RESEARCH ARTICLE

Enhancing Content - based Image Retrieval using Multi - Attention Capsule - Support Vector Machine - Convolutional Neural Network

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Received: 11 Nov 2025 Revised: 29 Nov 2025 Accepted: 13 Dec 2025

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ABSTRACT

Content-Based Image Retrieval (CBIR) within computer vision enable users to find visually similar image in extensive databases through image content, rather than relying on metadata or keyword-based systems. Artificial Intelligence (AI) and Deep Learning (DL) have changed Content-Based Image Retrieval systems in the last few years by making it possible for them to learn features automatically and understand images better. Deep learning-based CBIR solutions currently struggle to overcome four main limitations, which produce poor feature interoperability and feature selection, as well as restricted spatial evaluation models, in addition to background noise overfitting. The problems in feature retrieval and computational efficiency mainly affect retrieval accuracy when processing diverse complex datasets. The proposed Multi-Attention Capsule Support Vector Machine-Convolutional Neural Network (MAC-SVM-CNN) framework introduces a solution to resolve current CBIR challenges. This method divides its operation into three sequential processing stages which include preprocessing and then feature extraction before classification occurs. The Deep Attention-Guided Filtering (DAGF) method serves as the deep attention-guided filtering approach for image preprocessing. The field of feature extraction uses the Hierarchical Cross-Attention Vision Transformer along with Particle Swarm Optimization (HCA-ViT-PSO) process. The MAC-SVM-CNN serves as the classification method. Through the DAGF module, users receive enhanced images with reduced background disturbances, as attention-driven filters effectively eliminate noise. The HCA-ViT-PSO model attains multi-level discriminatory features through

cross-attention patch connections combined with PSO optimization for dimensional and relevant feature selection. The classification portion of MAC-SVM-CNN utilizes spatial-aware capsule layers together with attention mechanisms and a margin-maximizing SVM to perform efficient content similarity-based image ranking and matching.

Keywords: Content-based Image Retrieval, Image preprocessing, Particle Swarm Optimization, Deep Attention-Guided Filtering, Multi-Attention Capsule, Support Vector Machine, Vision Transformer, Spatial evaluation.

INTRODUCTION

The vital domain of CBIR within computer vision presents an approach for automatically collecting images from large databases through visual content analysis, rather than text-based metadata. The fundamental function of CBIR entails the extraction and comparison of image features based on color, texture, shape, and spatial arrangement to identify similar matches for any given query image [1]. The previous generation of Content-Based Image Retrieval systems used manual quality to get information from pictures. These systems, on the other hand, had a hard time understanding pictures and were very sensitive to changes in size, orientation, and noise. Deep learning and artificial intelligence have made content-based image retrieval systems much better, especially when it comes to finding similar images and extracting features. Research [2,3] shows that the models help CBIR systems find high-level semantic features that are similar to how people see things. The cool features added by Vision Transformer (ViT) and attention mechanisms, these models can tell the difference between things and understand the context very well. Modern AI-powered CBIR systems use a mix of local and global features to make sure they work very well when searching through multimedia databases, medical diagnostics, and surveillance. Even though they have got better, still the latest CBIR models hit big hurdles to actually use them. Pooling in a CNN strip away where parts of picture belong, so the image looks flat; meanwhile attention doesn't catch those tiny details that really count. When deep models are used on old data they often can't talk to other systems; they can't handle mixed data well and they end up overfitting [5]. Tech today holds back CBIR tools, so they can't hit the accuracy or scale that needed when they actually use them, therefore, they fall short. The new MAC-SVM-CNN method aims at the problems you see in image-search tools, therefore gives a different way to sort pictures. Hooking capsule nets with layers that zero-in on the key visual parts, then the system just shoots up stronger results. The output feels far more powerful. The user adds an SVM to the program, the system draws steady lines when it decides if two pictures match. That new MAC-SVM-CNN setup actually pulls off better image searches, it lets the system see where things are, therefore the results look clearer.

RELATED WORKS

Gu Y *et al*., found that the results were surprising. Deep Graph Based Multimodal Feature Embedding (DGMFE) a fresh way to pull up endomicroscopy images, where it merges many data types via graph neural networks. It pulls in both nearby details and the overall image, therefore the search works better. It gobbles up so much computer power. So, it just can't keep up when the data gets huge [6]. Kumar G V R M and his teammates built a stacked Siamese Neural Network (SSiNN). By spotting similar neural patterns, the system pulls matching pictures faster for content-based image retrieval. It uses a layered Siamese design to pull out features. It occupies lot of memory and still can't handle brand-new classes [7]. Pradhan J *et al*. built DNA-CBIR after studying how DNA codons line up and found that the outcome shifted and could pull deep features from similar sequences. It separates image features better, but it's still tricky, therefore using it on many different picture types is hard [8]. Siva Kumar M *et al*., have done the work. Also, the idea is simple that built a fast picture finder using layered nets which grabs the right images on spot. It runs faster and finds more accurately even noisy pictures still trip it up [9].Lu H *et al*., suggested that they invented Deep Fuzzy Hashing Network, which they call DFHN by Mixing fuzzy logic with hashing, authors end up

with short binary codes which will find things later. When it pulls data faster, accuracy drops when the pictures look almost identical [10]. PreethyByju and the team, studied and created a step-by-step image search tool for JPEG-2000 compressed satellite archives. The way it judges similarity improves a bit each round. If the connection is slow, the technique barely manages huge raw pictures, so its effectiveness drops [11].Alsmadi M K *et. al*. established a standard CBIR system using color, shape, and texture features as descriptive parameters. This method provides a clear interpretation but struggles to scale and lacks capabilities for semantic analysis [12]. M. Garg *et al*. say it works well and created a hybrid detection method that pulls together a fresh take on the Gray-Level Co-occurrence Matrix and a tweaked Local Binary Pattern which spots stuff older methods. Authors add extra texture data for higher precision, the mix of textures does not help us see the hidden shape behind crazy image sketches which can spot differences in photos that look almost the same, so the result ends up much clearer [13]. Ma L *et. al*., suggested that Deep Progressive Asymmetric Quantization (DPAQ-CI) using causal tricks, making fine-grain image processing better, refined features improved, therefore pictures look sharper. It gives better detail but cost big on training, so it still can't really explain much [14].Arai H et., suggested and created a disease-focused image embed tool called DOIE-PSS, it works with a fake scanner set-up which can pull 3-D brain MRIs quicker. It can smooth out the differences between scanners while still highlight disease details, but when author put it on other medical scan equipment it just doesn't work well [15]. Survey of various DL methodologies of CBIR systems (Table1).

PROPOSED METHODOLOGY

The proposed framework for content-based image retrieval utilizes a MAC-SVM-CNN architecture as a deep learning approach. It aims to enhance retrieval effectiveness by determining how well-suited an image category is for a given query. The features used for image retrieval come from the Corel 2K dataset, which is well-suited for image content analysis. This work goes beyond conventional models to use a combination of Hierarchical Cluster Analysis (HCA) and ViT (Vision Transformers) as the actual image feature extraction model. HCA is able to group images such that images within the same group are semantically similar. ViT, which is a Transformer-based architecture, is able to work well with the kind of features extracted with HCA. HCA + ViT is a really good feature extraction combination, though it's not one that it will find in many places, if at all. Architecture Diagram of Proposed method (Figure 1). The proposed Content-Based Image Retrieval system is depicted in Figure 1. This system uses advanced artificial intelligence techniques to match images accurately. The operation of the system initiates with a preprocessing step applied to the input image. The preprocessing algorithm, which is called Directional Adaptive Guided Filter (DAGF), was developed and it performs two operations: First, it identifies and enhances the regions of the input image that contain the most important visual information. At the same time, it effectively reduces the background noise that is present at the visual boundaries of these regions. In other words, it greatly improves the visual quality of the image so that it can extract the most meaningful features from it. The enhanced input image is still an image of the same visual content as the original input image. At this point, it has a superior quality image in hand that it was ready to use as a basis for performing feature extraction.

Deep Attention-Guided Filtering (DAGF)

So, this Deep Attention-Guided Filtering (DAGF) is the main way to prepare data for the CBIR architecture that should use. DAGF is a new way to filter images that uses deep learning and attention techniques to focus on the most important parts of the pictures. It makes sure that the important information and visual parts are in sync by getting rid of noise and keeping the important parts of the images. In terms of object-level focus, DAGF not only maintains object border (edge) visual quality but also good texture quality as well as good spatial quantity and spatial pattern quality. DAGF maintains these very different (and all very important) visual properties because they are all essential to good object identification both at the human and at the machine level. Preprocessing begins with the input image $I(x, y)$, which lies in the domain $R^{H\times W\times C}$. The points in this space correspond to the size and shape of the image, given by its height H and width W, and its number of color channels C, which are formatted in RGB. For our testing, we bled the images into the Corel2K-Image dataset from which our database arises. The way we applied attention in our work was by using a deep function $f_{att}(.)$which outputs an attention map A(x,y) that tells us were, in the image,

we should be looking. The output from $f_{att}(.)$is made adaptive by the $\sigma(\cdot)$activation function, which gives us values that range from 0 to 1.

$$A(x,y) = \sigma\left(f_{att}\big(I(x,y)\big)\right) \quad \text{Eq. (1)}$$

The attention-weighted map visually highlights important parts as high-weight areas, while minimizing background and noise areas through low weights. Structural regularization through guidance image $G(x,y)$ co-occurs with parallel processing of $I(x,y)$, which becomes the blurred version of $I(x,y)$. The calculation of $I_D(x,y)$ begins with blending between $I(x,y)$ and $G(x,y)$ based on the attention values at each (x,y).

$$I_D(x,y) = A(x,y).I(x,y) + \big(1 - A(x,y)\big).G(x,y)) \quad \text{Eq. (2)}$$

The equation protects essential features from being eliminated while it eliminates unimportant noise and irrelevant information. The output image $I_D(x,y)$ advances to the feature extraction process E. The end product of this stage produces a deep feature vector F.

$$F = E(I_D) \quad \text{Eq. (3)}$$

The optimized feature representation enables detection of intricate relationships between semantic and spatial properties in images that uses for classification and similarity measurements. The complete preprocessing process delivers superior retrieval outcomes that make the system very effective for content-based image search operations.

Hierarchical Cross-Attention Vision Transformer along with Particle Swarm Optimization (HCA-ViT-PSO)

The DAGF image enhancement outcome undergoes feature extraction via the HCA-ViT-PSO method to obtain crucial image attributes. The ViT method preprocesses images by dividing them into equally sized patches, which undergo tokenization before processing through the transformer layers. A key aspect of the ViT method is the crossover attention mechanism. This is a dominant architectural feature of the ViT method, which allows it to make use of the Cross-Attention mechanism. This is important because performing Cross-Attention in a ViT model can allow for very low-resolution fine details to be tightly bound with high-level, more abstract (and thus less detailed) visual features. A good way to think of Cross-Attention in the context of DAGF enhancement is that it allows for a very high-level understanding of the whole visual feat. By adjusting its updates through both personal best achievements and group best achievements, the system directs its search towards the optimal feature set for convergence. Content-based image retrieval systems employ the final, optimized feature vector $F = E(I_D)$, which gathers various spatial and semantic patterns along with discriminative characteristics to achieve high-accuracy image retrieval. The image that underwent preprocessing as $I_D(x,y)$ gets split into fixed-size image patches. Each segment of the image receives a patch embedding transformation to form a feature vector $p_i \in R^d$, while d signifies patch embedding dimensions across all n image pieces to create the total set $P = \{p_1, p_2, \dots, p_n\}$. Positional encoding e_i is added to every patch embedding to preserve the images' spatial structure before passing it to the Vision Transformer.

$$z_0 = [p_1 + e_1, p_2 + e_2, \dots, p_n + e_n] \quad \text{Eq. (4)}$$

The transformer layers organize their operations through hierarchical structures to process information at several semantic levels. The cross-attention mechanism M in these layers enables interaction of representations across levels through equation 5.

$$M(Q,K,V) = softmax\left(\frac{QK^T}{\sqrt{d_k}}\right)V \quad \text{Eq. (5)}$$

The input computations consist of $Q = z_l W_Q, K = z_{l'} W_K$, and $V = Z_{l'} W_V$, through which z_l and $z_{l'}$ refer to hierarchically separated representations while W_Q, W_K, and W_V stand for learnable weight matrices and d_k represents the key dimension for dot-product scaling. The dot-product attention receives modifications from the learnable projection weights W_Q, W_K, and W_V while the key dimension is d_k. PSO serves as an optimal feature selection method, which we use to enhance extracted features while minimizing redundancy. Each particle $X_i = [x_{i1}, x_{i2}, \dots, x_{id}]$ contains binary vectors $x_{i1}, x_{i2}, \dots, x_{id}$ that choose features or discard them while x_{ij} takes values in {0,1}. The update process for velocity and position values of each particle relies on equation 6.

$$v_i^{t+1} = \omega v_i^t + c_1 r_1 (p_i - x_i^t) + c_2 r_2 (d - x_i^t)$$
$$x_i^{t+1} = x_i^t + v_i^{t+1} \qquad \text{Eq. (6)}$$

The evolution of each ith particle velocity v_i^t at t iteration involves personal position p_i together with global best g through velocity controller operations with random values r_1, r_2 drawn from $U(0,1)$ applied to the current position x_i^t. The constants ω, c_1 and c_2 control inertia and the balance between exploration and exploitation. The algorithm provides the optimized feature vector as a result through equation 7.

$$F = PSO(I_D) \qquad \text{Eq. (7)}$$

The post-optimization vector consists only of the most vital features for classification, enabling retrieval. This final representation allows the CBIR system to operate on the reprocessed data with higher precision and efficiency.

Algorithm 1: HCA-ViT-PSO
Input: $I_D(x, y)$,
d,
W_Q, W_K, W_V
$\omega, c_1, c_2, r_1, r_2$
Number of i and t for PSO
Output: F

Start
Step-1 : Split $I_D(x, y)$ into fixed size patches
For each P:
Calculate $p_i \in R^d$ its embedding
Add e_i to each $p_i \in R^d$ like
$z_0 = [p_1 + e_1, p_2 + e_2, \dots, p_n + e_n]$
End for

Step-2: For each l, evaluate,
$Q = z_l W_Q, K = z_l' W_K, V = z_l' W_V$
Apply $M(Q, K, V) = sofmax\left(\frac{QK^T}{\sqrt{d_k}}\right)V$
Acquire $E(I_D)$ from final transformer output.
End for

Step-3: Each $X_i = [x_{i1}, x_{i2}, \dots, x_{id}]$ is a $x_{i1}, x_{i2}, \dots, x_{id}$ which representing as selected features (0 ,1)

Step-4: F evaluation must utilize a function that assesses classification accuracy and retrieval performance.
Update v_i^{t+1} and x_i^{t+1} for each t
Run PSO until both convergence and maximum t limits have been met.

Return the $F = PSO(I_D)$

Step-5: The improved accuracy can be achieved by using the final F with reduced dimensionality through CBI.
Stop

Figure 2 illustrates the workflow process of the HCA-ViT-PSO methodology employed by our CBIR system. Enhancement of preprocessed images starts by implementing the DAGF method. This modified image undergoes segmenting treatment into uniform patches before the implementation of patch embedding, producing vectors when d serves as the embedding dimension. Each embedded patch receives its assigned positional encoding, which maintains spatial relationships for the resulting input sequence. The sequence passes through multiple stages of a hierarchical Vision Transformer that combines low-level and high-level features through cross-attention mechanisms. The model gains improved capabilities in recognizing complex visual patterns, as it allows data to move seamlessly between different levels of semantics. PSO optimization of deep features occurs when each component examines the features for either retention or elimination. The system updates both the positions and velocities of particles, while ω controls inertia. The learning factors are c_1 and c_2. Additionally, r_1 and r_2 are random variables uniformly distributed between 0 and 1, and g represents the best overall position. An optimized feature vector retains the most significant discriminative elements for retrieval and classification operations, while also improving accuracy and reducing computational requirements.

Multi-Attention Capsule-Support Vector Machine-Convolutional Neural Network (MAC-SVM-CNN)
The HCA-ViT-PSO method produces optimized features upon execution, which are then delivered to the MAC-SVM-CNN classifier for precise image classification and retrieval tasks. The MAC-SVM-CNN represents a model that combines the benefits of attention mechanisms with capsule networks and SVM, as well as CNN capabilities. The feature vector delivered by HCA-ViT-PSO is fed into a multi-attention mechanism, which assigns specific weights to each feature component. The Capsule Network receives an attention-weighted vector from this stage to grasp relationships between various features as well as overall component connections. One capsule contains computational capability that generates a vector representing specific image class entities' instantiation parameters. The capsule routing capabilities help the network build organizational structures and study positional changes while focusing on detailed image analysis. After being obtained from the capsule network, the vectors are flattened before being processed with a CNN for further spatial feature abstraction. As the final step of the processing, an SVM classifier operates on the CNN output data. The SVM determines the optimal decision boundary between image classes by finding the maximum margin value for the support vectors. The MAC-SVM-CNN system achieves high accuracy in image content classification through its multi-scale attention and spatial hierarchy features. The proposed MAC-SVM-CNN model utilizes the pre-processed dataset images, which are converted into feature vectors $F = [f_1, f_2, \ldots, f_d]$, where f_i represents distinct image descriptors, such as textures, color patterns, and spatial arrangements, and d indicates the total number of extracted features. The softmax function determines attention weights α_i for essential features to stand out.

$$\alpha_i = \frac{\exp(s_i)}{\sum_{j=1}^{d} \exp(s_j)} \qquad \text{Eq. (8)}$$

The calculation uses raw attention scores s_i to determine the value of f_i. The weighted vector is computed as the final product of feature analysis through

$$F' = \sum_{i=1}^{d} \alpha_i f_i \qquad \text{Eq. (9)}$$

The classification process benefits from enhanced discrimination delivered through significant features. A self-attention mechanism S processes contextual encoding by deriving feature vector-based query Q and key K and value V matrices that serve as inputs for S.

$$S(Q,K,V) = softmax\left(\frac{QK^{\top}}{\sqrt{d_k}}\right)V \quad \text{Eq. (10)}$$

The equation of self-attention contains three weight matrices W^Q, W, W^V of key vector dimension d_k that compute $Q = FW^Q, K = FW^K, V = FW^V$. The system processes the attended features through a capsule network. A capsule v_j generates its output vector, which produces a value where the vector norm represents class j probability using the formula,

$$v_j = \frac{\|s_j\|^2}{1+\|s_j\|^2}\cdot\frac{s_j}{\|s_j\|} \quad \text{Eq. (11)}$$

$$s_j = \sum_i c_{ij}\hat{u}_{j|i} \text{ where}, \hat{u}_{j|i} = W_{ij}u_i \quad \text{Eq. (12)}$$

The lower capsule layer output u_i passes through W_{ij} and combines with c_{ij} to determine the result. The margin loss function is applied to train the capsule network after it has been used.

$$L_j = T_j.\max\left(0, m^+ - \|v_j\|\right)^2 + \lambda\left(1-T_j\right).\max\left(0, \|v_j\| - m^-\right)^2 \quad \text{Eq. (13)}$$

The presence of class j is denoted by $T_j \in \{0,1\}$, and the training process utilizes margins m^+ and m^- regularized by λ. The margin loss implementation activates true class capsules strongly and prevents other capsules from activating simultaneously. Multiple CNN layers serve the purpose of in-depth representation learning. The feature map produced by layer l contains the following information.

$$F_{CNN}^l = ReLU\left(W^{(l)} * F^{(l-1)} + b^{(l)}\right) \quad \text{Eq. (14)}$$

The learned convolutional weights $W^{(l)}$ and biases $b^{(l)}$ process the input data using the convolution operation, denoted by $*$. Different depth segments of these layers recognize hierarchical visual patterns, starting from edges and moving through patterns to objects. The classification process utilizes SVM to determine the optimal hyperplane boundaries for categorizing images. The original form of the algorithm achieves simplistic outcome solutions.

$$\min_{w,b}\frac{1}{2}\|w\|^2 \quad \text{Eq. (15)}$$

Subject to,

$$y_i(w^{\top}x_i + b) \geq 1 \quad \text{Eq. (16)}$$

The CNN-enhanced image feature vector x_i, together with its true label $y_i \in \{-1, +1\}$, operates under the decision parameters w and b. A kernelized dual formulation is implemented if the dataset proves not linearly separable.

$$\max_{\alpha}\sum_{i=1}^n \alpha_i - \frac{1}{2}\sum_{i,j=1}^n \alpha_i\alpha_j y_i y_j K\left(x_i, x_j\right) \quad \text{Eq. (17)}$$

With $K\left(x_i, x_j\right)$ as the kernel function, such as Radial Basis Function (RBF), and α_i as the Lagrange multipliers. The prediction relies on the computation carried out by equation 18.

$$\hat{y} = \text{sign}(w^{\top}x + b) \;\; \forall\, \hat{y} = \arg\max_j \|v_j\| \quad \text{Eq. (18)}$$

The decision procedure relies on a combination of SVM and capsule-based output systems. The processing techniques applied to the preprocessed dataset yielded high retrieval accuracy, demonstrating the effectiveness of the MAC-SVM-CNN framework.

