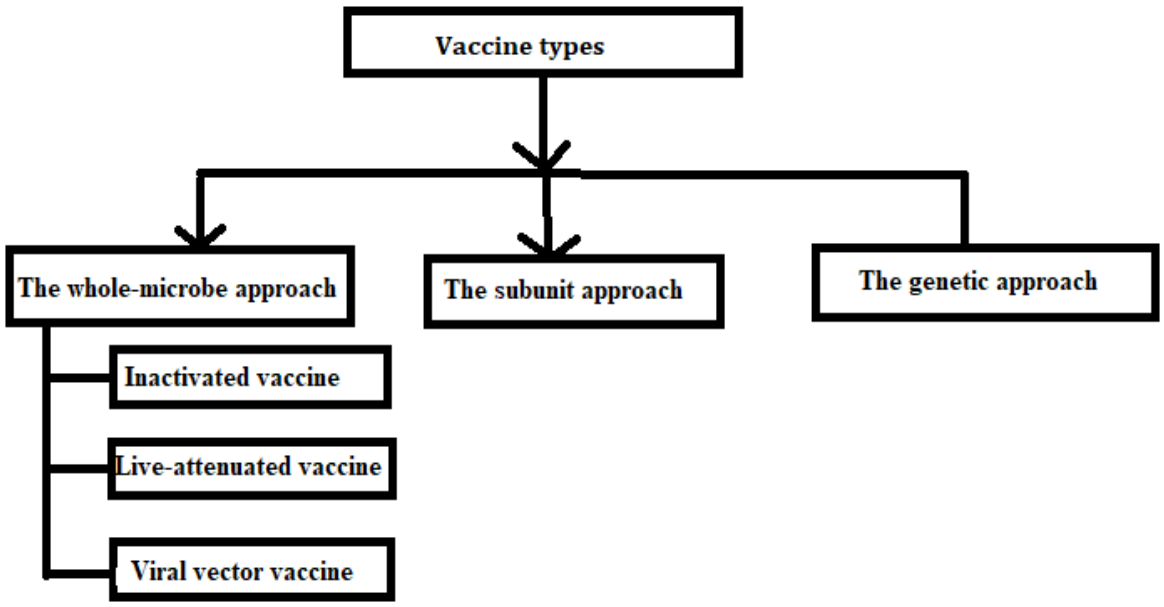

Fig. 1. Types of vaccine

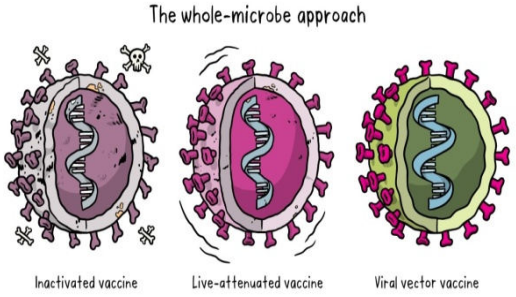

Fig. 2. The whole-microbe approach

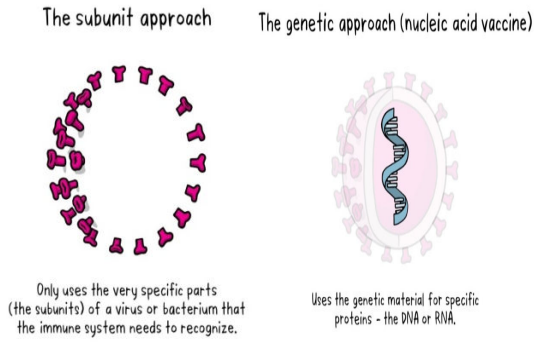

Fig. 3. The subunit approach

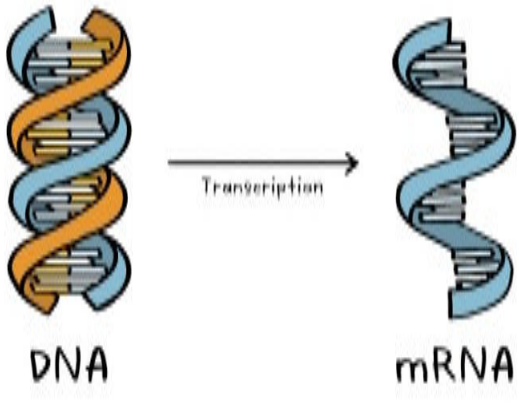

Fig. 4. The genetic approach (nucleic acid vaccine)