Algorithm 2: MAC-SVM-CNN
Input: $F = [f_1, f_2, \ldots, f_d]$ form feature selection process, and d
O**utput:** $\hat{y}$ predicted class label
Start
Step-1: For each f_i:
Compute s_i
Apply $\alpha_i = \frac{\exp(s_i)}{\sum_{j=1}^{d} \exp(s_j)}$
Generate $F^{'} = \sum_{i=1}^{d} \alpha_i f_i$
End for
Step-2: Calculate $Q = FW^Q, K = FW^K, V = FW^V$
Step-3: Utilize $S(Q,K,V) = softmax\left(\frac{QK^{\top}}{\sqrt{d_k}}\right)V$
For each j:
Evaluate $s_j = \sum_i c_{ij} \hat{u}_{j|i}\ \hat{u}_{j|i} = W_{ij} u_i$
Calculate $v_j = \frac{\|s_j\|^2}{1+\|s_j\|^2} \cdot \frac{s_j}{\|s_j\|}$
End for
Step-4: For each j:
Compute $L_j = T_j . \max(0, m^+ - \|v_j\|)^2 + \lambda(1 - T_j) . \max(0, \|v_j\| - m^-)^2$
For each l:
Apply $F_{CNN}^{l} = ReLU\left(W^{(l)} * F^{(l-1)} + b^{(l)}\right)$
Execute flattening operations on the last output of the CNN layer.
End for
End for
Step-5: Define $\min_{w,b} \frac{1}{2}\|w\|^2$ subject to $y_i(w^{\top} x_i + b) \geq 1$
Step-6: If data is non-linear
Utilize $\max_{\alpha} \sum_{i=1}^{n} \alpha_i - \frac{1}{2}\sum_{i,j=1}^{n} \alpha_i \alpha_j y_i y_j K(x_i, x_j)$
Predict $\hat{y} = \text{sign}(w^{\top} x + b)\ \forall\ \hat{y} = \arg\max_j \|v_j\|$
Forecast $\hat{y}$ and enhance classification accuracy
End if
Stop

RESULT AND DISCUSSION

The analysis of the MAC-SVM-CNN method utilizes a corel image database through image processing and CBIR techniques. The image database will be used to train and test 1,000 different classifiers, which will analyze images of ships, parachutes, and signboards as their categories. The CBIR system benefits from MAC-SVM-CNN because this approach delivers the best characteristic elements required for image classification. Temperature-based comparison methodologies can evaluate the previous content retrieval methods of CNN, KNN, LBP, and MAC-SVM-CNN on the corel2K database. You can make the MAC-SVM-CNN approach more accurate by looking at performance measurements like accuracy, precision, recall, and F1-score. Table 2 shows that the suggested MAC-SVM-CNN approach may increase the accuracy of image retrieval by comparing it to the CNN, KNN, and LBP, methods to get the test and validation accuracy. Also, Ship, Parachute, and Sign board all did better on the test and training datasets, with scores of 93.5%, 92.6%, and 96.5%, respectively. Figure 3 present the precision measurements for CNN, KNN, LBP, and the proposed MAC-SVM-CNN. Across all categories, the MAC-SVM-CNN achieves superior precision outcomes due to its integrated multi-attention mechanisms, SVM with capsule networks, and CNN-based spatial features. The precision of the MAC-SVM-CNN is 44.9% for ships, 47.4% for parachutes, and 50.3% for signboards, exceeding all other evaluated methods. Figure 4 shows the study comprises traditional and state-of-the-art models,

including CNN, KNN, and LBP, in conjunction with the proposed MAC-SVM-CNN framework. Through recall values, the methods show their capability to generate all necessary images in response to specific queries. All categories demonstrate that the proposed MAC-SVM-CNN approach yields superior performance measurements, suggesting it can better recognize essential content parts. The evaluation results from Figure 5, compare MAC-SVM-CNN against benchmark techniques CNN, KNN, and LBP. Each image category benefits from the MAC-SVM-CNN approach because it delivers superior results in F1 Scores, reaching 0.601 for ships, 0.626 for parachutes, and 0.656 for signboards. Figure 6, shows how deep learning methods performed relative to one another in classifying images of ships, parachutes, and signboards. The research evaluated two types of baseline models, consisting of CNN, KNN, and LBP, along with the proposed MAC-SVM-CNN system. The data from the graph verifies a top performance level of the proposed MAC-SVM-CNN approach for multi-class content-based image retrieval across all categories.

CONCLUSION

In conclusion, the study presents an adaptive CBIR framework that effectively addresses the significant limitations present in standard and deep learning retrieval methods. The system exhibits high performance across various challenging datasets through its precise implementation of preprocessing with DAGF, followed by HCA-ViT-PSO feature extraction, and lastly, the MAC-SVM-CNN classification method. The proposed method effectively reduces background noise while enhancing key visual characteristics that facilitate discriminative learning of data. Testing on the ships, parachutes, and signboards groups within the Corel2K-Image dataset reveals that the MAC-SVM-CNN method achieves superior results compared to current advanced algorithms. The model achieves its highest accuracy of 96.5%, indicating its excellence in performing scalable image retrieval with high precision. The cross-domain capsule routing system, along with its attention mechanism and SVM-based classification boundaries, ensures both high accuracy and explainable operation when confronted with input variations.

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Table 1: Survey of various DL methodologies of CBIR systems.

Author/Year	Methodologies	Application Domain	Used Dataset	Drawbacks
Carvalho E D *et. al.*, (2020),[16]	XGBoost	Breast Cancer	Public image database	Low generalization, manual feature extraction.
GururajC *et. al.*, (2020),[17]	Artificial Intelligence(AI)- based feature extraction	Content based image retravel	Artificial intelligence data	Lack of deep learning structure
AlshehriM *et.*	Fuzzy inference system	General CBIR	CBIR_dataset	Limited

al., (2020),[18]				scalability
AgrawalS *et. al.*, (2022),[19]	Deep CNN	Lung disease image diagnosis	Medical Imaging	High computational cost
LiX *et. al.*, (2021), [20]	AI,DL methods	CBIR	Oxford and Paris datasets	The outcomes have low accuracy.
AngadiS *et. al.*, (2023), [21]	Pre-trained CNNs	General CBIR	Wang dataset	Not evaluated across diverse datasets
PathakD *et. al.*, (2021), [22]	Group Normalized-Inception-Darknet- 53 (GN-Inception- Darknet-53)	CBIR	Corel-1 K, Corel-5 K, Corel-10 K, VisTex, Stex and ColorBrodatz	Increased complexity
Yogita Mistry *et. al.*, (2018), [23]	Color and Edge Directivity Descriptor (CEDD)	CBIR	WANG database	Lacks learning capability
GhozziY *et. al.*, (2022),[24]	Type-2 fuzzy nearness measure (IT2FNM)	CBIR	SIMPLI city database	Complex to implement
BibiR *et.al.*, (2022), [25]	VGG-19	CBIR	Wang-A, Wang-B,OT scene	Needs high computing resources

Table 2: Content Based Image Retrieval Using Various Methods and Images

Input image	Methods	Precision (%)	Recall (%)	F1-score (%)	Accuracy (%)
Ship	CNN	21.7	65.2	0.326	69.12
	KNN	32.4	72.7	0.448	72.3
	LBP	34.6	77.2	0.478	80.6
	MAC-SVM-CNN	44.9	91.1	0.601	93.5
Parachute	CNN	23.6	76.9	0.361	70.2
	KNN	27.8	81.5	0.415	74.1
	LBP	34.4	85.7	0.491	76.3
	MAC-SVM-CNN	47.4	92.5	0.626	92.6
Signboard	CNN	24.8	89.1	0.388	72.9
	KNN	33.5	89.5	0.488	75.36
	LBP	34.8	86.3	0.496	79.4
	MAC-SVM-CNN	50.3	94.8	0.656	96.5

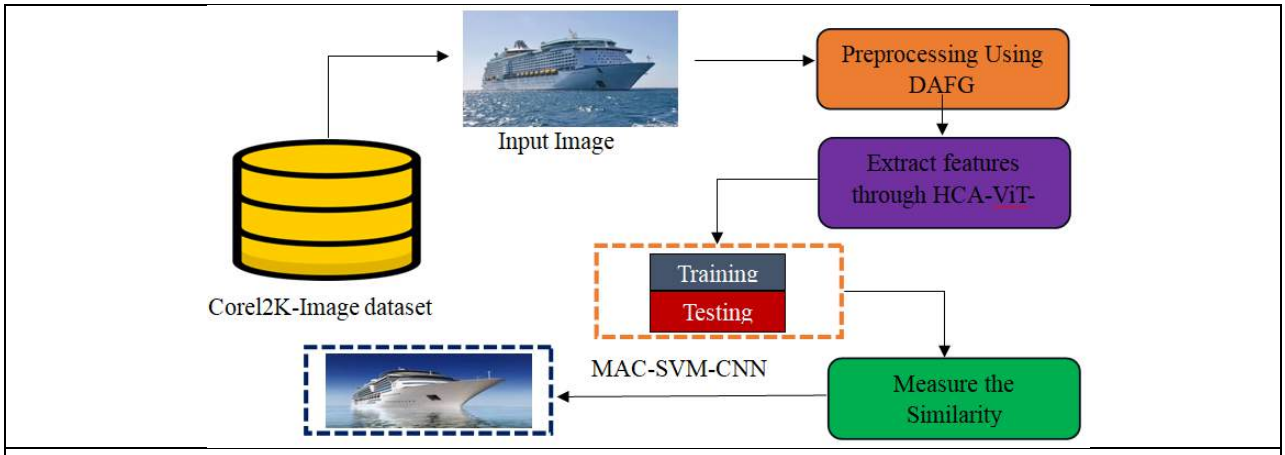

Figure 1: Architecture Diagram of Proposed method

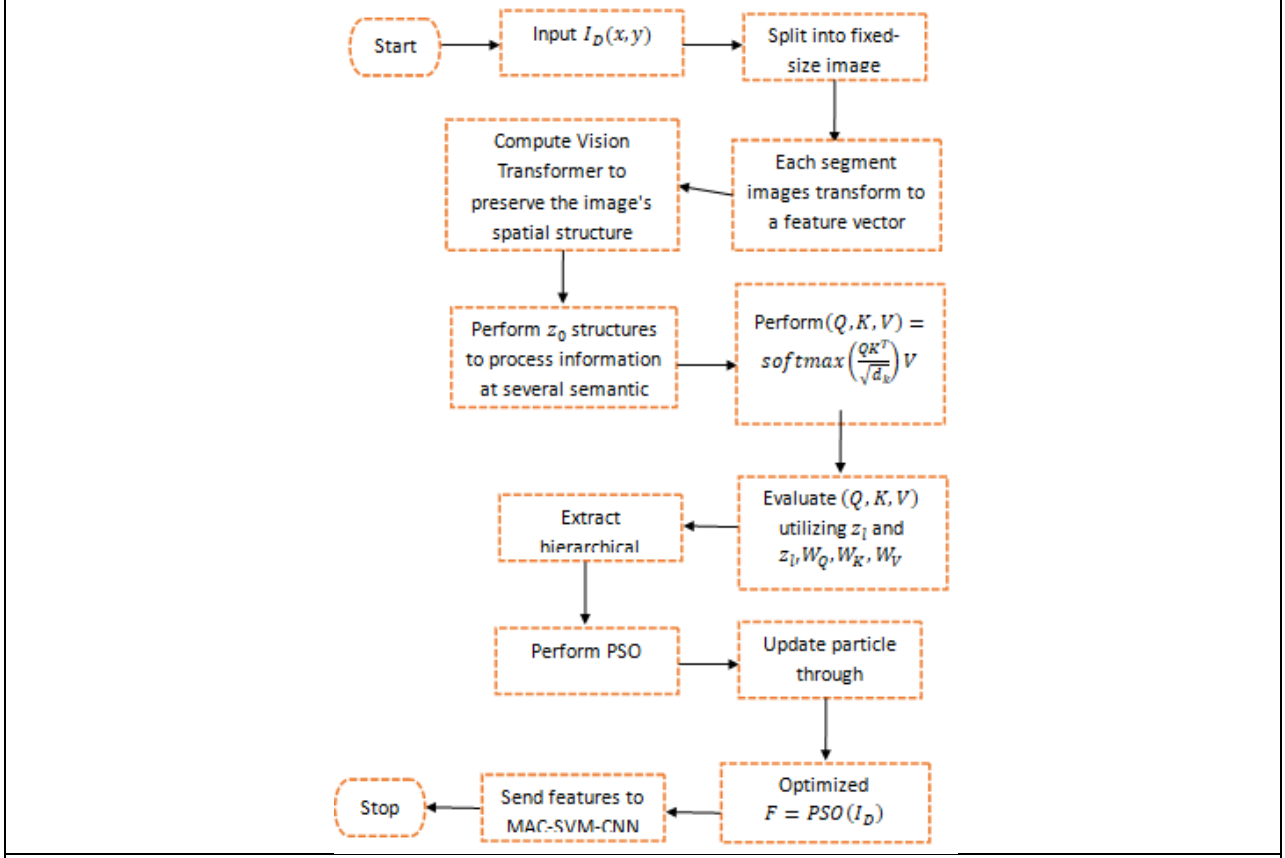

Figure 2: Flowchart diagram of the HCA-ViT-PSO method

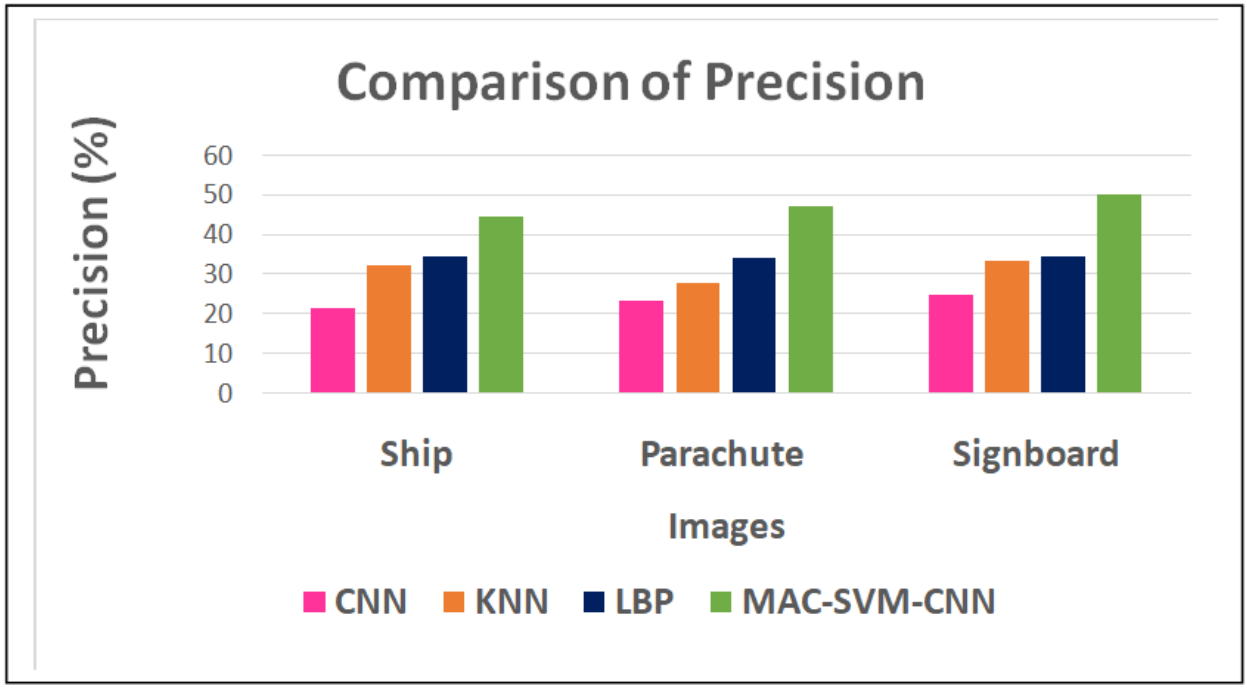

Figure 3: Precision Performance

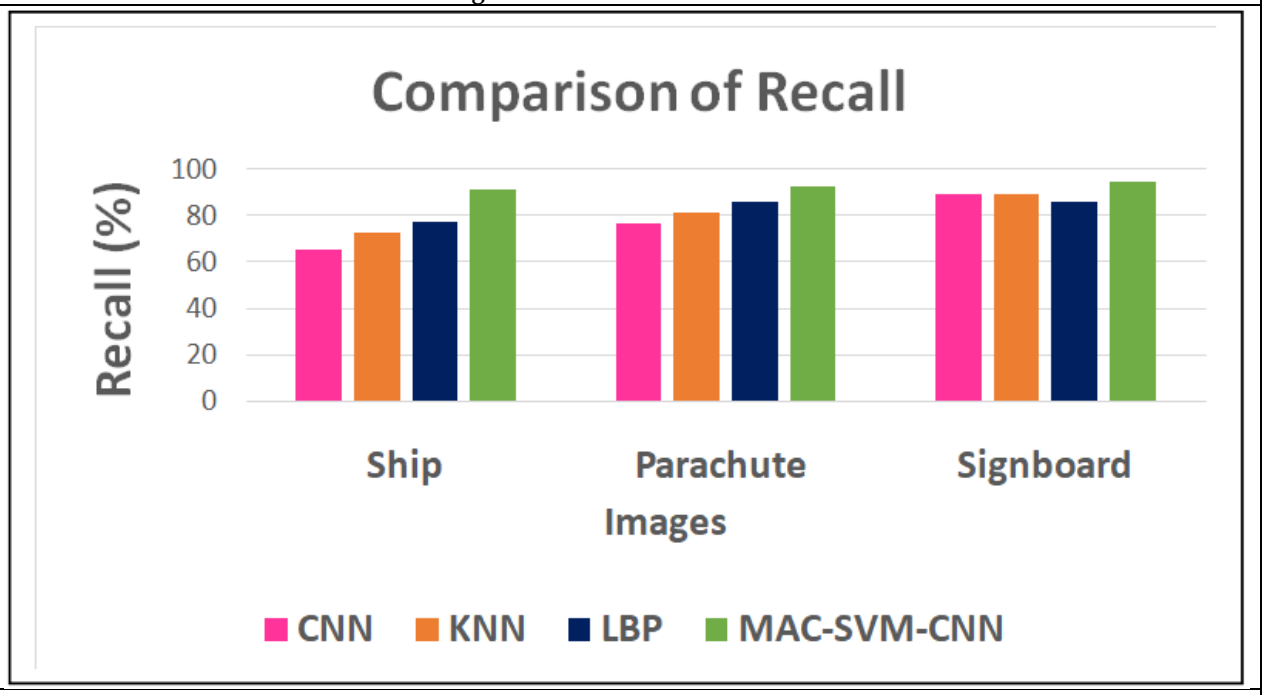

Figure 4: Recall Performance

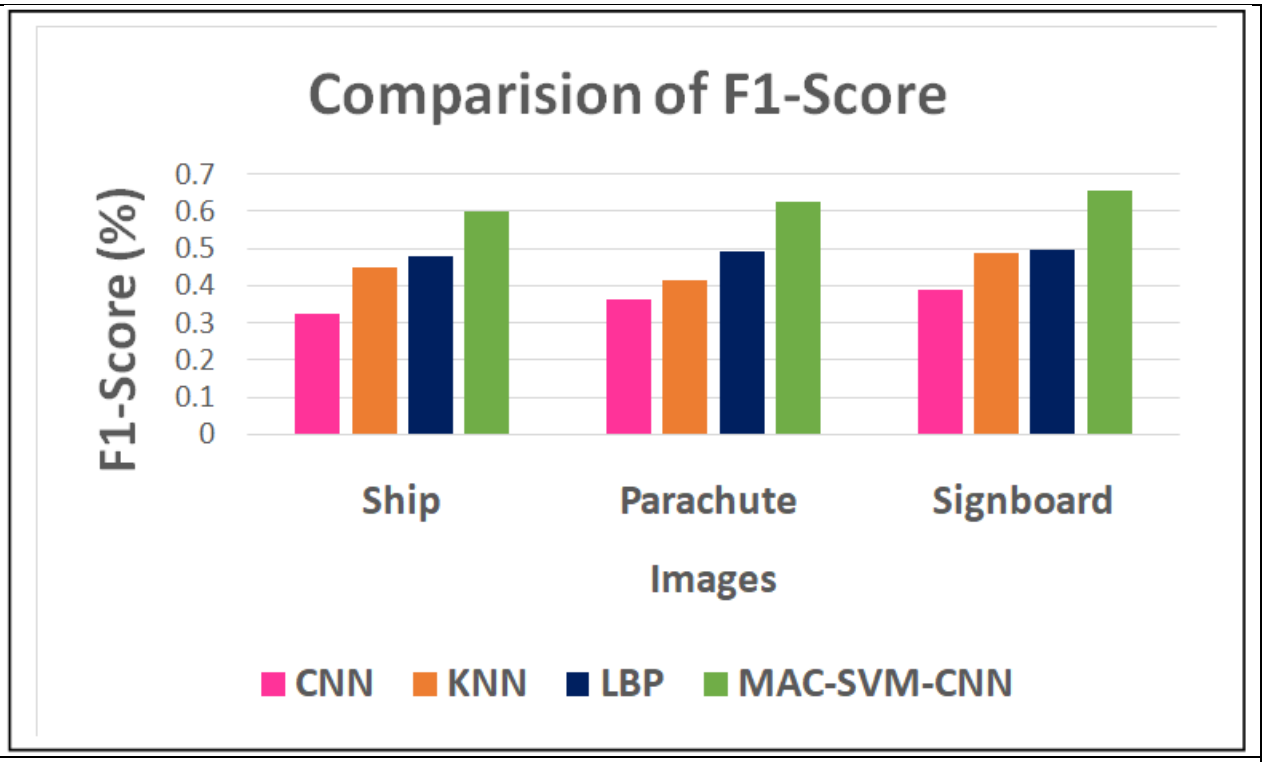

Figure 5: F1-Score Performance

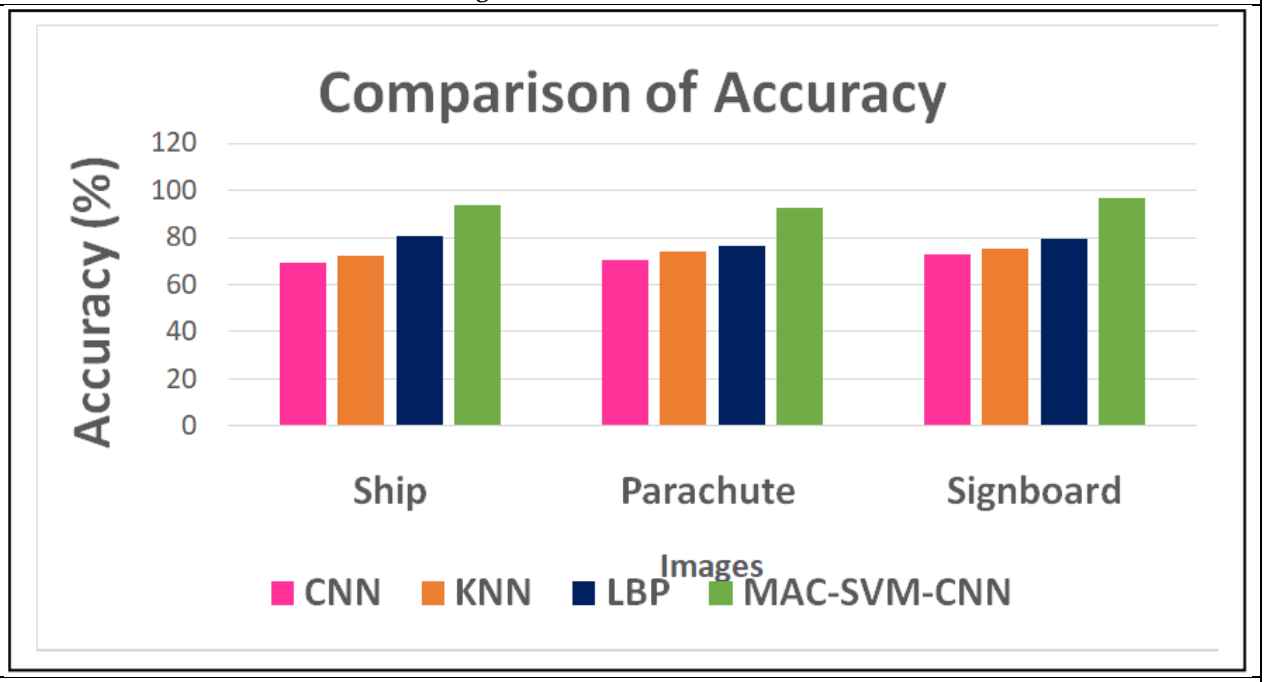

Figure 6: Accuracy Performance

REVIEW ARTICLE

A Review on Malathion : Pollution in Living Organisms with a New Approach of Fuzzy Logic Controller, Analysis and its Remediation

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Received: 14 Nov 2025 Revised: 18 Dec 2025 Accepted: 27 Jan 2026

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ABSTRACT

Malathion is an organophosphorus insecticide and pesticide commonly used in crops and residential applications. The negative effects of Malathion on human health and ecosystems are of great concern. In this work, an electrical logic tool Fuzzy Logic Controller (FLC) is used to analyse the causes and hazardous effects of Malathion to human and mammals. Based on expert's opinion the possible factors that cause damage to health and ecosystems due to Malathion is identified, which serve as the input to the FLC. The FLC establishes the causal relation between these factors computaionally. This approach can be used to study the interdependencies between the adverse effects of any pesticide in human health and environment due to prolonged exposure.

Keywords: Malathion; Fuzzy logic Controller, Mammals, Human beings, Minimal risk levels, Control & Preventive measures.

INTRODUCTION

The Organophosphorous [OP] compound Malathion, quietly known as carbophos, maldison, and mercaptothion was developed in 1950 during second world war, for its high insect potency andlow mammalian toxicity. OP is a non-systemic, wide spectrum compound hence utilizedas one of the safest & most selective insecticides. Based on the complete review of scientific evidence from the mutagenicity tests for bacteria, fruit flies, mice, hamsters, fish and human cell cultures bioassays conducted in 29 laboratories between 1978 and 1995 National Institute for Occupational safety and Health (NIOSH) identified Malathion as a *Mutagen*[1]. Between late 1970s and 2008,

malathion was the primary pesticide used in the USDA Boll Weevil Eradication Program to protect cotton crops in the southern United States [2]. The estimated average annual total domestic usage of malathion in the USA is approximately 15 million pounds of malathion as an active ingredient. Malathion is regulated by both Food and Drug Administration (FDA) and U.S. (EPA)Environmental Protection Act with a maximum amount of 8 parts per million (ppm) as residue on specific crops used for food.Its potential toxicity to humans requires, that an appropriate time lapse should be observed between the application time and entry/re-entry of a field worker.*It has been recommended not to enter or go to the fields sooner than 6 days after malathion spraying*. Exposure to high concentrations of malathion has been associated with severe toxicity and death in some cases.

Fuzzy Logic Controller (FLC):

The classical controllers are rigid in nature since the control methods are designed at one nominal operating point and HENCE they are not able to respond satisfactorily in dynamic operating point and disturbances. This main challenge is overcome by Fuzzy Logic Controller (FLC) and designed for that. Simulation is done using MATLAB Simulink. Compare to classical controller's fuzzy controllers are adopted to dynamic changes. In general, fuzzy means difficult to perceive, indistinct or vague in between right and wrong. The objective of Fuzzy Logic is formalization and eventual mechanization of two remarkable human capabilities and it is introduced by Lotfi Zadeh in 1965 to process imprecise data and the basic concept is Attempt to mimic Human control logic. Fuzzy Logic Controller (FLC) is a controller based on the concepts of fuzzy sets, linguistic variables and approximate reasoning to evaluate rules. FLC are range to range and range to point controllers and the input of FLC is membership function o/p also depends on membership function. In conventional controller we have control gain or control loss, which are combination of numerical values. In FLC instead of fixed gain or loss, a updated variables are used in terms of rules and they are linguistic in nature [3]. Such a typical rule can be written as follows:

IF E is Ai and CE is Bi then output is Ci
Where, Ai, Bi and Ci are the labels of linguistic variables of Error (E), Change of Error (CE) and output respectively. E, CE and output represent degree of membership.

PHYSICAL FACTORS

Adsorption Behaviour:

The adsorption of malathion was greater in soils with greater amounts of soil organic matter, whereas the destruction of the soil organic matter fraction of soils led to decreased adsorption [4]. Malathion is rapidly and effectively absorbed by practically all routes including the gastrointestinal tract, skin, mucous membranes, and lungs. However, the absorbed malathion is readily excreted in the urine, and does not accumulate in organs or tissues.

Bioconcentration Factor [BCF]:

Malathion did not bioconcentrate in a freshwater fish. Depending upon the suspended particles, impurities, salt content it shows various values of BCF. Despite the apparent tendency of malathion to partition into the tissues of aquatic organisms, the potential for biomagnification in the food chain is likely to be low because malathion appears to be metabolized by the aquatic organisms.

Toxicikinetics: Mechanism of Toxicology in human health:

The most influenced exposure routeof malathionto the general population is through the dermal contact, ingestion, and/or inhalation [5]. The majorexposure can adsorbedthrough skin when contacting contaminated products or surfaces, or through lung absorption by inhaling contaminated air. Domestic users of malathion are also at high risk of intoxication related to its application in residential areas near homes and gardens for medflies and mosquitoes control. Absorbed malathion can be transported by the blood and distributed to many organs and tissues including the liver where it is metabolized to form maloxon.

Degradation & Pathways:
Malathion is degraded in the environment through two main pathways, ***activation and degradation*** [6]

Activation of the compound involves oxidative desulfuration, yielding the degradatemalaoxon, a cholinesterase inhibitor with greater toxic properties than its parent compound. Activation may also be achieved by photooxidation, chemical oxidation, or biological activation, which occurs enzymatically through the activity of mixed function oxidases.

Degradation of malathion occurs through both **chemical and biological** means, with hydrolysis being the most important pathway [7]. Biological degradation through the hydrolytic pathway is mainly achieved through the enzymatic activity of carboxylesterases and phosphatases, and to a lesser extent through the activity of reductase. Malathion may also be degraded through des- or dealkylation of the O-methyl or O-ethyl groups, mediated by a phosphatase/mixed-function oxidase system [8]

The effects of light including ultraviolet [UV] radiation through photolysis on both malathion and its degradatemalaoxon. An estimated atmospheric photooxidation half-life of 1.5 days based on the reaction of malathion with photochemically produced hydroxy radicals [9]. Malathion degradation in the atmosphere occurs mainly due to indirect photolysis (photooxidation) rather than resulting from direct photolysis.

Spreading & Transportation:
Malathion released in the atmosphere as a result of its use on agricultural crops and/or residential areas may form droplets that fall on ground covers including plants, animals, soils, water resources, buildings, and/or other structures. Malathion deposited on these platforms maysubsequently be transported away through the action of rainfall/precipitation and wind.

Breaking Down of Malathion in various sources:
Malathion is usually transformed or degraded within a few weeks through the processes of photolysis, hydrolysis, and/ or biodegradation by microorganisms.It is rapidly degraded by soil bacteria, low concentrations are expected to be present in groundwater. Reported half-lives in soil range from 1 to 17 days.

In water, malathion breaks down quickly by hydrolysis or by the action of bacteria present in the water. The half-lives of malathion in water were estimated as 1.65 days at pH 8.16, and 17.4 days at pH 6.0 .
In air, malathion is broken down by reacting with other chemicals formed naturally in the air by sunlight, to form a more toxic product called malaoxon. Malathion may be transported in the atmosphere as a vapour form or adsorbed onto particulate matter [10]. It has been detected in the fog of remote pristine areas, indicating that long-range travel may occur under some conditions.

Architecture of FLC
The fuzzy logic controller has many advantages than the conventional PI controllers. The main reason for fuzzy controller is that it does not need any accurate mathematical model of the system which is going to be control and can work with imprecise inputs. It can also handle nonlinearity and more robust than conventional nonlinear controllers [11]. Practically it doesn't need fast processors and it needs less data storage in the form of membership functions and rules than conventional look up table for nonlinear controllers. The block diagram of Fuzzy logic controller and the internal structure of the controller are shown in Figure [1].

A basic architecture of FLC contains fuzzification, inference mechanism, fuzzy rule base, defuzzification. Fuzzification converts binary data into fuzzy data it has two processes that is derive the membership function for input and output variables. Defuzzification process is to derive the desired crisp output value by combining the membership functions with fuzzy rules. It converts fuzzy o/p values to control signals. It derived by two categories,

one is off line defuzzification, here all input and output membership functions are based on actual experience i.e, specified application. Online method is real time controllability has higher control accuracy [12].

Malathion and Health Effects in Human:

The most frequently detected pesticides malathion in the FDA's total diet studies is a great potential for exposure of the general population by consumption of food containing residues of the chemical.

The median lethal dose (LD50) of malathion is estimated to be 2100 mg/kg in man. *These data are discussed in terms of three exposure periods: acute (14 days or less), intermediate (15–364 days), and chronic (365 days or more*).Levels of significant exposure for each route and duration are presented with the data as showing *no-observed-adverse-effect levels (NOAELs)*or *lowest observed-adverse-effect levels (LOAELs)* reflect the actual doses (levels of exposure) used in the studies [13].

Malathion inhalation and excretion in Human body: Malathion enters the body through the air we breathe containing malathion during / after it has been sprayed for public health uses. After exposure, it enters body quickly and passes into the bloodstream which can easily go to many organs and tissues. Most of the malathion is broken down in the liver into other substances, called metabolites. Itdo not tend to accumulate in the body, and leave mostly in our urine within a few days.

Carcinogenic Effect

In April 2000, U.S. EPA classified malathion as having "suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential by all routes of exposure". An epidemiological study at six Canadian provinces pointed out that the cancer risk of non-Hodgkin's lymphoma was twice in men exposed to malathion compared to healthy men who had not been exposed to malathion [14,15]. Also, occupational exposure to pesticides has been reported to be associated with an increase risk or incidence of different types of carcinomas such as non-Hodgkin's lymphoma [16], Hodg-kin's lymphoma, leukemia [17], multiple lymphoma [18], pancreatic cancer [19], gastric cancer [20], lung cancer [21], bladder and colon cancer [22], and gall bladder sarcoma [23].

Various affects due to Malathion

Malathion classification on the basis of hazards level

Hematological Effects

When high levels of malathion exposed to persons, it induce DNA abnormalities [24], decrease human immunity [25] and cause non-Hodgkin's lymphoma [26]. Acute malathion treatment resulted in bone marrow failure and plastic anemia [27].Persons who were in direct contact with malathion in the pesticide manufacturing company found an inverse relationship between hemoglobin concentration and duration of employment. Eight individuals who had worked in the processing unit for >20 years had mean hemoglobin levels of 11.30 g/dL compared to 15.5 g/dL measured in four matched controls employed for >20 years[28].

Renal Effects

Regarding renal effects,in humans after the exposure ofunknown formulation of malathion a 65-year-old man was developed with transient renal insufficiency with massive proteinuria 3 weeks after spraying intensively with malathion [29].

Body weight Effects:

There were no exposure-related changes in body weight when absorbed during the study of aerosol bombs of acute malathion.

Neurophysiological Effects:

(a)14 workers were exposed to 57 % malathion of pesticide formulation for 4-5 hours /day duration for 4-6 months. *There were no evidence of neuromuscular insufficiency and no significant alterations in motor nerve conduction velocity or any indication of altered synaptic transmission*[30].

(b)11 workers were exposed to Organic Phosphates, a significantly higher percentage of peripheral neuropathies evaluated by electromyograph [EMG] recordings were observed among pesticide workers when compared to control ones [31, 32]. *A slight reduction (3%) in sensory nerve conduction velocity.*

Cholinesterase activities

Concentration-related effects: Females seemed more pronounced than in males.

Plasma cholinesterase activity: Decreased 30 and 70% in the mid-exposure level and high exposure level females.

RBC cholinesterase activity: Decreased 22 and 27% in *midexposure* level males and females &43 and 44% in *high-exposure* level males and females.

Brain cholinesterase activity: Decreased 41% in high-exposure level females.

Fuzzy Inference System

Fuzzy set allows objects or members to represent a smooth boundary whereas classical represent sharp boundary, and the membership function takes the value in the interval 0 and. It is derived by different methods like triangular waveform, trapezoidal, sigmoidal, guassian, bell shaped, s curved waveform and each one possess its own specialty. For that purpose, min inference rule and centroid defuzzzification technique have been used. The input membership function and output membership function are shown in Figure 2, 3 and .4

Discussion of Simulation and Result

In this work malathion and its health effects are analyzed with eight fuzzy rules1. Report in human actions, 2. Malathion inhalation and excretion in Human body. 3. Carcinogenic Effect, 4. Hematological Effects, 5. Renal Effects, 6. Body weight Effects, 7. Neurophysiological Effects, and 8. Cholinesterase activities. To design fuzzy inference system for this analyses 8X8 rules are used as it is unsupervised one. The connection matrix for fuzzification and defuzzification are derived based on experts opinion as given in the equation 1 and 2.

$$T_f(F) = \begin{bmatrix} 0 & HHMHVHVHH \\ H & 0 & VHVHHHMM \\ HVH & 0 & MHHLL \\ MVHVH & 0 & MHLL \\ LMMVL & 0 & VHVHH \\ VLVLVLMH & 0 & MM \\ LVLVLVLLL & 0 & VH \\ LVLVLVLLMM & 0 \end{bmatrix} \quad [1]$$

$$T_d(F) = \begin{bmatrix} 0 & 0.3 & 0.3 & 0..2 & 0.3 & 0.4 & 0.4 & 0.3 \\ 0.3 & 0 & 0.4 & 0.4 & 0.3 & 0.3 & 0.2 & 0.2 \\ 0.3 & 0.4 & 0 & 0.2 & 0.3 & 0.3 & 0.1 & 0.1 \\ 0.2 & 0.4 & 0.4 & 0 & 0.2 & 0.3 & 0.1 & 0.1 \\ 0.1 & 0.2 & 0.2 & 0.05 & 0 & 0.4 & 0.4 & 0.3 \\ 0.05 & 0.05 & 0.05 & 0.2 & 0.3 & 0 & 0.2 & 0.2 \\ 0.1 & 0.05 & 0.05 & 0.4 & 0.05 & .01 & 0 & 0.4 \\ 0.1 & 0.06 & 0.06 & 0.06 & 0.1 & 0.2 & 0.2 & 0 \end{bmatrix} \quad [2]$$

Malathion in Insects

Malathions bind to the enzyme acetylcholinesterase (AChE) at nerve endings throughout the bodies of insects and other organisms [33]. AChE plays a key role in the synaptic transmission of nerve impulses and attack the tiny pores

of spiracles. Its inhibition causes the blockage to signal transmission leading to intoxication manifested by restlessness, hyper-excitability, convulsions, paralysis, and death [34].

Malathion in mammals

The signs and symptoms of malathion toxicity are different in mammals because in mammals AChE is not active in the central nervous system, but rather in nerves that connect with muscles [35].

Carcinogenic Effect:

In a two-year dietary study, researchers administered oral doses of 2,359, 739, or 868 mg/kg/day exposures of malathion to rats, results observed an increased incidence of liver and nasal/oral tumors in rats and increased incidence of liver tumors in mice [36].

Hemotologic effects

Malathion on high doses, suppress the immune system, affect the hemato- poietic system, deleterious effects on hematological parameters of treated animals [37]. Chronic exposure of malathion to a group of animals in a researchsignificantly decreases RBCs, Hb, and P.C.V% [Packed cell volume] values [38].

Neurological effects

Malathion is found to inhibit the release of acetylcholinesterase at the synaptic junction.Neuropathy target esterase (NTE), causesOrganophosphorus-induced delayed polyneuropathy (OPIDP) due to the consumption of malathion. When higher level of dosages causes neurological effects and nerval syndrome disorders. [39].

Reproductive & Developmental effects:

Malathion influences the reproductive function by two mechanisms via its cellular toxic action and its effect reduced sperm count, obviously decreased the levels of testosterone [40]

Hepatic effects&5.6 Renal effects:

Renal effect tests were conducted to rats with the aerosol application of 96.4% pure malathion at a concentration of up to 2,010 mg/m3, 6 hours/day, 5 days/week for 13 weeks. It showed no significant alterations in the renal effectand body weight during the study [41].

Discussion of Fuzzy stimulation and Results

Further the effects of malathion in mammals are examined in six different categories, like 1. Carcinogenic Effect, 2. Hematologic effects, 3. Neurological effects, 4. Reproductive &amp, 5. Developmental effects, 6. Hepatic effects and Renal effects. It is effectively analyzed with the aid of 6X6 fuzzy rules as given below.

$$T_f(F) = \begin{bmatrix} 0 & H & H & M & H & VH \\ H & 0 & VH & VH & H & H \\ H & VH & 0 & M & H & H \\ M & VH & VH & 0 & M & H \\ L & M & M & VL & 0 & VH \\ VL & VL & VL & M & H & 0 \end{bmatrix} \quad [3]$$

$$T_d(F) = \begin{bmatrix} 0 & 0.3 & 0.3 & 0..2 & 0.3 & 0.4 \\ 0.3 & 0 & 0.4 & 0.4 & 0.3 & 0.3 \\ 0.3 & 0.4 & 0 & 0.2 & 0.3 & 0.3 \\ 0.2 & 0.4 & 0.4 & 0 & 0.2 & 0.3 \\ 0.1 & 0.2 & 0.2 & 0.05 & 0 & 0.4 \\ 0.05 & 0.05 & 0.05 & 0.2 & 0.3 & 0 \end{bmatrix} \quad [4]$$

The obtained fuzzy model is a realistic sensitive model which leads good performance as the fuzzification mimics human knowledge system. It can easily optimize the huge information's into a specific operating points. It is observed that the fuzzy inference system is a vital tool for explaining the effects of malathions over human and mammals.

MRL[Minimal Risk Levels]:

An acute-duration inhalation MRL of 0.2 mg/m^3 was derived for malathion based on a no-observedadverse-effect-level (NOAEL) of 65 mg/m^3 for inhibition of RBC cholinesterase activity in rabbits exposed to a malathion aerosol [42].

An oral MRL in Humans:

Case 1: An oral MRL study for group of people were conducted withmalathion aerosolof 0, 5.3, 21, and 85 mg/m3 concentrationsof 2 hours/day for 42 days. Up to 21 mg/m^3, there was no irritation or toxic effects, we observed with a complaints of nasal and eye irritation within 5–10 minutes only at the exposure to 85 mg/m^3 of malathion aerosol.

Case 2:An intermediate-duration oral MRL of 0.02 mg/kg/day was derived for malathion based on inhibition of plasma and RBC cholinesterase activity in humans with 15-364 days exposure. [43].

First phase, Five male volunteers were made to consume0.11 mg malathion/kg/day daily in the capsules form blended with corn oil approximately for 32 days.

Second phase, After the completion of first phase -for three weeks and then were administrated as daily capsules with malathion providing about 0.23 mg malathion/kg/day for 47 days.

Third phase, 0.34 mg malathion/kg/day for 56 dayssubjected in the third phase.

Various Tests were conducted using the tests,

The MRL was derived by dividing the NOAEL of 0.23 mg/kg/day by an uncertainty factor of 10 (to account for sensitive subpopulations).ThePlasma content and RBC cholinesterase was determined twice weekly prenatal, during, and the post administrations of malathion.

(i) Routine blood counts and urinalyses were conducted at the end of each study period.

The *reports were quite common that,* administration of 0.11 mg malathion/kg/day for 32 days or 0.23 mg/kg/day for 47 -No clinical signs.

But the phase three activity of 0.34 mg malathion/kg/day for56 days caused a maximum depression of 25% in plasma cholinesterase approximately 3 weeks after cessation of treatment.

DISPOSAL

Incineration in a furnace equipped with an afterburner and a scrubber is the recommended method of disposal for malathion [44,45]. If incineration is not an available option, malathion may be disposed of by absorbing in vermiculite, dry sand, earth, or a similar material and then being buried at a designated landfill site [46].

Membrane Techniques: **Type I** & **Type II**: Malathion issubjected to molten salt combustion using potassium chloride. This process is very attractive due to the destruction of malathion is >99% and the products of combustion can be safely re-used as a fertilizer (United Nations 1985).

Adsorption Techniques & Hydrolysis: In soil and sediments, the major degradation process of malathion is microbially mediated biodegradation, occurs mainly through enzyme-catalyzed hydrolysis. The predominant pathway for the biodegradation of malathion has been reported to be carboxylesterase activity. Half-life values in soil of 3–7 days have been reported for the degradatemalaoxon. Little malathion appears to volatilize from soil and while malathion is moderately to highly mobile in soils, leaching of malathion through the soil and into groundwater is unlikely due to the rapid degradation of the compound in the environment [47].

Regulatory Guidelines

According to the National Institute for Occupational Safety and Health (NIOSH)'s guidelines, workers should not be exposed to malathion concentrations greater than 10 mg/m^3 during a 10-hour workday, 40 hours per week. NIOSH also recommends that an atmospheric concentration of 250 mg/m^3 malathion be considered as being immediately hazardous to human health and life.

CONCLUSION AND REMEDIAL MEASURES:

This review highlights the most recent applications of malathion as the use of fertilizer, pesticide and its impacts to human health, mammals & insects. The data were configurated with different dosages, time duration and concentration with the wide range of testing studies. The minimal risk level, choloniesterase behaviour, oxidative reaction gives a keynote to the researchers.

Remedial Measures: To reduce the risk of exposure of malathion it is important to wash the foods prior to eating them. When contaminated vegetables or other produce grown in a backyard garden is eaten as it is, found to that there is a presence of toxicity.