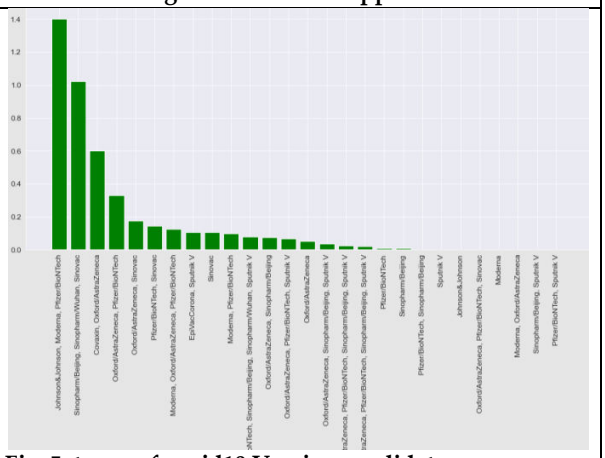

Fig. 5. types of covid19 Vaccine candidates

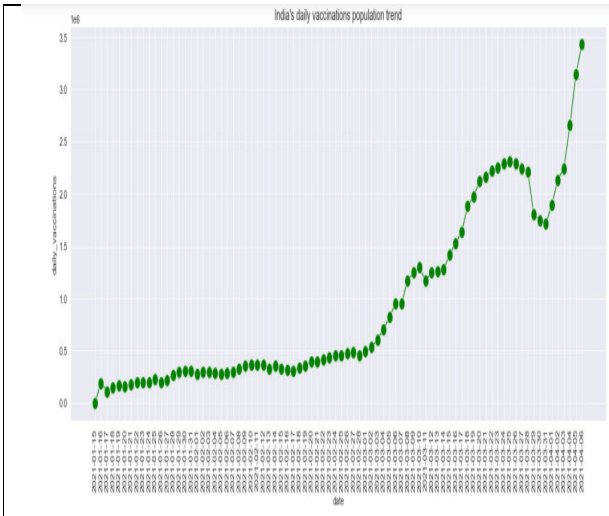

Fig. 6. India daily vaccination Vs Population

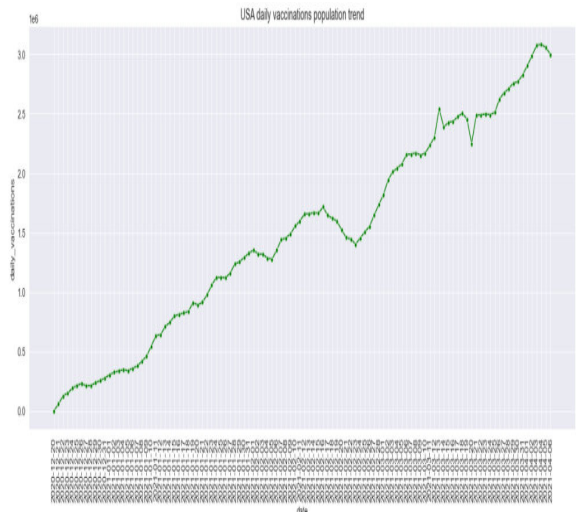

Fig. 7 :USA daily vaccination Vs Population

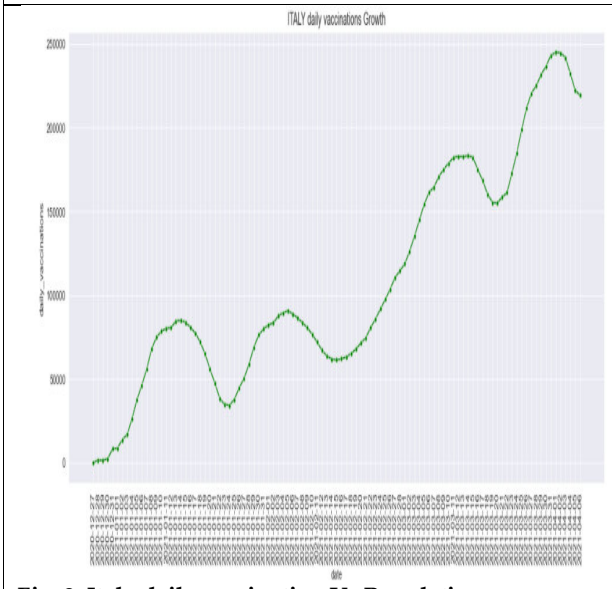

Fig. 8. Italy daily vaccination Vs Population

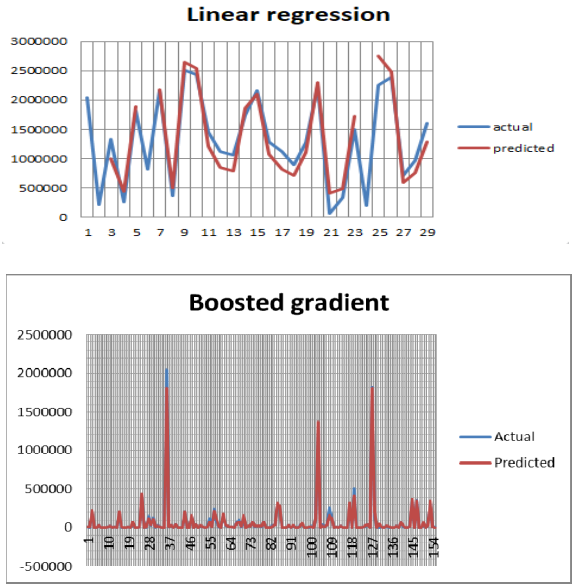

Fig. 9. Daily Vaccinations Prediction modelusing Machine Learning Algorithms.