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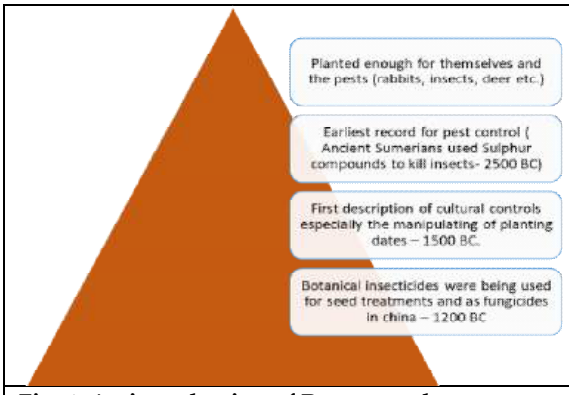

Fig. 1. An introduction of Pest control

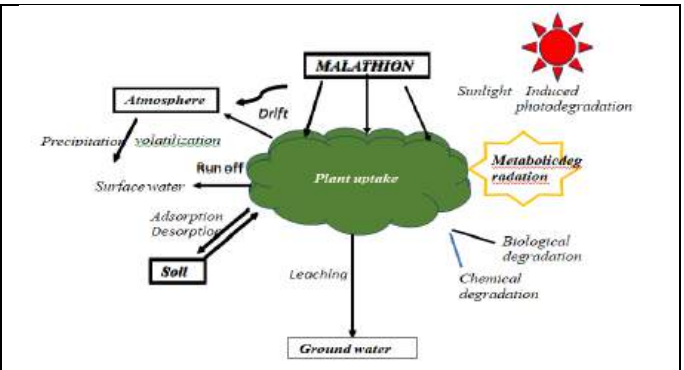

Fig.2. Malathion: Chemical action in soil, water, air – Image drawing [Malathion pathways in the environment, Transport mechanisms]

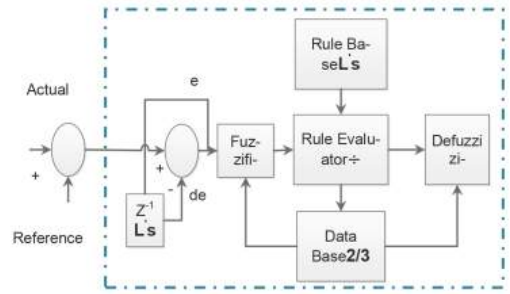

Fig. 3.Internal Structure of FLC

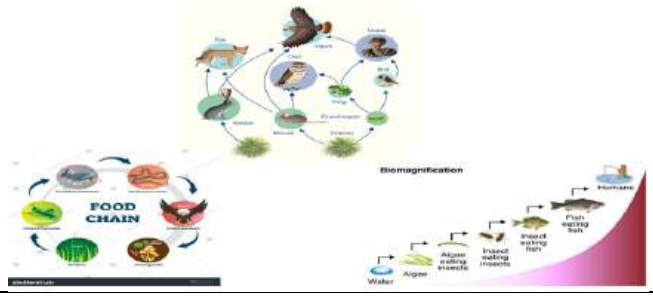

Fig. 4. Malathion classification on the basis of hazards level

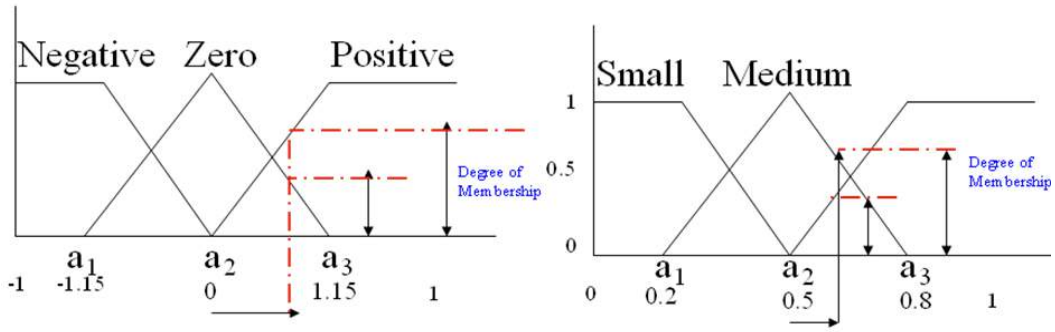

Fig.5. Input Membership Function

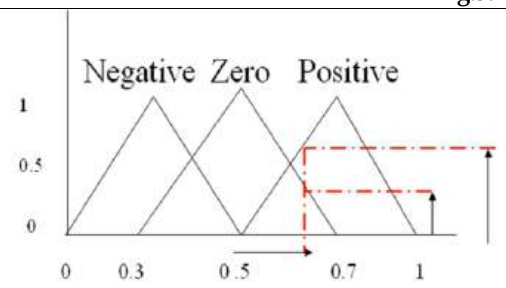

Fig.6. Output Membership function

	Small	Medium	large
Negative	Positive	Positive	Zero
Zero	Positive	Zero	Negative
Positive	Positive	Zero	Negative

Fig. 7. Rules set of IPFC

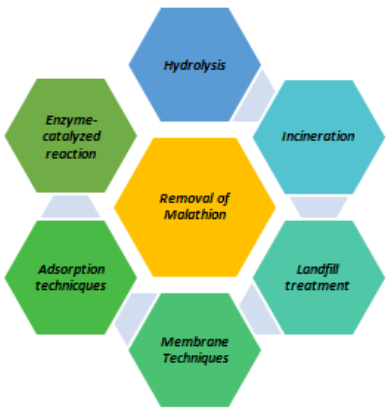

Fig. 8. Disposal of Malathion

Indian Journal of Natural Sciences www.tnsroindia.org.in ©IJONS

Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Strategic Deployment of Mathematical Models in the Financial Industry

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Received: 03 Nov 2025 Revised: 22 Nov 2025 Accepted: 22 Dec 2025

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ABSTRACT

The financial industry relies on quantitative methods to understand the market dynamics, handle uncertainty, and make investment decisions. Within the increase of complexity in financial markets, mathematical modeling is very necessary for the purpose of risk assessment, predicting the value of assets, and understanding the factors that play a vital role in investor returns. This paper uses two mathematical models that are commonly used: the Capital Asset Pricing Model and Geometric Brownian Motion, to analyze the behavior of stock prices, particularly in the Indian market. With CAPM, we tried to evaluate the systematic risk and expected return for the State Bank of India with the help of ten years' monthly market data and using the yield of a 10-year Government of India bond as the risk-free rate. On the other hand, GBM will be used for predicting future prices for Reliance Industries using simulations based on daily log-returns between 2022 and 2024.Our findings show that SBI has a high beta and has high sensitivity to market movements and their fluctuations. This sensitivity is more seen in times of crisis, such as the COVID-19 pandemic period, while GBM simulations for the Reliance company indicate strong volatility connected with wide forecast bands, implying that its price behavior over recent years was notably driven by market shocks and sudden fluctuations. These two models show how mathematics can encapsulate key aspects of financial behavior and provide structured views of risks and returns even when real markets are highly subject to volatility and sharp shifts.

Keywords: Mathematical Models, CAPM, GBM, Risk Management, Financial Forecasting

INTRODUCTION

Mathematics plays a vital role in modern finance; it speaks the basic language through which risk, return, valuation, and market dynamics are comprehended, and it doesn't just work with numbers. Financial markets function on numbers and numerical data, and mathematical modeling helps in converting the raw data into useful insight that can help in our decision-making. From a clear and precise perspective, the quantitative methods help investors, analysts, and main institutions to understand stock performance, their evaluation, as well as predict future returns and detect the variations in market movements. In the current times of changing economic transformations, global linkages, and highly sensitive market responses, mathematical modeling has made it much more relevant and easier to draw conclusions. Markets these days feel more unpredictable than ever. The adverse effect of geopolitics, inflation, policy swings, and new tech — they all shake things up. At the same time, we're compiled with real-time data and have powerful tools to analyze it. With risk getting more complicated and unpredictable due to such factors, mathematical models step in to help us make sense of it all. They cut through the noise, reduce uncertainty, help us spot trends, and give us a framework for smarter financial decisions and choices. This paper takes a close look at two go-to mathematical models mainly applied in finance. The first is the Capital Asset Pricing Model (CAPM). It measures how much risk a stock carries compared to the overall market and finds out what kind of returns you should expect. The second is the Geometric Brownian Motion (GBM) model, which captures the wild, continuous ups and downs of stock prices. It's a favorite for predictions and simulations.The goal of this project is to show how these models can actually make financial analysis in banking and the stock market sharper. How these models improve finances. We're applying CAPM to the State Bank of India (SBI) and GBM to Reliance Industries. We can quantify risk and model future predictions, and finally find both the theoretical and actual returns. This particular method shows the importance of mathematical models in aiding investment decisions and dealing with uncertainty and risks that come with finance.

LITERATURE SURVEY

If you look back, a lot of financial market theory traces its roots to the early versions of the Capital Asset Pricing Model, dating as far back as the 1860s. The real backbone is the mean-variance model, introduced by Markowitz in his work on choosing the best mix of assets when you're facing uncertainty. Later, Black, Jensen, and Scholes confirmed that certain components-especially the beta of security returns — were crucial, especially when looking at returns above the average. Then there's the Fama and MacBeth model. They took CAPM further by using cross-sectional regression to study the relationship between risk and average returns for stocks on the NYSE. Models like CAPM are sometimes called Lintner and Sharpe models, recognizing the key contributions of both researchers. Jiang, in "The Application of Mathematical Models in Finance," digs into how these models shape our understanding of finance. The paper lays out just how complex financial theory is, but also shows how mathematical tools — especially those with geometric underpinnings — have pushed the field forward. Statistical models play a big role for banks, especially when it comes to setting credit policies and managing risk. Credit rating agencies, for example, can get a lot smarter about managing credit risk by building their own internal rating systems and mathematical models. The Capital Asset Pricing Model, or CAPM, really changed the game in finance math. It lets you figure out how risk and return play off each other across different investment groups, which makes it a go-to tool for managing portfolios. Gao's 2023 paper, "The Impact of COVID-19 on Five Categories of Industries Based on CAPM Model," discusses the impact of how the pandemic shook up different sectors of the market. COVID-19 has emphasized how it has affected and brought many challenges to the economy globally. Studying this stuff matters. When you look at the stock market, you can see it reflecting the ups and downs caused by COVID across various industries. The findings are interesting: after the pandemic, banks took on more risk (their beta values went up), while e-commerce, automakers, and pharma saw lower betas. So, the pandemic didn't hit every industry the same way—risk and return shifted depending on where you looked.

Paper Description

This paper explores how mathematical models help us understand, measure, and predict financial risk in the Indian stock market. We worked on two major stocks—State Bank of India and Reliance Industries Limited. For the analysis, I used the Capital Asset Pricing Model (CAPM) and the Geometric Brownian Motion (GBM) model. The goal? To show how math isn't just theory—it actually sharpens real decisions in areas like volatility, return prediction, and risk assessment. SBI stands in for the banking sector here. It's a good example for showing how CAPM links systematic risk to expected returns. On the other hand, RIL's business is all over the place and pretty volatile, making it ideal for illustrating how GBM handles randomness in stock prices. CAPM lays out a straight-line relationship between how a stock moves and how the whole market moves, which makes it easy to figure out beta (that's the measure of systematic risk). GBM treats stock prices as a never-ending random walk, factoring in both drift and volatility.

Implementation Methodology

Data Collection

SBI Monthly Adjusted Closing Prices

For the data, I started with SBI's monthly adjusted closing prices from January 2014 to December 2024,a solid ten years. These adjusted prices cover everything: dividends, splits, bonuses, you name it. That makes them the best way to calculate real returns. I used this data to work out SBI's monthly log-returns, compare them to the risk-free rate, run the CAPM regression, estimate beta, and see how expected returns stack up against what really happened. SBI makes sense here because it's India's biggest public-sector bank and a heavyweight in the NIFTY 50 index, so it's perfect for market risk modeling.

NIFTY 50 Monthly Adjusted Closing Prices

I gathered the NIFTY 50 Index's monthly adjusted closing prices for the same ten-year stretch. The NIFTY 50 is the main benchmark for the National Stock Exchange—tracking India's top 50 large-cap companies across all the big sectors. This index matters because it's the CAPM standard for market returns. It's the reference point for calculating excess returns, figuring out SBI's beta, and measuring both expected and realized performance. CAPM always compares an asset to the whole market, so NIFTY 50 is the obvious choice.

Reliance Industries Daily Adjusted Closing Prices

For Reliance, I used daily adjusted closing prices from January 2022 to December 2024. Reliance is a giant—spread across retail, telecom, and energy—and its stock price bounces around a lot in the short term. This volatility makes it perfect for showing off stochastic modeling with GBM. Daily data is key here, since GBM needs lots of observations to nail down drift and volatility. With this dataset, I calculated daily log-returns, figured out the drift (μ) and volatility (σ), simulated future price paths, and got a handle on daily unpredictability and risk using the stochastic approach. Reliance fits well for this kind of modeling because it's highly liquid, has a huge market cap, and consistently shows the kind of price behavior GBM is built for Running the GBM model gave me a solid simulation setup: daily log-returns, yearly estimates for drift and volatility, the discrete-time GBM formula, ten sample future price paths, and templates for plotting those results—charts, histograms, the works. These pieces make it possible to really dig into risk and uncertainty for Reliance.

Data Pre-Processing

Data pre-processing is an essential step in getting raw financial time-series data ready for comprehensive quantitative analysis. This phase guarantees that datasets are organized, sanitized, altered, and prepared for the mathematical processes necessary for CAPM regression and GBM simulation.

Data Purification and Alignment

The research utilizes genuine financial time-series data from the Indian stock markets:

- SBI share prices: Monthly adjusted closing figures spanning a decade.
- NIFTY 50 index: Monthly closing values adjusted for calculations of market returns.
- Risk-free rate: yield on the 10-year sovereign bonds of the Government of India (GOI).
- Reliance Industries share prices: Daily adjusted closing figures for 2022–2024.

All adjusted closing prices guarantee that dividends, splits, and other corporate activities are accurately accounted for.

Computation of Log Returns

The datasets were meticulously synchronized to uphold temporal coherence. For CAPM calculation, monthly returns for SBI and NIFTY 50 were determined using:

Log Return Formula

$$R_t = \ln\left(\frac{P_t}{P_{t-1}}\right)$$

SBI → monthly logged returns (for CAPM)
NIFTY 50 → monthly logarithmic returns (for CAPM)
Dependence → everyday log returns (for GBM)

Converting Risk-Free Rate to Monthly

The risk-free rate is the yearly yield on a 10-year Government of India bond.CAPM requires a monthly risk-free interest rate.

$$R_{f,monthly} = \frac{R_{f,annual}}{12}$$

Next, we deduct this rate from both stock and market returns for each month.

Calculation of Excess Return (for CAPM)

CAPM is ineffective with raw returns. It utilizes surplus returns:

SBI excess Return Calculation (for CAPM)

$$R_{i,t}^{excess} = R_{i,t} - R_{f,t}$$

Market Excess Return (NIFTY)

$$R_{m,t}^{excess} = R_{m,t} - R_{f,t}$$

Preparing Inputs for GBM (for Reliance)

Utilizing the daily log returns of Reliance:

1. Everyday Drift

$\mu_{daily} = mean(r_t)$

2. Daily Fluctuation

$\sigma_{daily} = std(r_t)$

3. Yearly Calculation

GBM utilizes yearly drift and volatility:

$\mu = \mu_{daily} \times 252$

$\sigma = \sigma_{daily} \times \sqrt{252}$

(252 = days of trading in a year.)
These constitute the ultimate GBM parameters.

Final Output
After preparation:
CAPM dataset contains:
Monthly return log of SBI
Monthly return log of NIFTY 50
Risk-free rate per month
Monthly SBI surplus return
Excess return from the market on a monthly basis
GBM Dataset Includes:
Daily log returns for Reliance
Daily fluctuations and variability
Yearly fluctuation and variability
Recent stock price for simulation
This finalizes data preparation and generates clean, model-ready datasets.

CAPM Implementation (State Bank of India)
Model Specification
Regression setup:
$R_{i,t}^{excess} = \alpha + \beta\left(R_{m,t}^{excess}\right) + \epsilon$

Where:
- $R_{i,t}^{excess}$- Excess return of SBI at time t
- $R_{m,t}^{excess}$- Excess return of the market at time t
- α- Intercept
- β- Slope representing Systematic risk
- ϵ- Error term

Regression Procedure
The regression was conducted using the Regression function in Excel's Data Analysis ToolPak. The actions taken were:
- SBI excess return as an independent variable (X).
- Market excess return as dependent variable (Y).
- Output Regression table includes α, β, R^2 and Regression statistics.

CAPM Expected Return Formula
$E(R_i) = R_f + \beta\left(R_f - R_m\right)$

Where:
- R_f-Risk-free rate
- R_m- Excess Market return
- β- Estimated from regression

Summary
The CAPM application established a strong empirical structure for assessing SBI's risk features through-
Monthly excess returns- A linear regression formula, Statistical evaluation, and finally Templates for visualizing additional assessment.

Geometric-Brownian Motion Implementation (Reliance)
Model framework
The Geometric-Brownian Motion stochastic differential equation is:

$$dS_t = \mu S_t dt + \sigma S_t dW_t$$

Where:
S_t- Stock price at time t
μ- Drift (expected return)
σ- Volatility
W_t- Brownian Motion

The analytical solution is:
$$S_t = S_0 \exp\left(\left(\mu - \frac{1}{2}\sigma^2\right)\right)t + \sigma W^t$$

Summary
The GBM execution generated a well-organized stochastic simulation setting that included- Daily log-return values, projected shift and variability yearly parameter collection, equation for discrete-time GBM, 10 projected future price trajectories, and templates for visualizing path charts, histograms, and comparative studies.
These components facilitate thorough risk and uncertainty assessments for Reliance Industrie.

CONCLUSION

This section lays out what I found from applying CAPM to SBI and GBM to Reliance, looking at the results through the lens of market behavior, risk patterns, and how well these models actually predict what's coming next.

CAPM Results for SBI

Regression Output
The CAPM regression of SBI's monthly excess returns against NIFTY 50's monthly excess returns produced the subsequent important statistics:

Interpretation of Beta
A beta of 1.59 suggests:
- SBI has significant systemic risk.
- Its returns magnify market fluctuations.
- The bank is very responsive to macroeconomic and policy-related cycles.
- Investors in SBI can anticipate increased volatility amid market declines.

This corresponds with SBI's business engagement in interest rate cycles, credit cycles, and significant market variations.

Expected Return Vs Actual Return

Using CAPM model, we conclude:

- Calculated CAPM Expected Return= -20.68%
- Actual mean monthly return (Annualized)= -6.02%

Interpretation:

A significant difference exists between the theoretical expectation of CAPM is substantial in size and negative, and the current achieved performance, which is adverse yet less severe.

Conclusion for CAPM

Despite CAPM accounting for SBI's elevated systematic risk, it undervalues true performance because of the elevated instability during times of crisis and structural alterations overlooked by the model.

GBM Results for RIL

Estimated Parameters

Interpretation

Daily fluctuations are significant, whereas yearly fluctuations are stable due to the scaling of time.

Negative drift indicates a mild downward trend in the observed timeframe (2022–2024), signifying:global oil fluctuations, telecommunications industry rivalry and post-pandemic adjustment.

GBM Simulation Outcomes

Using the latest price: $S_0 = ₹1210.61$

Final Simulated Prices:

Understanding of Distribution

- The average simulated price is a bit less than the current price, aligning with the negative trend.
- The 5th–95th percentile range signifies the 90% confidence interval.
- The price is expected to stay between ₹1118 and ₹1277 for the upcoming year.

Observations

CAPM determines the relationship between SBI and the market NIFTY 50, showing how it is majorly valuable for managing the overall portfolio risk. The expected return shown is adversely affected by crisis periods like COVID-19, as shown in this project. GBM gives a probability on price predictions, which helps with structural planning. Its simulations are mostly consistent and capture realistic ups and downs in volatility.

Final Insights

Together, these models show that SBI exhibits real, systematic market risk. Still, its actual performance doesn't always match up with what CAPM predicts, because of the deeper structural issues and the impact of crises. Reliance shows moderate fluctuations and a tight prediction range, giving steady long-term trends.

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Table 1. Regression Output

Parameter	Value	Evaluation
β	1.59	SBI exhibits considerably higher volatility compared to the market; a 1% shift in market return results in a 1.59% variation in SBI return.
α	Minor Positive	Suggests slight outperformance in relation to risk, though statistically insignificant.
R^2	Moderate(~0.55)	CAPM accounts for roughly half of the variation in SBI returns.

Table 2. Estimated Parameters

Parameter	Value	Evaluation
Daily drift(μ_c)	–0.0001377	Marginally negative anticipated daily return.
Annual drift(μ)	–3.47%	Anticipated yearly trend is slightly negative.
Daily volatility(σ_c)	0.6787	Significant short-term fluctuation.
Annual volatility(σ)	10.77%	Average yearly volatility.

Table 3. GBM Simulation Outcomes

Statistic	Value
Mean final price	₹1186.89
5th Percentile	₹1118.37
95th Percentile	₹1277.00

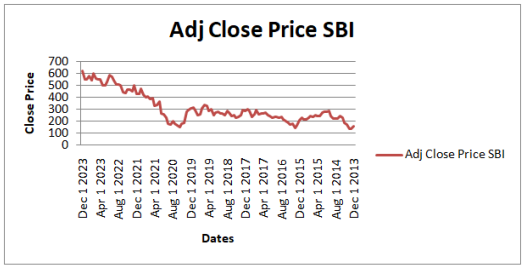

Figure 1: Adjusted closing price history of SBI between 2014 and 2024, illustrating long-term growth trends, cyclical fluctuations, and macroeconomic influences on stock performance

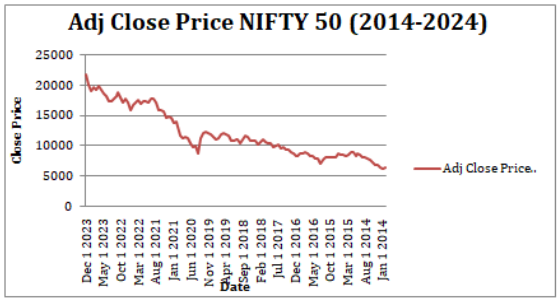

Figure 2: Trend of adjusted closing prices for the NIFTY 50 from 2014 to 2024, depicting overall market fluctuations and benchmark performance pertinent to CAPM.

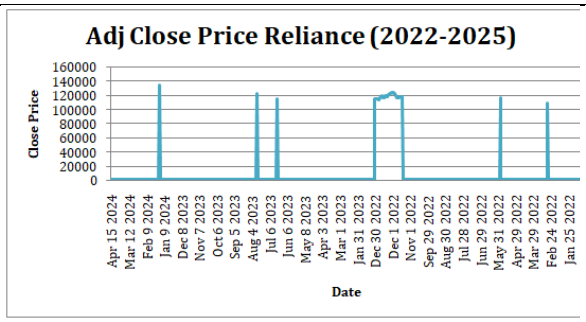

Figure 3: Daily adjusted closing price of Reliance Industries spanning 2022 to 2024, illustrating short-term variations and volatility trends pertinent for GBM modeling

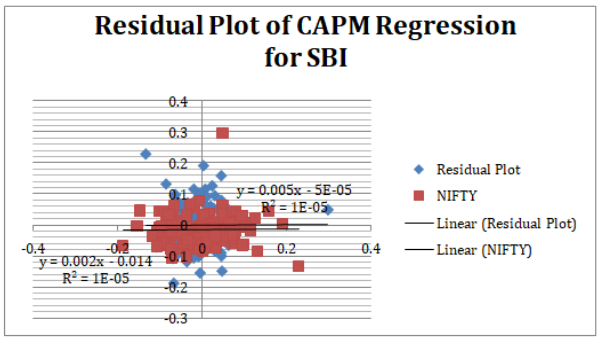

Figure 4: Residual plot of the CAPM regression for SBI, illustrating deviation patterns and evaluating the suitability of the linear model

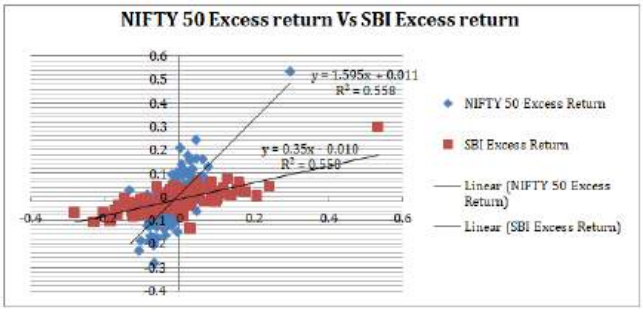

Figure 5: Scatter plot depicting SBI excess returns against NIFTY 50 excess returns, featuring the fitted CAPM regression line, demonstrating the estimated beta and relationship of systematic risk.

Indian Journal of Natural Sciences www.tnsroindia.org.in ©IJONS

Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

REVIEW ARTICLE

Integrative Ayurvedic and Neurobiological Approach to Opium De – Addiction : A Comprehensive Review

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Received: 26 Nov 2025 Revised: 18 Mar 2025 Accepted: 18 Dec 2025

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ABSTRACT

Opioid addiction is a major global health crisis characterized by neurobiological dysfunction, cognitive decline, psychiatric comorbidities, and high relapse rates. Conventional therapies often provide temporary symptomatic relief but fail to address long-term neuropsychological recovery. To critically review opioid addiction's neurobiological mechanisms and evaluate Ayurvedic therapeutic strategies—including *Panchakarma*, *Medhya Rasayana*, and *Satvavajaya Chikitsa* within an integrative treatment framework. A systematic literature search was conducted following PRISMA 2020 guidelines across PubMed, Scopus, Web of Science, Google Scholar, and AYUSH Research Portal. Studies related to opioid neurobiology, Ayurvedic addiction management, and integrative models published in the last 20 years were included. Eligible data were synthesized thematically. Opioid addiction disrupts mesolimbic dopamine signalling, enhances stress-axis reactivity, diminishes cognitive control, and increases relapse vulnerability. Ayurvedic detoxification procedures (*Vamana, Virechana, Basti, Nasya*), *Medhya Rasayana* herbs (Bacopa monnieri, Convolvulus pluricaulis, Celastrus paniculatus, Withania somnifera), and *Satvavajaya* therapies (meditation, pranayama) demonstrate potential benefits in neuroprotection, stress modulation, cognitive enhancement, and emotional stabilization. The mechanisms align with contemporary neurobiological evidence. *Ayurveda* provides a multidimensional therapeutic model that addresses physiological detoxification, cognitive restoration, emotional regulation, and long-term relapse

prevention. Integrating Ayurvedic therapies with modern treatment modalities may offer an evidence-based, holistic strategy for opioid de-addiction. Further clinical trials are needed for validation.

Highlights:

- Opioid addiction causes profound neurobiological, cognitive, and emotional dysregulation.
- Ayurvedic therapies provide detoxification, neuroprotection, and psychological stabilization.
- *Panchakarma* and *Medhya Rasayanas* align mechanistically with modern addiction neuroscience.
- *Satvavajaya Chikitsa* enhances emotional resilience and reduces relapse risk.
- Integrative Ayurvedic–neuroscience models may improve long-term addiction outcomes**.**

Keywords: *Opium addiction; Panchakarma; Rasayana therapy; Medhya Rasayana; Satvavajaya Chikitsa; Neurobiology of addiction; Ayurvedic detoxification*

INTRODUCTION

Opium addiction, characterized by the compulsive use of opium-derived substances, leads to dependence and withdrawal symptoms [1]. Derived from *Papaver somniferum* [2], opium has both medical and recreational applications but carries substantial risks, including cognitive impairment and mental health disturbances [3]. This review examines the psychological impact of opium addiction and outlines Ayurvedic management strategies such as *Shodhana Chikitsa* (detoxification) [4], *Shamana Chikitsa* (palliative care), and *Rasayana Chikitsa* (rejuvenation) [5]. Opioid addiction remains a major global health crisis, with rising consumption and increasing opioid-related mortality, particularly due to the proliferation of potent synthetic opioids such as fentanyl [6]. Within this context, Ayurvedic therapies represent promising complementary approaches for detoxification, withdrawal mitigation, and cognitive restoration.

Objectives

- Examine the neurobiological mechanisms of opioid addiction, focusing on disruptions in reward pathways, neurotransmission, and cognition.
- Summarize key Ayurvedic interventions for addiction management, including *Rasayana* therapies (rejuvenation), *Medhya Rasayanas* [6] (cognition-enhancing neuroprotective herbs), and Panchakarma procedures such as Vamana (therapeutic emesis), *Virechana* (therapeutic purgation), *Basti* (medicated enema therapy), *Nasya* (nasal administration), and *Raktamokshana* (bloodletting), along with commonly used herbal formulations.
- Evaluate integrative therapeutic approaches combining modern neuroscientific evidence with Ayurvedic principles to enhance detoxification, cognitive restoration, emotional regulation, and long-term relapse prevention.

MATERIALS AND METHODS

This systematic review was conducted in accordance with PRISMA 2020 guidelines. The methodological process included the following steps:

Literature Search

A comprehensive search strategy was applied across major biomedical and integrative medicine databases including PubMed, Scopus, Web of Science, Google Scholar, and the AYUSH Research Portal. Search terms included combinations of keywords related to opioid addiction neurobiology, *Ayurvedic* treatment modalities, *Panchakarma, Rasayana*, and integrative de-addiction approaches (*Figure 1: PRISMA Flow Diagram*).

Eligibility Criteria

Peer-reviewed articles published within the last 20 years were included if they examined (a) the neurobiological mechanisms of opioid use disorder, (b) Ayurvedic therapeutic interventions relevant to addiction management, or (c) integrative or comparative addiction frameworks. Studies not written in English, duplicates, commentaries, dissertations, and those unrelated to addiction or Ayurveda were excluded.

Data Extraction

Relevant data from the included studies were systematically extracted and organized into thematic categories. The major domains included:

(i) Neurobiological processes underlying opioid dependence,
(ii) Ayurvedic detoxification and rejuvenation therapies,
(iii) *Rasayana*-based cognitive and emotional restoration
(iv) Integrative therapeutic models.

Data Synthesis

A qualitative thematic synthesis was performed to compare, contrast, and integrate findings from modern neuroscientific and Ayurvedic literature. Emphasis was placed on mechanistic overlap, therapeutic complementarities, and translational relevance.

Quality Assurance

The systematic approach ensured that all included evidence contributed to an objective, comprehensive, and integrative understanding of opioid addiction and its management through Ayurvedic and contemporary therapeutic frameworks

Fig.1. diagram presents the structured process used to identify, screen, assess, and include studies in the systematic review. A total of 1,346 records were identified, of which 1,194 were screened, 112 full-text articles were assessed for eligibility, and 52 studies met the final inclusion criteria.

OBSERVATIONS AND DISCUSSION

Opium addiction is a significant global and national health crisis, with severe social and economic consequences. Globally, around 292 million people used drugs in 2022, with 60 million using opioids. Opioids are responsible for nearly 80% of drug-related deaths, with approximately 600,000 fatalities recorded in 2019, largely due to overdose (Fig.2). *This line graph illustrates the temporal trends in overdose deaths associated with major drug categories, including heroin, cocaine, methamphetamine and other stimulants, prescribed opioids (e.g., oxycodone), and fentanyl-related substances. The data show a sharp rise in fatalities linked to synthetic opioids, particularly fentanyl, after 2014, highlighting the escalating severity of the opioid crisis in the United States.*

In India, the situation is particularly alarming, with 2.1% of the population using opioids three times the global average. Opioid use is significantly higher among males (4%) compared to females (0.2%), and even children aged 10 to 17 years are affected (Fig:3). The increasing prevalence and high mortality rates highlight the urgent need for comprehensive and integrative treatment strategies, combining *Ayurvedic* detoxification, cognitive restoration, and psychological resilience-building with modern therapies for sustainable recovery. *Fig. 3 bar chart illustrates the prevalence of opioid use across the Indian population, showing national overall rates (2.1%), significantly higher prevalence among males (4%), and comparatively low prevalence among females (0.2%).*

Neurobiological Foundations of Opium Addiction

Mechanisms of Action

Opium addiction is primarily driven by its ability to alter the brain's reward system. Opioids bind to mu-opioid receptors (MORs) in the ventral tegmental area (VTA), nucleus accumbens , and prefrontal cortex, leading to inhibition of gamma-aminobutyric acid (GABA)-ergic interneurons(Fig.4). This disinhibition results in excessive dopamine release throughout the mesolimbic reward pathway [6]. The resulting surge in dopamine produces intense euphoria, reinforcing compulsive drug-seeking behavior and contributing to the development and maintenance of addiction.Furthermore, the amygdala and hippocampus, which are involved in emotional learning and memory formation, play a crucial role in linking opioid use with pleasurable experiences, reinforcing the addiction cycle [7].

Fig.4 diagram depicts the major neural pathways involved in opioid dependence. Activation of mu-opioid receptors inhibits GABA interneurons, increasing dopaminergic output from the ventral tegmental area (VTA) to the prefrontal cortex and limbic structures. The amygdala and hippocampus contribute to emotional memory formation, while locus coeruleus hyperactivity underlies withdrawal symptoms. Together, these circuits drive reward reinforcement, compulsive drug-seeking behavior, and withdrawal dysregulation

Tolerance and Dependence

Chronic opioid use leads to adaptive changes in neuroplasticity, diminishing opioid receptor sensitivity and resulting in tolerance, where increased doses are required to achieve the same euphoric effects [8]. Prolonged opioid exposure downregulates endogenous opioid production, making the brain reliant on external opioids for normal functioning [9]. When opioid consumption ceases, the hypothalamic-pituitary-adrenal (HPA) axis becomes hyperactive, leading to withdrawal symptoms such as anxiety, irritability, hyperalgesia (increased pain sensitivity), and dysphoria [10]. The noradrenergic system in the locus coeruleus is also hyperactivated, contributing to symptoms like sweating, nausea, and tremors [11].

Psychological Impact of Opium Addiction

Cognitive Impairments

Opium addiction is strongly associated with progressive cognitive decline. Attention and working memory deficits are common, with affected individuals experiencing difficulty concentrating and retaining information, leading to impaired problem-solving abilities [12]. Executive dysfunction arises due to opioid-induced disruption of prefrontal cortex activity, resulting in compromised decision-making, reduced impulse control, and poor planning, all of which contribute to compulsive drug-seeking behavior [13]. Additionally, reduced neurogenesis is observed with chronic opioid exposure, particularly within the hippocampus, negatively influencing learning capacity and memory consolidation [14].

Emotional Dysregulation

Opioid dependence significantly alters emotional processing due to its suppressive effects on the limbic system. Emotional blunting, characterized by apathy and reduced social engagement, arises from diminished amygdala activation [15]. Increased stress sensitivity occurs as dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis heightens stress reactivity, making individuals more susceptible to anxiety and irritability [16]. Additionally, anhedonia**,** or the inability to experience pleasure, results from the downregulation of dopamine receptors in the nucleus accumbens, thereby increasing vulnerability to depressive symptoms [17].

Behavioral Changes

Opium addiction results in marked behavioral disturbances. Compulsive drug-seeking behavior emerges as striatal neuroadaptations cause the brain to prioritize opioid use over essential needs [18]. Risk-taking and impulsivity increase due to impaired decision-making, predisposing individuals to unsafe sexual behaviors, financial instability,

and criminal involvement [19]. Furthermore, social withdrawal becomes prominent as individuals disengage from family, occupational duties, and social environments, contributing to a progressive decline in quality-of-life [20].

Psychiatric Comorbidities

Opioid addiction is frequently accompanied by a range of psychiatric comorbidities. Major depressive disorder (MDD) is common, driven by opioid-induced dysregulation of serotonin and dopamine pathways, leading to low mood, hopelessness, and suicidal ideation [21]. Generalized anxiety disorder (GAD) often develops or worsens due to heightened stress reactivity and persistent worry associated with chronic opioid use [22]. Personality disorders, particularly antisocial and borderline traits, further contribute to impulsivity, aggression, emotional instability, and an increased risk of relapse [23].

Ayurvedic Approach to Opium De-Addiction (Fig.5)

***Shodhana Chikitsa* (Detoxification Therapy)**

Ayurveda places primary emphasis on *Shodhana* (detoxification) as the initial step in de-addiction, targeting the elimination of *Ama* (metabolic toxins) and residual opioid by-products from the body. Among the key detoxification procedures, *Raktamokshana* (bloodletting therapy) is used to alleviate toxin accumulation in the bloodstream, which is often associated with fatigue and systemic inflammation; controlled bloodletting facilitates toxin removal and improves blood oxygenation [24]. *Vamana* (therapeutic emesis) is particularly beneficial in managing *Kapha*-related disturbances observed during opioid withdrawal, as it helps clear the gastrointestinal and respiratory pathways, restore appetite, and reduce nausea and lethargy [25].

***Shamana Chikitsa* (Palliative Therapy)**

Shamana Chikitsa (palliative therapy) stabilizes the body and mind following detoxification, helping to reduce withdrawal-related anxiety, depression, and cravings. Key interventions include *Medhya Rasayanas (Table:1)* (neuroprotective and cognition-enhancing herbs) such as *Brahmi* (*Bacopa monnieri*), which improves cognition, memory, and emotional regulation [26]; *Shankhpushpi* (*Convolvulus pluricaulis*), known for its mood-stabilizing and anxiolytic effects [27]; and *Jyotishmati* (*Celastrus paniculatus*), which acts as a neurostimulant and enhances synaptic connectivity [28]. Additionally, adaptogenic *herbs* such as *Ashwagandha* (*Withania somnifera*), which modulates cortisol, improves sleep, and supports adrenal recovery [29], and *Guduchi* (*Tinospora cordifolia*), which promotes hepatic detoxification, enhances immune regulation, and supports HPA-axis balance [30], play a crucial role in restoring systemic and psychological stability during the de-addiction process.

***Rasayana* Therapy (Rejuvenation and Neuroprotection)**

Swarnaprashana (gold therapy) is traditionally described as enhancing cognitive resilience, emotional stability, and neuronal function, with some evidence suggesting that gold nanoparticles may support synaptic transmission [31]. *Chyawanprash*, a classical polyherbal formulation containing *Amla* (*Emblica officinalis*) and *Pippali* (*Piper longum*), is noted for its rejuvenative properties, improving vitality, digestion, immunity, and neuronal repair [32].

***Satvavajaya Chikitsa* (Ayurvedic Psychotherapy)**

Satvavajaya Chikitsa (Ayurvedic psychotherapy) focuses on strengthening mental and emotional regulation to reduce psychological dependence on opioids. *Dhyana* (meditation) has been associated with increased gray matter density in brain regions responsible for self-control, thereby helping to reduce cravings and impulsive behaviours [33]. *Pranayama* (breathwork practices), including techniques such as *Anulom Vilom*[*] and *Bhramari*[**], promotes autonomic stability and modulates neurotransmitter activity, effectively mitigating withdrawal-related anxiety and emotional distress [34].

Fig. 5. schematic illustrates the convergence of neurobiological mechanisms and Ayurvedic therapeutic principles in a unified de-addiction framework. Neurobiological pathways include dopamine reward regulation, HPA-axis modulation, neuroplastic repair, and cognitive control circuits. Ayurvedic interventions include Panchakarma detoxification, Rasayana-based neuroprotection,

Satvavajaya emotional regulation, and Medhya cognition-enhancing therapies. Together, these approaches support integrated detoxification, neuroregulation, and relapse prevention.

* Anulom Vilom Pranayama is a yogic breathing technique that involves alternate nostril breathing to balance the nervous system, calm the mind, and enhance respiratory and mental regulation. ** Bhramari is a humming-bee breath that calms the brain and reduces anxiety.

Fig.6. diagram illustrates the Ayurvedic therapeutic framework for addiction management, including Shodhana (detoxification through Vamana, Virechana, Basti, and Nasya), Shamana (stabilization with Medhya Rasayanas such as Brahmi (Bacopa monnieri), Shankhapushpi (Convolvulus pluricaulis), Ashwagandha (Withania somnifera), and Guduchi (Tinospora cordifolia)), and Satvavajaya (mind–behavior therapies including meditation and pranayama). Collectively, these interventions support cognitive restoration and reduce relapse risk

CONCLUSION

Ayurveda offers a comprehensive, multidimensional framework for managing opioid dependence by integrating detoxification *(Shodhana*), restorative herbal interventions (*Shamana* and *Rasayana*), and cognitive–behavioral strengthening (*Satvavajaya Chikitsa*). These interventions address key neurobiological disturbances such as dopamine dysregulation, HPA-axis hyperactivity, impaired executive control, and emotional instability. Evidence shows promising overlap between Ayurvedic mechanisms such as antioxidant effects, neuroendocrine modulation, and enhancement of synaptic plasticity and modern neuroscience findings. While integrative Ayurvedic-modern protocols have significant potential for sustainable recovery, high-quality clinical trials are needed to establish standardized treatment guidelines, optimal dosages, and measurable outcomes.

Author Contribution

Author 1: Review of literature, writing review and editing Manuscript preparation, Data acquisition and analysis. **Author 2 and 3**: Conceptualization, Methodology/Study design, Manuscript editing, Grammar and Spelling check,

ACKNOWLEDGEMENT

Nil

Validation Data availability statement: Not applicable.

Financial support and sponsorship - Nil.

Conflicts of interest- There are no conflicts of interest

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Table 1. *Medhya Rasayana* (neuroprotective and cognition-enhancing herbs)herbs and their Neurobiological Actions

Herb	Scientific name	Ayurvedic action	Neurobiological relevance
Brahmi	*Bacopa monnieri*	Medhya, Smriti-enhancing	Improves synaptic plasticity, reduces oxidative stress
Shankhapushpi	*Convolvulus pluricaulis*	Nerve calming, anxiolytic	Enhances GABAergic tone, reduces anxiety
Jyotishmati	*Celastrus paniculatus*	Buddhi vardhaka	Enhances cholinergic transmission, memory
Ashwagandha	*Withania somnifera*	Adaptogen, anxiolytic	Reduces cortisol, neuroprotective
Guduchi	*Tinospora cordifolia*	Immunomodulator	Regulates HPA axis, antioxidant

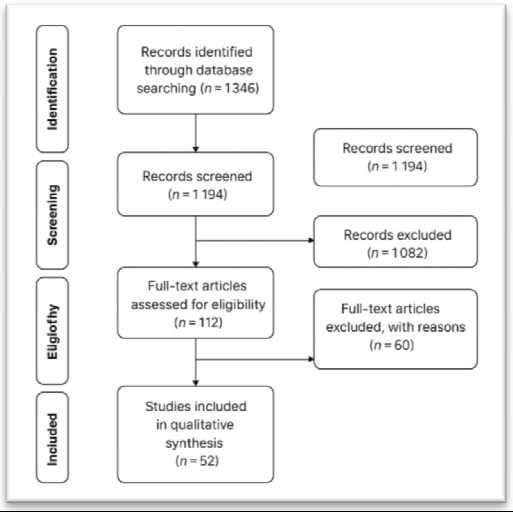

Figure 1. PRISMA 2020 Flow Diagram for Study Selection.

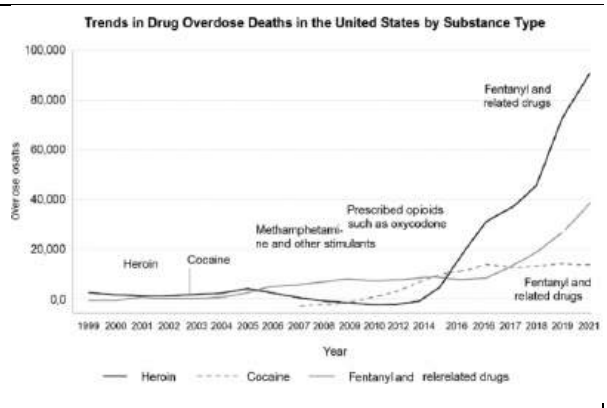

Fig 2: Trends in Drug Overdose Deaths in the United States by Substance Type (1999–2021)

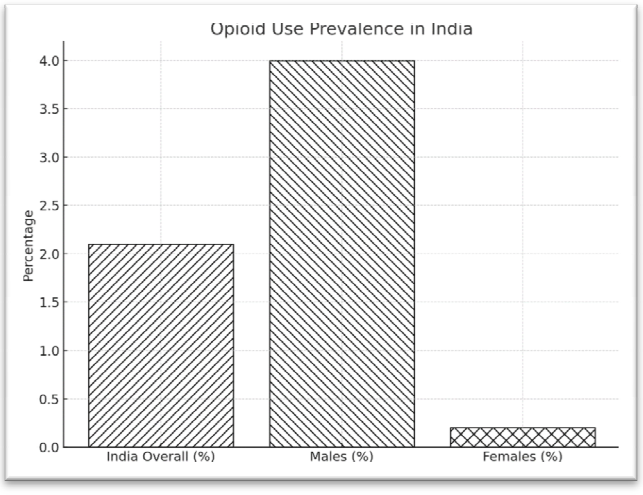

Fig. 3: Opioid Use Prevalence in India (%).