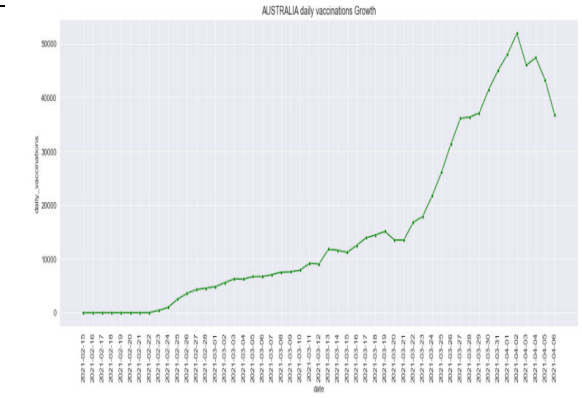

Fig. 10. Australia daily vaccination Vs Population

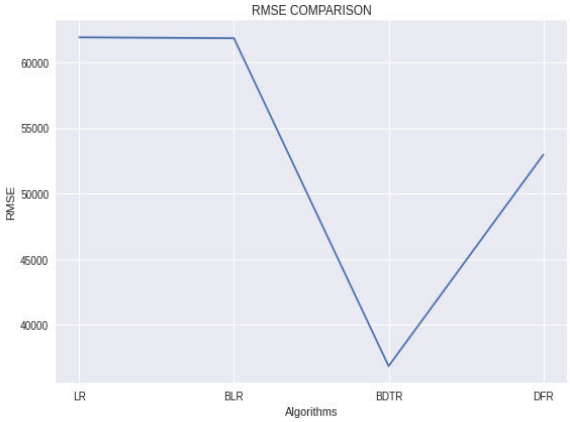

Fig. 11. RMSE comparison

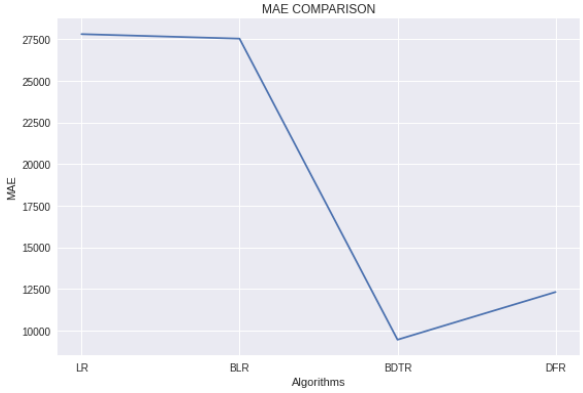

Fig. 12. MAE comparison

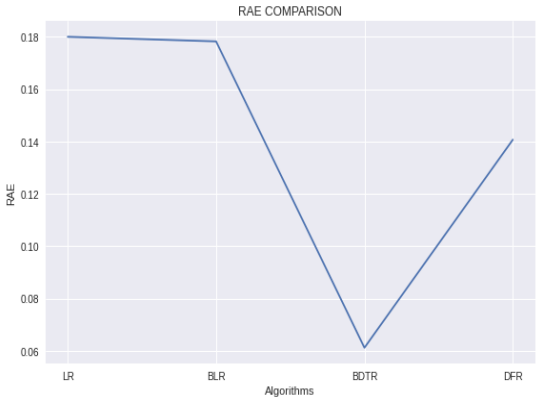

Fig. 13. RAE comparison

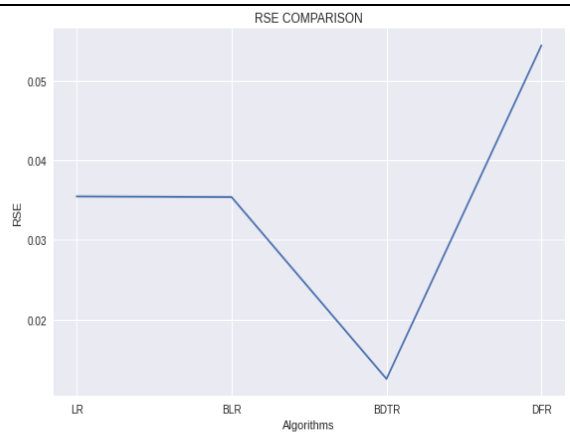

Fig. 14. RMSE comparison

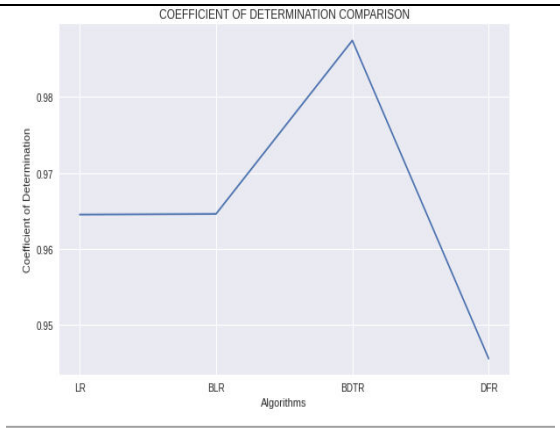

Fig. 15. COE comparisons