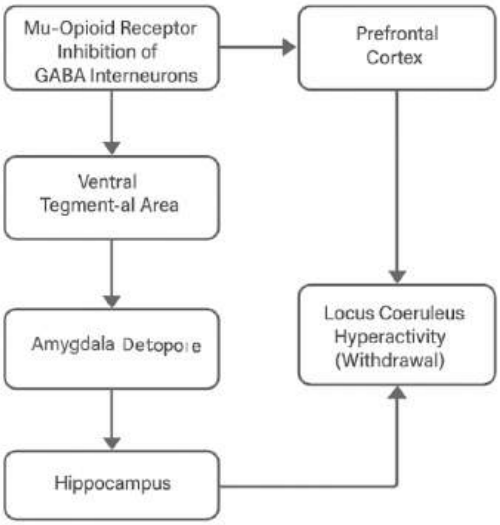

Fig. 4. Neurobiological Circuit of Opioid Addiction.

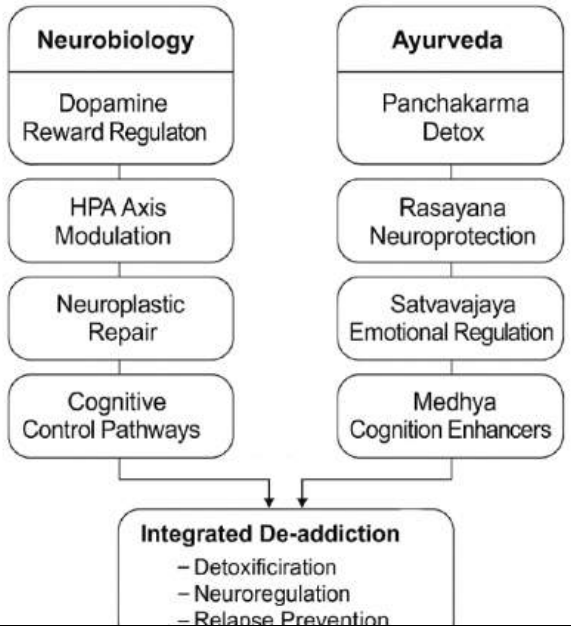

Fig. 5. Integrative Neuro-Ayurvedic Model for Opioid De-addiction.

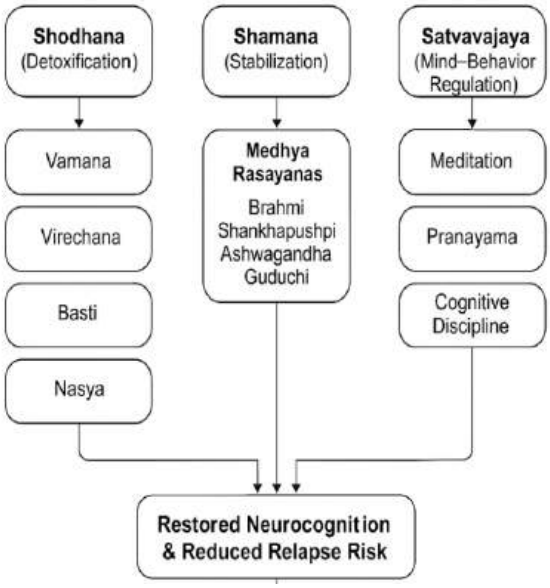

Fig. 6. Ayurvedic Treatment Pathway for Opioid De-addiction.

RESEARCH ARTICLE

Green Marketing Strategies and Consumer Purchase Intentions for Eco - Friendly Products in India

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Received: 12 Nov 2025 Revised: 16 Dec 2025 Accepted: 06 Jan 2026

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ABSTRACT

The negative impact on the environment, changing climate, and growing global concern for the environment have led to both consumers and businesses to give the highest priority to the environment. In this regard, green marketing has been a very helpful tool for those companies that want to not only sell more and keep the environment clean but also control the consumption patterns of sustainability. The present research looks at the effects of the green marketing approaches on the buyer intentions of the Indian market, which is one of the fastest growing global consumer economies, marked by an increase in the environmental consciousness and demand for sustainable products. The questionnaire is given to 500 urban consumers living in four main metropolitan cities, the study assesses what influences the major green marketing elements like eco-labeling, green packaging, and corporate social responsibility (CSR) communication on the purchase decisions. The use of correlation and multiple regression techniques disclose that eco-labeling and the consciousness of the environment are the main tendencies towards the purchase of the product, and these are followed by green packaging and CSR initiatives. Pricing issues are still the main obstacle to getting more buyers even though consumers have a good opinion on the eco-friendly products. The results bring out the necessity of having solid environmental claims, open

sustainability practices, and pricing strategies that are in line with the competition to win over consumers and get the market accepted. For the companies and the marketers, this study is an important source of literature on green consumerism which will also provide them with the necessary insight to plan and promote sustainable consumption behaviors in India.

Keywords: Environmentally friendly products, Ecologically related marketing, Indian consumers, Green marketing programs and strategies, Green marketing practices, and Indian consumers are stimulated to make eco-friendly buying choices.

INTRODUCTION

The concerns about the environment that are growing together with the rapid depletion of natural resources have moved the world towards sustainable consumption. Green marketing, which is mainly trying to sell the product based on its environmental attributes, has emerged as a major tool for the companies trying to establish long-term consumer relationships [1]. Urbanization, disposable incomes, and environmental consciousness in India are all conditions that are very conducive to the green marketing strategies [6]. On the one hand, Indian consumers are more aware of eco-friendly products than ever before, but on the other hand, there is no steady demand for such products. Different consumers' perceptions, trust issues, and in general, price sensitivity are the main causes of inconsistency that can be observed in the results of different studies [4]. In addition to their values and beliefs, research shows that consumers' acceptance of green products depends on very many factors having either a positive or negative impact, such as product characteristics, communication, and promotion, as well as social influences [2],[7]. Therefore, it is vital to study the impact of green marketing strategies on the purchase intentions of the Indian market in order to create a precise sustainable marketing framework.

LITERATURE REVIEW

The requirement for all industries and green marketing to move from a niche strategy has been primarily driven by consumers' demand for transparency and sustainable practices [8]. Eco-labeling has become one of the most important methods for companies to exhibit their devotion to the environment and the needs of consumers, which has, in turn, influenced the environment-friendly direction of consumer choices [9]. Also, through the use of eco-friendly packaging, sustainable materials, and waste reduction, the consumers' views can be greatly affected [10]. CSR activities not only help to create a strong trust among customers but also aid in the creation of a good brand image, thereby, increasing consumer loyalty[5]. Intention to purchase is influenced by attitudes, social norms, and perceived control over the behaviour [2]. Many different research works have verified that concern for the environment is directly linked with the adoption of green purchasing habits [11]. But on the other side, the green product market is always beset with the problems of high prices along with the doubts about the eco-friendliness of the products which result in low demand [12]. India is witnessing a rise in environmental awareness but it is not reflected uniformly across all population categories in terms of purchasing habits [13]. The urban population is found to be more open to trying and accepting eco-friendly products than the rural population [14]. The whole concept of digital influence in the area of sustainable consumption is becoming more and more important as it is doing so at a fast pace [15].

METHODOLOGY

This study utilizes a quantitative study strategy that will help to clarify the influence of green marketing strategies on the consumption intentions of eco-friendly products among Indian consumers. The whole methodology has been laid down in such a way that it guarantees the findings to be reliable, valid, and applicable to other contexts. This part

describes the research method, sampling plan, instrument construction, data gathering process, and the different analytic methods employed in the investigation.

Research Approach

For the measurement of consumer attitudes, perceptions, and purchase intentions, a quantitative survey-based approach was selected. Quantitative research is systematically and objectively pet. It is quite common in marketing and consumer-behavior studies, mainly when the relationship between variables is analyzed by applying statistical methods. The study takes an explanatory point of view and tries to find out the impact of specific green marketing strategies (eco-labeling, green packaging, CSR communication, etc.) on purchase intentions.

Population and Sampling

The Indian consumers aged between 18 and 45 years, who were aware of the green products or had at least once bought them, were the target population. Non-probability convenience sampling was adopted because of the vast area covered by India and the related logistic problems. Although fully non-random, this method is still suitable for exploratory consumer behavior research, especially when the respondents have to be previously exposed to sustainable products. The total number of respondents who took part in the study is 500. The respondents were taken from the four major metropolitan cities—Delhi, Mumbai, Bangalore, and Chennai since these urban centers have good environmental awareness, the widest product availability in the market, and also the most exposure to green marketing campaigns. The distribution across cities was made with the goal of capturing different socio-economic and cultural backgrounds in the urban consumer group.

Instrument Development

A structured questionnaire was made by taking reliable scales from past studies on green marketing and consumer behavior.

The questionnaire had four main parts:

Demographic data (age, sex, income, education).

Environmental awareness (assessed by 5 items taken from Chan, 2001).

Attitudes toward green marketing strategies: Eco-labeling (4 items), Green packaging (4 items), CSR communication (3 items)

Purchase intention towards eco-friendly products (5 items from Ajzen's TPB model) All items were scored on a 5point Likert scale where 1 = Sturdily Disagree and 5 = Effectively Agree. The assess was pre-verified on a small crowd of 30 participants to check if the questions were understandable and if the measurement was consistent. Some minor changes were made based on the feedback.

Data Collection Procedure

To make the surveys more accessible and get more responses, they were done in both online and offline ways for four weeks.

- Google Forms was used for the online surveys, while email, WhatsApp groups, and social media sites were utilized to spread the word.
- The offline questionnaires were given out in selected cities in shopping malls, supermarkets, and university campuses.

The respondents who provided the answers to the questionnaires were assured that their identities would not be revealed and that their responses would be kept secret, and the others were allowed to participate if they wished. The number of responses gathered was 532, but after eliminating the invalid ones, only 500 valid responses remained, which were the result of filtering out the incomplete surveys and inconsistent answers through screening.

Reliability and Validity Testing

To make sure the data was of high quality, both reliability and validity tests were performed:

- Cronbach's alpha was utilized to evaluate the internal consistency of each construct. The results for all the constructs were higher than 0.78, which is well above the suggested minimum of 0.70.
- Validity of the content was secured by adopting measurement items from earlier studies that had been validated.
- Validity of the construct was proven by factor analysis (KMO value = 0.84), which signified that the data was suitable for subsequent statistical analysis.

Data Analysis Techniques

The statistical analysis was performed through SPSS 26.0 program. The subsequent methods were used successively:
Descriptive Statistics: Presented the respondents' demographic characteristics and key variable mean scores.

Correlation Analysis: Found out the degree and the nature of the relationships between green marketing strategies and purchase intentions.

Multiple Regression Analysis: Provided support for the impacts of eco-labeling, green packaging, CSR communication, and environmental awareness on consumer purchase intention.

ANOVA Tests: Conducted to compare the differences in purchase intentions of different demographic groups (age, income, education).
The cumulative effect of using these statistical methods was to yield a very detailed understanding of how green marketing strategies affected consumer behavior in the Indian market.

RESULTS AND DISCUSSION

The research brought out very important factors of the impact of green marketing methods on the purchase intent of consumers in India. The responses of the 500 participants were subjected to a range of statistical methods, including, but not limited to, descriptive statistics, correlation analysis, regression modeling, and ANOVA. This section gives a detailed account of the demographic traits, the mean values of the major variables, the statistical results, and the discussion.

Demographic Profile of Respondents

The respondents' demographic characteristics are built up in Table 1. The sample represented a variegated urban population in terms of different age groups, income levels, and education categories.

Descriptive Statistics

Descriptive analysis was conducted to gauge the respondents' perceptions on green marketing strategies and their purchase intention. The findings are shown in Table 2. Mean values show a high level of environmental awareness and a positive perception of eco-labeling, whereas CSR communication received a lower score but still above the mid-point, indicating a fair trust in corporate environmental claims

Correlation Analysis

To evaluate the relationships relating the green marketing constructs and the purchase intention, Pearson correlation coefficients were calculated. The findings are represented in Table 3.
Notes:$p < 0.01$ for all correlation values.
The correlation between eco-labels and the purchase intention was the highest (r = 0.71), which implies that the eco-labels positively support the consumers' trust up to a great extent.

Regression Analysis

A several regression testing was functioned to find out the extent to which green marketing influences the consumer's purchase intention. The results have been got in Table 4.

Summary of the Model

R = 0.81

R^2 = 0.66

Adjusted R^2 = 0.65

F = 118.42, **p** < 0.001

The model accounts for 66% of the change in the purchase intentions, thus indicating a very robust predictive performance. The variable eco-labeling has been disclosed as the greatest predictor ($\beta = 0.38$), which is in accordance with the previous correlation findings.

ANOVA – Differences Based on Income Groups

One-way ANOVA was used to assess the variations in purchase intention between the different income groups. ANOVA Results for Purchase Intention by Income Level (Table 5). The analysis revealed a significant difference ($p = 0.001$) in purchase intention across income groups, indicating that the higher-income group of respondents was more willing to buy eco-friendly products.

Figures

Mean Scores of Green Marketing Constructs (Figure 1)

Description

A bar chart illustrating the average of each construction: Environmental Awareness: 4.12, Eco-Labeling: 4.02, Green Packaging: 3.89, CSR Communication: 3.76, Purchase Intention: 3.94 This graph shows that the highest scores were given to environmental awareness and eco-labeling.

Regression Impact of Predictors on Purchase Intention (Figure 2)

Description

The Y-axis of the clustered bar graph with standardized beta values presents eco-labeling (0.38), environmental awareness (0.31), green packaging (0.24), CSR communication (0.19) as the bars. Eco-labeling, which is the tallest bar, consolidates its leading impact.

Purchase Intention by Income Groups (Figure 3).

Description

A line or bar graph representing income categories, where the upper category made considerable buyers' eco-friendly products' price willingness scores clearly visible. The consumers with income higher than ₹75,000 were much more inclined to purchase environmentally friendly products than the others.

CONCLUSION AND RECOMMENDATIONS

The research has come to a conclusion that the adoption of green marketing strategies—most notably eco-labeling, green packaging, and CSR activities—affect the consumer's willingness to buy eco-friendly products in India to a great extent. It is recommended that marketers concentrate on the offered product's transparency, eco-certifications' fortification, and the environmental benefits communication all the more effectively. Price sensitivity can be handled further through the methods of subsidies, loyalty programs, or even cheap but sustainable materials thus adoption can take place. Long-term research should focus on the areas of digital influence, comparing different cultural consumers, and sustainability behavioral shifts.

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Table 1: Demographic Characteristics of Respondents (N = 500)

Demographic Variable	Category	Frequency	Percentage (%)
Gender	Male	280	56%
	Female	220	44%
Age	18–25	160	32%
	26–35	210	42%
	36–45	130	26%
Monthly Income	< ₹25,000	110	22%
	₹25,000–₹50,000	210	42%
	₹50,001–₹75,000	110	22%
	> ₹75,000	70	14%
Education	Undergraduate	150	30%
	Graduate	240	48%
	Postgraduate	110	22%

Table 2: Mean and Standard Deviation of Key Variables

Construct	No. of Items	Mean	Standard Deviation
Environmental Awareness	5	4.12	0.61
Eco-Labeling	4	4.02	0.67
Green Packaging	4	3.89	0.72
CSR Communication	3	3.76	0.69
Purchase Intention	5	3.94	0.74

Table 3: Correlation Matrix

Variables	1	2	3	4	5
Environmental Awareness	1				
Eco-Labeling	0.63**	1			
Green Packaging	0.52**	0.61**	1		
CSR Communication	0.48**	0.55**	0.49**	1	
Purchase Intention	0.66**	0.71**	0.59**	0.53**	1

Notes: p < 0.01 for all correlation values.

Table 4: Regression Model Summary

Predictor Variable	Beta (β)	t-value	Significance (p-value)
Environmental Awareness	0.31	6.21	0.000
Eco-Labeling	0.38	7.85	0.000
Green Packaging	0.24	5.12	0.000
CSR Communication	0.19	4.01	0.001

Table 5: ANOVA Results for Purchase Intention by Income Level

Source	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	4.412	3	1.471	5.32	0.001
Within Groups	136.221	496	0.274		
Total	140.633	499			

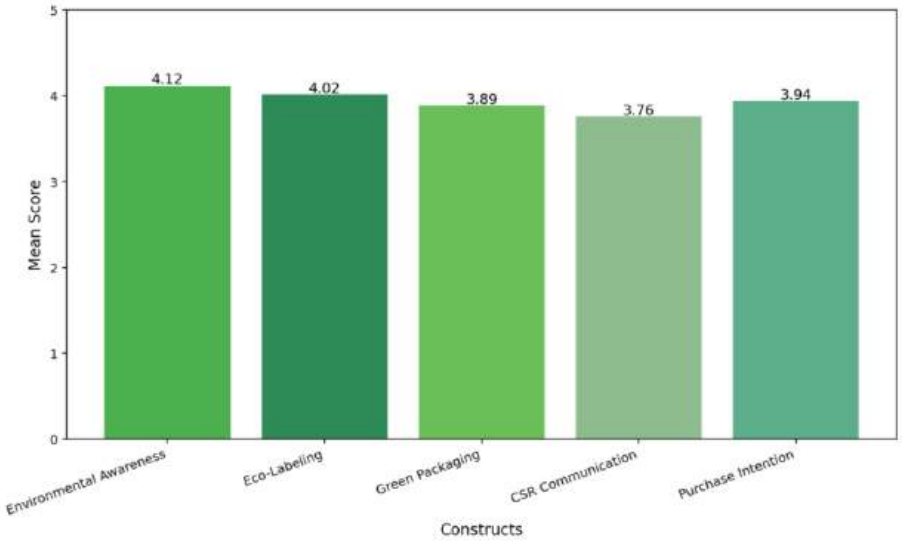

Figure 1: Mean Scores of Green Marketing Constructs

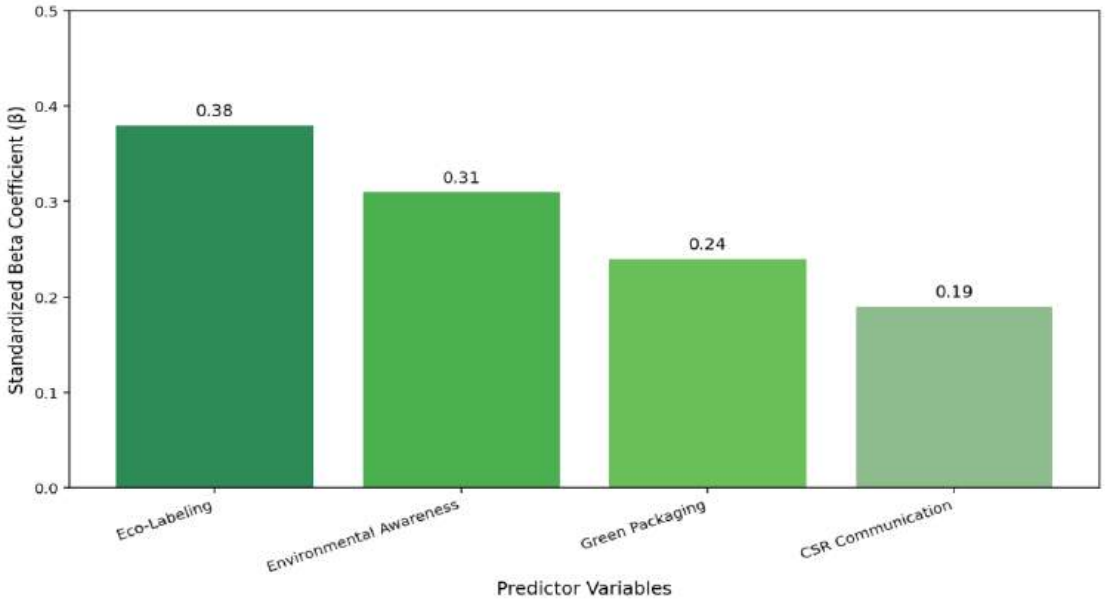

Figure 2: Regression Impact of Predictors on Purchase Intention

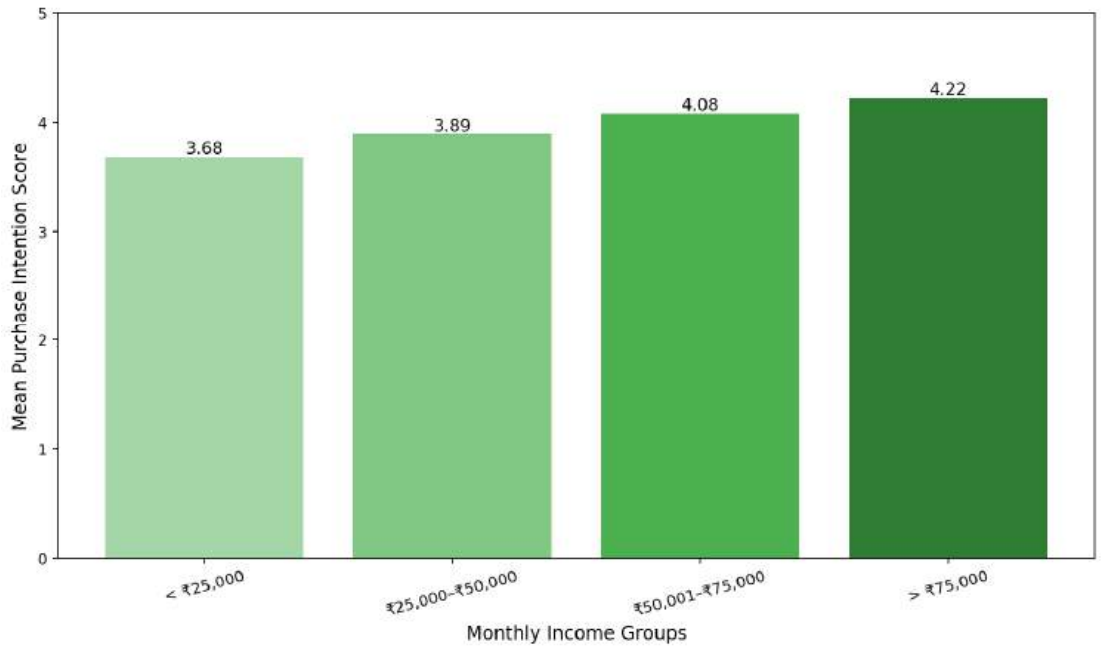

Figure 3: Purchase Intention by Income Groups

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Spectral, Optical, Electrical, Thermal and Dieletric Characterization of 2-Aminothiazole Single Crystal

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Received: 06 Oct 2025 Revised: 10 Nov 2025 Accepted: 18 Dec 2025

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ABSTRACT

2-aminothiazole single crystal was grown by slow evaporation method. The crystal has been characterized by UV-Visible NIR spectrum, Photoluminescence, Thermal analysis and Dielectric analysis to confirm its suitability for optical applications. The various optical and electrical properties has been calculated from the UV-Visible spectrum. Photoluminescence spectra revealed the violet light emission observed at 380 nm. The grown crystal was thermally stable up to 170˚C , confirmed from the thermo gravimetric analysis. The crystal exhibits high dielectric behaviour at low frequency and the dielectric behaviour is low at higher frequencies.

Keywords: Optical properties, Photoluminescence, Dielectric constant and loss, Thermal studies.

INTRODUCTION

Aminothiazole have many applications in both human and veterinary medicine [1].Organic molecular materials are appealing in controlling the light beam by an electric field because they offer many possibilities to tune their optical properties and obtain large electro-optic effects [2]. The main advantage of organic materials is that their structures can be easily altered to get the craved optical properties [3, 4]. Optical properties of the crystalline materials provide

information regarding the composition, nature and quality of the crystal. The Optical behaviour of the materials is important to determine their usage in optoelectronic devices [5]. The FTIR, FT-Raman and DFT of 2-aminothiazole have been already reported [6].The optical band gap of the 2-Aminothiazole have been calculated using Tauc'splot as 3.05 eV. The optical constants have been reported earlier [7].The title compound has been screened for its suitability in the fabrication of optoelectronic devices.

EXPERIMENTAL

2-aminothiazole (1.00g) was dissolved in 20 ml ethanol. The dissolved solution was then filtered. The filtered solution was allowed for slow evaporation in room temperature. Brown blockcrystal was obtained after two weeks on slow evaporation of the solution. Figure 1 shows the chemical diagram of 2-aminothiazole. The grown crystals are shown in figure 2.

RESULTS AND DISCUSSION

UV VISIBLE ANALYSIS

The optical properties of a material are important, as they provide information on the electronic structures and types of optical transitions[8].The UV-Visible absorption spectrum of 2-aminothiazole was recorded using Perkin Elmer Lamda 35 spectrophotometer in the wavelength range of 190 nm to 1100 nm. The UV-Visible absorption spectrum is shown in figure 3. The peak at 270 nm is due to the electron transitions from the highest occupied molecular orbital (HOMO) to the lowest unoccupied molecular orbital (LUMO) corresponding to the n→π^* electronic transition [9].

Optical Conductivity

The optical conductivity (σ_{op}) response of 2-aminothiazole crystal is derived from the value of the refractive index and absorption co-efficient by the following expression [10],

$$\sigma_{op} = \frac{\alpha nc}{4\pi}$$

The variation of the optical conductivity with wavelength is shown in figure4 (a). The optical conductivity as a function of photon energy (hυ) is shown in figure4 (b).

Optical Resistivity

The optical resistivity of a material is equal to the reciprocal ofits optical conductivity. The optical resistivity can be measured using the relation [11],

$$Poc = \frac{1}{\sigma_{op}}$$

Where, σ_{op} is optical conductivity. The variation of the log of optical resistivity with wavelength is shown in figure5 (a). The variation of optical resistivity with photon energy is shown figure5 (b). The low value of the optical resistivity at high photon energy suggests that the sample possesses enhanced optical quality with lesser defects and this parameter is of vital importance for NLO applications [12].

Electrical Conductivity

The value of electrical conductivity of a material is related with the optical conductivity value of the crystal using the following equation [13]

$\sigma_e = \frac{2\lambda\sigma_{op}}{\alpha}$

The electrical conductivity decreases with the increasing photon energy [14]. The variation of electrical conductivity with wavelength is shown in figure6 (a). The electrical conductivity as a function of photon energy (hυ) are shown in figure 6 (b).

Electrical Resistivity

The electrical resistivity of a material is equal to the reciprocal of its electrical conductivity. The electrical resistivity is calculated using the below relation [11],

$$Pec = \frac{1}{\sigma_e}$$

The variation of electrical resistivity with wavelength are shown in figure7 (a). Corresponding to the wavelength 500 nm electrical resistivity suddenly increases and drops down. This increasing optical resistivity region is suitable for NLO applications. The electrical resistivity as a function of photon energy (hυ) are shown in figure7 (b).

Electric Susceptibility

Susceptibility is the response of the medium to light [15]. Electric susceptibility (χ_c) can be calculated from the following relation [16, 17].

$\varepsilon_r = \varepsilon_0 + 4\pi\chi_c = \eta^2 - k^2$

$\chi_c = \eta^2 - k^2 - \varepsilon_0/4\pi$

ε_0 is the dielectric constant in the absence of any contribution from free carriers. The complex dielectric constant is given by ε_c. The real and imaginary part of dielectric constant from extinction coefficient are given as [17-19].

$\varepsilon_c = \varepsilon_r + \varepsilon_i$

$\varepsilon_r = n^2 - k^2$

$\varepsilon_i = 2nk$

Where $\varepsilon_r$and ε_i are real and imaginary part of dielectric constant. The electric susceptibility is calculated as χ_c = 0.1214. The real ε_r and imaginary ε_i values of dielectric constant are 1.5257 and 3.7391×10^{-6}.

Photoluminescence Analysis

The intrinsic behavior in the forbidden band region of the grown crystal is indicated by the luminescence phenomenon using Varian Corey Eclipse photoluminescence spectrophotometer. The photoluminescence excitation spectrum was recorded in the range of 300 nm to 600 nm. The excitation wavelength of 370 nm is as shown in figure 8. The emission spectrum reveals that the 2-aminothiazole crystal shows the presence of sharp intense peak at 370 nm (3.35eV) violet emission and a weak peak observed at 540 nm (2.29eV) green emission. The absence of visible emission bands has indicated that the high crystal quality and perfect crystallinity of the grown crystals [20,22]. This excitation spectrum indicates the emission of violet..The bandgap energy is calculated from the formula [21],

$$Eg = \frac{1240}{\lambda}$$

The calculated band gap energy is 3.26 eV.

Thermal Analysis

The thermal analysis provides the measure of the weight loss and the thermal stability of the grown crystal. TG-DTA analysis was carried out using SDT Q600, TA instruments in the temperature range of 30℃ – 320℃at the heating rate at 10℃ per minute in air atmosphere.. TG and DTA graph of 2-aminothiazole is shown in figure 9. TG curve reveals

the decomposition occurs in the temperature range between 170 ℃ and 600 ℃ with the mass change 89.24%. From DTA curve, the first and second endothermic peaks are observed at 65 ℃ and 165 ℃ reveals the melting point of the 2-aminothiazole single crystal. The sharpness endothermic peaks represent the melting point of the crystal [22,23].

Dielectric Analysis

The dielectric constant and dielectric loss was measured using Jognic's model 2816 B LCRZ meter. The experiment was carried out in the frequency range of 50 HZ to 200 KHZ. The high value of dielectric constant at low frequency may be due to the presence of all polarizations, namely space charge, orientation, electric and ionic polarizations [24]. The electrical energy is absorbed by the material and is dissipated in the form of heat. This dissipation of energy is called dielectric loss [25]. The figure 10 and 11 shows the variation of dielectric constant and dielectric loss in the range of frequency. It is clearly shows that the values of dielectric constant and dielectric loss decrease with increase in frequency. According to Miller rule, the dielectric constant and dielectric loss at higher frequency clearly shows that the material defect less and with good optical quality. So it is suitable for nonlinear optical applications [26-28].

CONCLUSION

Optically good quality single crystal of 2-aminothiazole single crystal was grown by slow evaporation method. UV-Visible absorption analysis reveals the electron transitions around wavelength 270 nm which confirms the formation of $n \rightarrow \Pi^*$ in grown crystal. From photoluminescence analysis violet excitation peaks observed at 380 nm for grown crystal. The grown crystal is thermally stable up to 170 ℃ which was confirmed by TG-DTA analysis. Dielectric analysis confirmed high optical quality and less defect concentration in the grown crystal.

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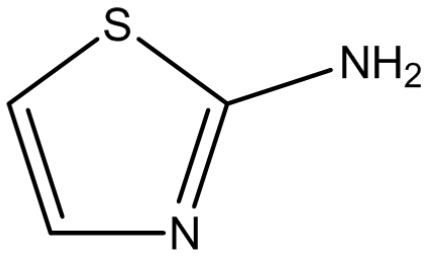

Figure 1 Chemical diagram of 2-aminothiazole

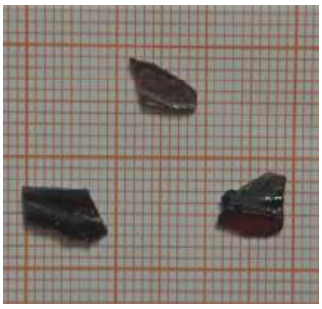

Figure 2 Crystals of 2-aminothiazole

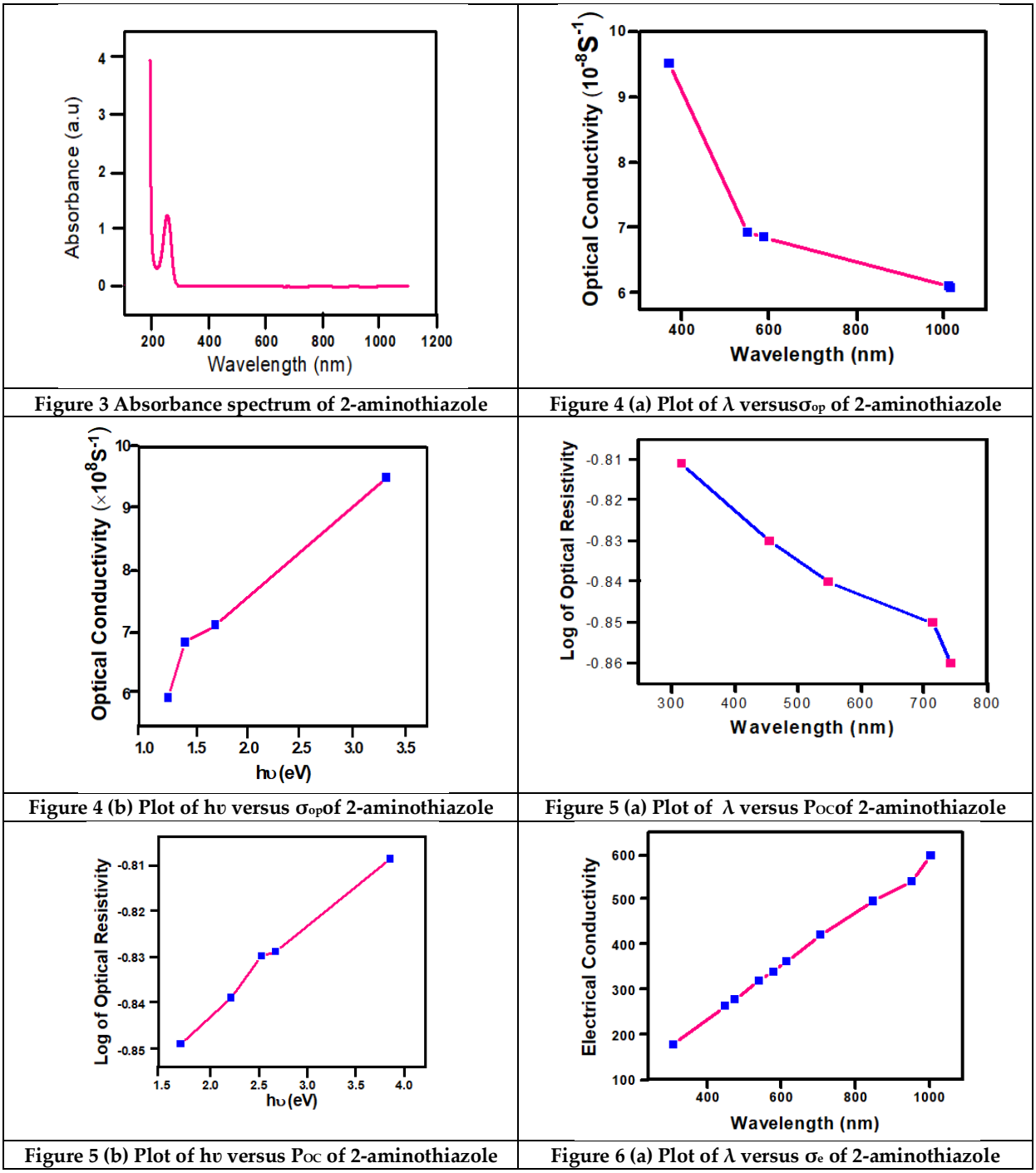

Figure 3 Absorbance spectrum of 2-aminothiazole

Figure 4 (a) Plot of λ versusσ_{op} of 2-aminothiazole

Figure 4 (b) Plot of hυ versus $\sigma_{op}$of 2-aminothiazole

Figure 5 (a) Plot of λ versus $P_{OC}$of 2-aminothiazole

Figure 5 (b) Plot of hυ versus P_{OC} of 2-aminothiazole

Figure 6 (a) Plot of λ versus σ_e of 2-aminothiazole

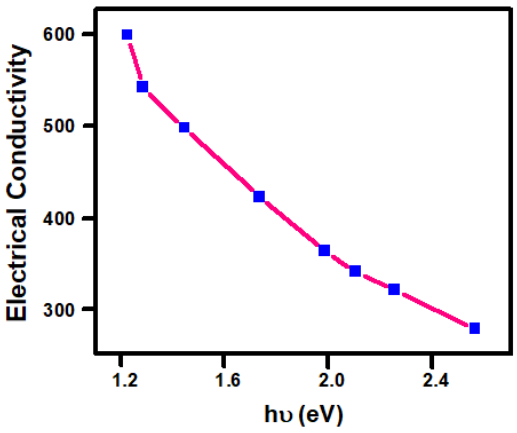

Figure 6 (b) Plot of hυ versus $\sigma_e$of 2-aminothiazole

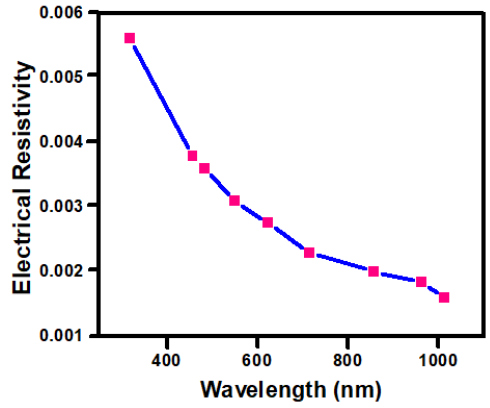

Figure 7 (a) plot of λ versus$P_{ec}$of 2-aminothiazole

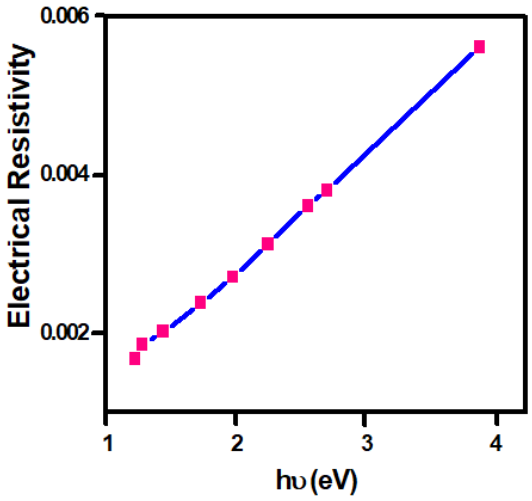

Figure 7 (b) Plot of hυ versus$P_{ec}$of 2-aminothiazole

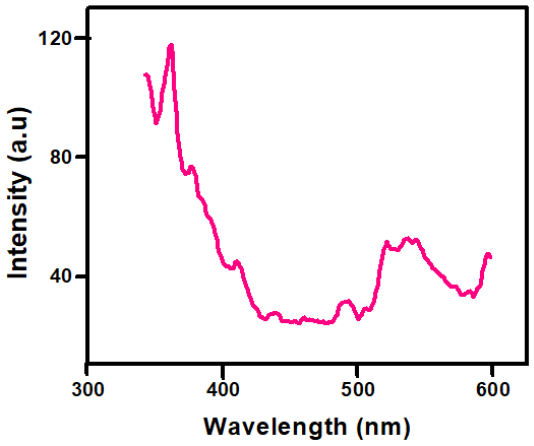

Figure 8 Excitation spectrum of 2-aminothiazole

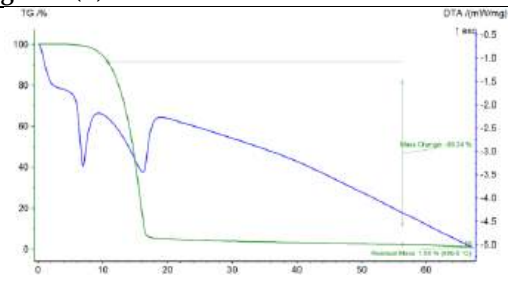

Figure 9 TGA-DTA graph of 2-aminothiazole

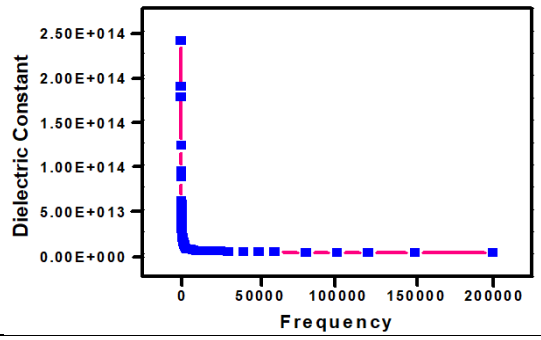

Figure 10 Frequency versus dielectric constant

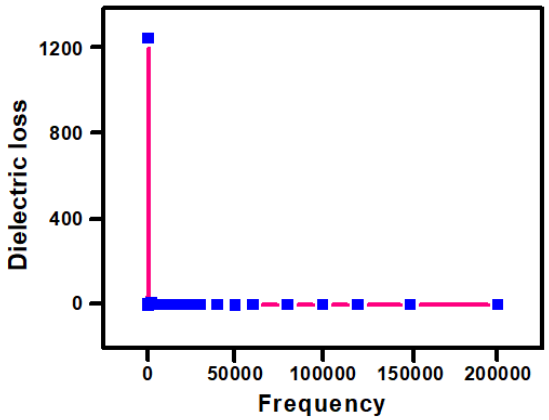

Figure 11 Frequency versus dielectric loss

RESEARCH ARTICLE

Economic Barriers to Green Product Consumption among Low - Income Households in Bengaluru's Sub-Urban Areas: A Survey - Based Quantitative Study

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Received: 12 Nov 2025 Revised: 20 Dec 2025 Accepted: 20 Jan 2026

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ABSTRACT

Environmentally friendly goods usually have a price premium associated as well as supplementary access costs that may limit adoption amongst economically disadvantaged consumers. The paper studies how affordability related barriers influence the consumption of green products among low-income families in sub-urban areas of Bengaluru. A cross sectional survey is suggested with a structured questionnaire to specifically capture perceived price premium, household budget constraints, access/transaction costs and perceived affordability as well as perceived fairness. The study illustrates (i) association testing which is the Chi-square test; (ii) strength and direction testing of association using Pearson correlation; and (iii) predictive influence testing of one or more explanatory variables findings through multiple regression. The model lends support to the claim of affordability and economic impediments as primary predictors of green product consumption in low income context.

Keywords: Green Products, Affordability, Price Premium, Low-Income Households, Survey, Chi-Square, Correlation, Regression.

INTRODUCTION

Sustainable consumption is now a mantra for environmental protection and production responsibility. Yet in most markets, green products are more expensive because they're made with eco-materials, certified or produced cleaner

or a company has to change its supply chain. This "green premium" can also be a prohibitive factor for cash-strapped households, who put value, low pricing and financial certainty above all. The literature indicates in fact that, when money is short and purchasing power limited, the willingness of consumers to buy green may only just be skin deep if at all. Experience from India and other developing settings suggests that perceived affordability, price sensitivity and access barriers affect whether consumers act on intended positive attitudes to purchase. In the suburbs i.e. outlying areas of Bengaluru, there is a high proportion of households under cost burden (Housing, Transport, Food and Utilities). In these situations, green consumption may be driven more by household economics (i.e., perceived price premium, budget constraints and additional access/transaction costs of time, travel and limited retail availability) than based on moral intention. There is meagre evidence of empirical research in the context of low income residents in sub-urban Bengaluru and hence an opportunity for a targeted quantitative research.

REVIEW OF LITERATURE

Price premium and willingness to pay for green products

A common issue in green consumption literature is the price premium associated with environmentally friendly products and its detrimental effect on purchase intention of low income consumers. Yadav & Pathak (2017) demonstrate that perceived behavioural control and intention significantly influence green purchasing behaviour in a developing country context, implying the feasibility aspect of being green when resources are scarce. In a related study, Prakash & Pathak (2017) report that the green purchase intention for eco-friendly packed goods is influenced by psychological and control determinants but in low involvement, price sensitive markets the capability to act factor still holds pertinence. Paul, Modi & Patel (2016) find in India that attitude and perceived behavioral control have significant predictive power for intention to be associated with behavior, thereby indicating that affordability limitations can attenuate the translation of intentions into behaviors.

Kirmani & Khan (2018) concentrate on India per se and 'explains' the willingness to pay a premium for green products, as underlined by consumer related evaluations of costs versus benefits. Biswas & Roy (2016) directly investigate willingness to pay for green products in the emerging-economy context and ensure that economic motives underlie premium payment behaviours. Hao et al. (2019) demonstrate that consumers' willingness to pay for green packaging is contingent on how the premium can be perceived and rationalized. Shi & Jiang (2023) also posit that willing to pay the premium price is influenced by reference group and awareness, hinting that social influence can be of importance – however affordability may still stand in the way.

Affordability constraints and the "attitude–behavior gap"

There is a large body of work on why positive environmental attitudes often do not result in green buying. Testa et al. (2021) critique the drivers of green consumption and argue that structural barriers, including economic-related ones are among the primary causes for divergence between concern and purchase. Sharma, Aswal & Paul (2023) provide a similar but more generalized aggregate picture and several recurrent determinants (attitude, norms, control, trust) as well as market/practical constraints constraining the actual buying. Patiño-Toro et al. (2024) additionally chart antecedents of green purchase intention/behavior and note that roadblocks vary by consumer segment and setting—encouraging localized research. Megha (2024) examines green consumption studies with the lens of literature synthesis and finds mixed results across socio-demographics—further supporting the evidence from particular segments like lower income households.

Nekmahmud & Fekete-Farkas (2020) expand the TPB in an emerging market and find that intentions and behavior depends on several factors, such as price perception, perceived benefit. Ogiemwonyi et al. (2023) also highlight that attitudes mediate this relationship but in terms of the effects of environmental factors suggest that barriers in particular can interfere with the link between attitude and purchase.

Willingness-to-pay evidence from meta-analysis and food/organic parallels

The evidence from sustainability/organics product categories is particularly relevant for green goods because the latter are also typically associated with premium prices. Li & Kallas (2021) aggregate evidence from around the world and verify that the size of consumers' willingness to pay premiums differs by product and attribute, but the premiums do exist and matter in all situations. Katt & Meixner, 2020) systematically review determinants of wtp for organic food and outline the ways in which perceived advantages and consumer values interplay with premium willingness. Smoluk-Sikorska et al. (2023) note, market price premiums can outstrip consumer willingness to pay resulting in a practical affordability gap. De Pelsmacker, Driesen & Rayp (2005) – which concentrated on fair-trade coffeeoffer their seminal evidence that ethical preferences do not necessarily translate into premium payments across all segments (and one which has direct bearing on the low-income constraint).

India / emerging market evidence on price sensitivity and availability

In India-related evidence, Srivastava & Gupta (2023) explicitly connect **price sensitivity** with green purchase intention and add that green product availability and interventions can shape buying outcomes—implying that affordability and access work together. Sun, Li & Wang (2022) show motivational framing ("for me" vs "for others") affects intention, but intention still interacts with economic feasibility in real purchase contexts. Kumar, Prakash & Kumar (2021) show that responsible purchase intention in an emerging market is influenced by consumer assessments of benefits and constraints, reinforcing the role of affordability-linked perceptions.

Research gap

Most studies either (i) examine general consumers, (ii) analyze intention rather than consumption, or (iii) treat economic barriers indirectly. A focused study on economic barriers among low-income households in Bengaluru's sub-urban areas can provide locally relevant evidence for marketers and policymakers.

Statement of the Problem

Green products are promoted as environmentally beneficial, yet adoption among low-income households remains limited. In Bengaluru's sub-urban areas, economic pressures may increase price sensitivity and reduce the feasibility of paying a green premium. Without local evidence, interventions may fail to address the real drivers of non-adoption. This study therefore investigates the economic barriers (price premium, budget constraints, access costs, affordability perceptions, and perceived value) influencing green product consumption among low-income households.

Objectives of the Study

i. To measure the level of green product consumption and key affordability-related perceptions among low-income households in Bengaluru's sub-urban areas.
ii. To test the association between household income categories and green product consumption using the Chi-square test.
iii. To examine the relationship and predictive influence of economic barriers on green product consumption using correlation and regression analysis.

Scope of the Study

The scope is limited to low-income households in selected sub-urban areas of Bengaluru. The study focuses on economic barriers (price premium perception, budget constraints, access/transaction costs, perceived affordability, and value for money) and their relationship with green product consumption behavior (purchase frequency/regularity).

Research Model and Hypotheses

Key variables

- **Dependent Variable (DV):** Green Product Consumption (frequency/regularity index)
- **Independent Variables (IVs):**
  - Perceived Price Premium (PPP)
  - Household Budget Constraint (HBC)
  - Access/Transaction Cost (ATC)
  - Perceived Affordability (PA)
  - Perceived Value for Money (VFM)
- **Control:** Income category

Hypotheses

Chi-square hypothesis

- $H0_1$: Income category and green product purchase status are independent.
- $H1_1$: Income category and green product purchase status are associated.

Correlation hypotheses (examples)

- $H0_2$: There is no significant relationship between perceived affordability and green product consumption.
- $H1_2$: Perceived affordability is significantly related to green product consumption. (Repeat similarly for PPP, HBC, ATC, VFM.)

Regression hypotheses

- $H0_3$: Economic barrier variables do not significantly predict green product consumption.
- $H1_3$: Economic barrier variables significantly predict green product consumption.

RESEARCH METHODOLOGY

Research design

Descriptive and explanatory, cross-sectional survey design (quantitative). The descriptive component profiles barriers; the explanatory component tests associations and predictions using inferential statistics.

Sampling technique

- **Stage 1 (Area selection):** Multi-stage sampling to select sub-urban wards/settlements of Bengaluru (e.g., peripheral/transition zones).
- **Stage 2 (Household selection):**Stratified sampling within selected localities using income categories that qualify as "low income" (defined operationally by your cut-off—monthly household income).

Sample size

n = 384 is commonly used for large urban populations with 95% confidence and 5% margin of error.

Sample unit and sample area

- **Sample unit:** Household decision-maker for routine purchases (grocery/household goods)
- **Sample area:** Selected sub-urban localities of Bengaluru (clearly list wards/areas in the final paper)

Data collection

- **Primary data:** Structured questionnaire (5-point Likert scale) administered through field survey or assisted interviews (recommended for low-income respondents).
- **Secondary data:** Prior studies and review papers for construct selection and tool justification.

Statistical tools used

1. **Chi-square test** – association between income group and purchase status
2. **Pearson correlation** – direction/strength between economic barrier variables and consumption
3. **Multiple linear regression** – predictive impact of economic barriers on consumption

Data Analysis and Interpretation (with hypothesis testing)

Descriptive Statistics

Interpretation: Economic pressure variables (price premium, budget constraint) are high on average, while perceived affordability and green consumption are relatively lowconsistent with affordability constraints limiting adoption in low-income households.

Chi-square test (Income × Purchase status)

$H0_1$: Income category and green product purchase status are independent.

$H1_1$: Income category and green product purchase status are associated.

Chi-square result: $\chi^2(2) = 26.15$, $p < 0.001$; Cramer's V = 0.261

Decision: Since $p < 0.05$, reject $H0_1$.

Interpretation: Purchase status differs significantly across income groups. As income rises within the "low-income" band, the share of green purchasers increases, supporting the argument that affordability constraints suppress adoption.

Correlation analysis (Pearson)

$H0_2$: No significant relationship exists between each economic barrier variable and green consumption.

$H1_2$: A significant relationship exists.

Decision: For each variable, $p < 0.05$ → **reject $H0_2$**.

Interpretation:

- Greater affordability and higher value-for-money perceptions are associated with greater green consumption.
- The perceived price premium is a significantly positively correlated factor for green consumption; the stronger budget restrictions and higher access costs are both negatively correlated.
- These findings are consistent with the economic barrier framing introduced in previous work on price premium and affordability limitations.

Multiple regression analysis (DV: Green Consumption)

$H0_3$: Economic barrier variables do not significantly predict green consumption.

$H1_3$: Economic barrier variables significantly predict green consumption.

Model summary: $R^2 = 0.431$, Adj. $R^2 = 0.422$, $F = 47.59$, $p < 0.001$

Decision: Since model $p < 0.05$, **reject $H0_3$**.

Interpretation: Economic factors are the most influential predictor of green product purchase. Perceived affordability is the most positive predictor, while perceived price premium is the most negative one. A budget constraint and cost of access also limit consumption. This corroborates the finding that economic viability (not just attitude) is a key determinant of green adoption among low-income households.

FINDINGS

i. The consumption of green products among low-income households appears to be restricted thereby revealing a significant price barrier.

ii. Income level is strongly associated with green purchase status (i.e., purchasing power divides even among low-income populations).

iii. Energy consumption features negative effects purely on perceived price premium, budget constraints and access costs to green; perceptions of affordability (good value for money) have positive effects purely on green.
iv. Regression results reveal that economic constraints collectively account for a significant portion of the variance in consumption, suggesting a policy and market design oriented to affordability.

Suggestions

i. Price interventions: Create low-unit packs, involve subsidies, or discount schemes in sub-urban retail.
ii. Low access cost: Deepen distribution through kirana stores, community outlets and last-mile delivery with low delivery fee.
iii. Value perception: stress "cost-saving in the long run" (endurance/health and safety) in order to enhance value-for-money perceptions.
iv. Micro-incentives: reward points/cashback for buying certified green products repeatedly.
v. Policy support: local awareness + price support programmes can be more effective than just awareness alone.

Limitations

i. Cross-sectional design cannot confirm causality.
ii. Self-reported measures may include recall and social desirability bias.
iii. Low-income classification depends on operational cut-off and may vary across localities.
iv. Product categories may differ in premium magnitude; results may vary by category (FMCG vs appliances).

CONCLUSION

Affordability is established as the predominant barrier to green product consumption by low-income households in Bengaluru sub-urban region. Evidence suggests that perceived price premium, household budget constraint and access/transaction costs are major hindrance to the consumption while affordability perception and value for money drive adoption. The findings contribute to the case that fostering green consumption in low-income markets calls for affordability-oriented, rather than attitudinal, intervention.

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Table 1: Descriptive statistics

Variable	Mean	SD
Perceived Affordability	2.99	0.71
Perceived Price Premium	3.85	0.59
Budget Constraint	3.93	0.56
Access Cost	3.39	0.69
Value for Money	3.57	0.71
Green Consumption (DV)	2.23	0.75

Table 2: Income category vs Purchase

Income category	No	Yes	Total	Yes %
≤15k	161	14	175	8.0
15k–25k	124	27	151	17.9
25k–35k	37	21	58	36.2

Table 3: Correlation with Green Consumption

Variable	r	p
Perceived Affordability	0.418	<0.001
Perceived Price Premium	-0.353	<0.001
Budget Constraint	-0.243	<0.001
Access Cost	-0.235	<0.001
Value for Money	0.245	<0.001

Table 4: Regression Coefficients

Predictor	B	SE	Beta (Std.)	t	p
Perceived Affordability	0.364	0.043	0.342	8.436	<0.001
Perceived Price Premium	-0.334	0.050	-0.263	-6.620	<0.001
Budget Constraint	-0.288	0.053	-0.216	-5.470	<0.001
Access Cost	-0.247	0.042	-0.229	-5.845	<0.001
Value for Money	0.166	0.043	0.157	3.898	<0.001
Income (control)	0.142	0.045	0.136	3.172	0.002

Indian Journal of Natural Sciences www.tnsroindia.org.in ©IJONS

Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Analysis of Similarity Reductions and Invariant solutions of DJKM Equation Arising in Nonlinear and Weakly Dispersive Inhomogeneous Media

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Received: 03 Nov 2025 Revised: 26 Nov 2025 Accepted: 31 Dec 2025

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ABSTRACT

In this research paper, the Date-Jimbo-Kashiwara-Miwa equation (DJKM) is solved analytically utilizing the similarity transformations approach via classical Lie-group theory. The similarity transformation method (STM) reduces the number of independent variables by one at each step. The STM is applied to Date-Jimbo-Kashiwara-Miwa equation and after successive application it reduces an ordinary differential equation. This can be solved further to get invariant solutions of the DJKM equation. This research has the potential to solve Date-Jimbo-Kashiwara-Miwa equation in a more general approach. Fluid mechanics, oceanography, optical fiber, fluid dynamics are all applications of the system.

Keywords: Lie symmetry analysis, Invariant solutions, Similarity transformation method and DJKM Equation.

INTRODUCTION

Nonlinear partial differential equations (NPDEs) are used to solid-state physics, plasma physics, applied physics, and applied mathematics, among other scientific areas. Quantum physics, electrodynamics, biology, fiber optics, chemical physics, and astrophysics are among the fields of physics that may be studied with NPDEs. We must obtain accurate solutions to the NPDE (Gabar and Wazwaz, 2024). The Date-Jimbo Kashiwara-Miwa (DJKM) equations are used to

build models in mathematical physics with weak nonlinear restoring forces and frequency dispersion with low surface tension and long wave lengths (Akram G.et.al., 2021).In integrable systems, the Jimbo-Kashiwara-Miwa (JKM) equation is a crucial nonlinear PDE that builds upon traditional models such as the KdV and KP equations. It was first proposed by Jimbo, Kashiwara, and Miwa in the 1980s and emerged from the research of soliton theory and isomonodromic deformations (Kumar, M. and Manju, K., 2022).The Lie group analysis, introduced by Mathematician Sophus Lie (Chauhan A.et.al., 2020), plays a powerful role in finding solutions to PDEs. Lie groups of transformation can be used in many methods of analyzing solutions PDEs. Dynamic mathematical and physical phenomena express exact solutions of partial differential equations (Bibi, K. and Khalil, A., 2021).

The DJKM equation has been extensively researched, and its solitary wave solutions have been reported in many different kinds of studies. Its two-dimensional dynamics are still not well understood, though. With applications to fusion and space plasma systems, this study focuses on obtaining invariant solutions to improve our knowledge of anisotropic environments and wave interactions in magnetized plasmas.

The DJKM is a $(2+1)$-dimensional nonlinear integrable PDE that describes multidimensional wave propagation. The Date-Jimbo Kashiwara-Miwa (DJKM) equation is a member of the Kadomtsev-Petviashvili(KP).Kadomtsev-Petviashvili (KP) equation is one of these whose base solution is of fundamental importance in equations and mathematical physics. In this present work, we explored the below-mentioned $(2+1)$-dimensional Date-Jimbo-Kashiwara-Miwa[1] (DJKM) equation

$$\frac{\partial^5\omega}{\partial x^4.\partial y}+4\frac{\partial^3\omega}{\partial x^2.\partial y}\frac{\partial\omega}{\partial x}+2\frac{\partial^3\omega}{\partial x^3}\frac{\partial\omega}{\partial y}+6\frac{\partial^2\omega}{\partial x.\partial y}\frac{\partial^2\omega}{\partial x^2}+\frac{\partial^3\omega}{\partial y^3}-2\frac{\partial^3\omega}{\partial x^2.\partial t}=0 \qquad (1)$$

The function$\omega(x,y,t)$ represent the wave amplitude which implies how the height of the wave changes in space with respect to the coordinates (x,y) and the time t.

A wide range of methods has been found to find invariant and exact solutions of non-linear partial differential equations like the generalized Generalized Kudryashov method (Gabar and Wazwaz, 2024), inverse scattering transformation, Backlund transformation (Adem, A.R.et.al.,2019),Hirota method, Darboux transformation, first integral method, homotopy asymptotic, (G/G) expansion method (Naher, H. and Abdullah, F.A., 2014), Painleve technique, Exp-function method (Bibi, K. and Khalil, A., 2021), Hereman-Nuseir method, ansatz method, sine Gordon expansion method (Akram G.et.al., 2021), the Riccati method (Iqbal, M.A.et.al.,2021), but the Lie symmetry method (Xu, P.et.al.2023)-(Tanwar, D.V. and Kumar, M., 2021) is very innovative and result-oriented approach for attaining the solutions of non-linear partial differential equations(NPDEs).

The authors also attempted to solve this form of DJKM analytically through the application of Lie symmetry (Qasim, M.et.al.2025) - (Kosmann-Schwarzbach, Y., 2010.), but the reduction could not be resolved further. It opens the entry for further research in this field. In the present work, using similarity variables obtained from the Lie similarity generator, the $(2+1)$-dimensional Date-Jimbo-Kashiwara-Miwa equation is transformed into a linear PDE, and subsequently, by using the similarity transformation method of this linear PDE, new exact solutions of the Date-Jimbo-Kashiwara-Miwa equation are obtained.

INFINITESIMALS VIA LIE-SYMMETRY ANALYSIS

In this section, infinitesimals of the DJKM are derived by using the one-parameter Lie group similarity transformations method (STM). Such transformations can be treated as:

$$\begin{aligned}
x^* &= x+\epsilon\xi_x+O(\epsilon^2),\\
y^* &= y+\epsilon\xi_y+O(\epsilon^2),\\
t^* &= t+\epsilon\tau+O(\epsilon^2),\\
\omega^* &= \omega+\epsilon\eta+O(\epsilon^2),
\end{aligned} \qquad (2)$$

where ξ_x, ξ_y, τ and $\eta$are known as infinitesimals (Olver, P.J., 1993)- (Bluman, G.W., 2010)which are in general the function of (x, y, t, w).since obtaining the infinitesimals ξ_x, ξ_y, τ and η in above transformationis not an easier work in view of handling the calculation manually, so author have obtained them by using symbolic program in maple.
Thus, authors get the infinitesimals ξ_x, ξ_y, τ and η as

$$\begin{aligned}
\xi_x &= \frac{x f_1'(t)}{4} + f_3'(t), \\
\xi_y &= \frac{y f_1'(t)}{2} + f_2(t), \\
\tau &= f_1(t), \\
\eta &= -\frac{xy f_1''(t)}{4} - \frac{f_1'(t)\omega}{4} - \frac{f_2'(t)x}{2} - y f_3'(t) + f_4(t),
\end{aligned} \tag{3}$$

SIMILARITY REDUCTIONS AND INVARIANT SOLUTIONS

Date-Jimbo-Kashiwara-Miwa equation(DJKM)

In order to derive analytical solutions for DJKM (1), Lagrange's characteristic equations are

$$\frac{dx}{\frac{x f_1'(t)}{4} + f_3'(t)} = \frac{dy}{\frac{y f_1'(t)}{2} + f_2(t)} = \frac{dt}{f_1(t)} = \frac{d\omega}{-\frac{xy f_1''(t)}{4} - \frac{f_1'(t)\omega}{4} - \frac{f_2'(t)x}{2} - y f_3'(t) + f_4(t)}, \tag{4}$$

Now, in order to proceed further, we considered the following cases:

Case (I): For

$$\begin{aligned}
&f_1(t) = a_1 t + a_2, \quad f_1'(t) = a_1, \quad f_1''(t) = 0, \\
&f_2(t) = a_3, \qquad\qquad\quad f_2'(t) = 0, \\
&f_3(t) = a_4, \qquad\qquad\quad f_3'(t) = 0,
\end{aligned}$$

are arbitrary constants, then similarity reduction of the Eq. (1) provides

$$\omega = \frac{1}{a_1 (t+a)^{\frac{1}{4}}} \int f_4 (t+A)^{-\frac{3}{4}} dt + \vartheta(X,Y)(t+A)^{-\frac{1}{4}}, \tag{5}$$

While$\vartheta(X,Y)$ are similarity functions of X and Y, which can be shown by

$$X = \frac{x-\alpha}{(t+A)^{1/4}}, Y = \frac{y-\beta}{(t+A)^{1/2}}, \tag{6}$$

Where$A = \frac{a_2}{a_1}, \alpha = -\frac{4a_4}{a_1}, \beta = -\frac{2a_3}{a_1}$ are arbitrary constants.

The similarity reduction of the DJKM Eq. (1) yields the following system:

$$2\vartheta_{XXXXY} + 8\vartheta_{XXY}\vartheta_X + 4\vartheta_{XXX}\vartheta_Y + 12\vartheta_{XY}\vartheta_{XX} + 2\vartheta_{YYY} + 3\vartheta_{XX} + X\vartheta_{XXX} + 2Y\vartheta_{XXY} = 0, \tag{7}$$

Case (II): For$b_1 = 0$, Eq. (7) provides:

$$\frac{dX}{b_2 + \frac{b_1 X}{2}} = \frac{dY}{b_3 + b_1 Y} = \frac{d\vartheta}{-\frac{b_3 X}{4} - \frac{b_2 Y}{4} - \frac{b_1 \vartheta}{2} - \frac{b_1 XY}{2} + b_4}, \tag{8}$$

On solving, one can have

$$Y_1 = b_3 X - b_2 Y \text{ and similarity functions } \vartheta = \frac{b_4 X}{b_2} - \frac{XY}{4} - \frac{\vartheta_1(Y_1)}{b_2}, \tag{9}$$

WhereY_1 is similarity variable and ϑ_1 is similarity function.

Thus, similarity reduction of DJKM (1) is given by the following ordinary differential equations (ODEs).

$$b_2 b_3^4 \vartheta_1^{'''''} + 4b_4 b_3^2 \vartheta_1^{'''} - 6b_3^3 \vartheta_1^{'''} \vartheta_1^{'} - 6b_3^3 \left(\vartheta_1^{''}\right)^2 + b_2^3 \vartheta_1^{'''} = 0, \quad (10)$$

Case (IIa):on solving Eq. (10), one can find

$$\vartheta_1 = AY_1 + B, \quad (11)$$

So, the solution of DJKM (1) is

$$\omega = \frac{a_2}{a_1}\left(\frac{b_3\left(x+\frac{4a_4}{a_1}\right)}{\left(t+\frac{a_2}{a_1}\right)^{1/4}} - \frac{b_2\left(y+\frac{2a_3}{a_1}\right)}{\left(t+\frac{a_2}{a_1}\right)^{1/2}}\right) + B, \quad (12)$$

Wherea_1, a_2, a_3, a_4, b_2 and b_3, B are arbitrary constants.

Case (IIb): On solving Eq. (10), one can find

$$\vartheta_1 = \frac{\frac{2}{3}(c_1 Y_1 + c_2)^{\frac{3}{2}}}{c_1} + c_3, \quad (13)$$

So, the solution of DJKM (1) is

$$\omega = \frac{\frac{2}{3}\left[\frac{c_1 b_3}{a_1\left(t+\frac{a_2}{a_1}\right)^{\frac{1}{4}}}\left(x+\frac{4a_4}{a_1}\right) - \frac{c_1 b_2}{\left(t+\frac{a_2}{a_1}\right)^{\frac{1}{2}}}\left(y+\frac{2a_3}{a_1}\right) + c_2\right]^{\frac{3}{2}}}{c_1} + c_3, \quad (14)$$

Where$a_1, a_2, a_3, a_4, b_2, b_3, c_1, c_2$ and c_3 are arbitrary constants.

ANALYSIS AND DISCUSSIONS

In this section, physical properties of the analytical solutions of the Date-Jimbo-Kashiwara-Miwa (1) is described.3-D Type profile of the solutions are explored. The main aim of this exercise is to look into what the answers are like based on how they are shown graphically. The animated behaviour of the solutions is dicovered using symbolic computations. With respect to variations in time and space, the wave amplitude function varies.Thus,as seen in Figures(1-2). The authorswere successful in capturing the dominating behaviour of an animation frame. The authors have given the constants suitable values, which reflect the dynamics of profiles since arbitrary constants are an vital part of analytical solutions.

Fig. 1: The wave amplitude shows 3-D type profile and helpful to suggest an offshore structure, which describes the fluid flow during $t = 5$. The arbitrary constants are taken as $a_1 = 8.256, a_2 = 3, a_3 = 4.1493, a_4 = 4, , b_2 = 6, b_3 = 7$and $B = 8$. The lump type profiles are extensively helpful in describing localized waves in the ocean, localized chemical waves and localized optical pulses that do not dissipate as they are are non-dispersive, localized in space and preserve the shape. This fact can help to draw significant conclusions for undestanding the physical nature of the invariant solutions obtained. Fig. 2: The wave nature shows asymptotic behaviour for and at time $t = 7$ treating $a_1 = 8.256, a_2 = 3, a_3 = 4.1493,\ a_4 = 4, b_2 = 6, b_3 = 7, c_1 = 3, c_2 = 4$ and $c_3 = 5$. As the space range for x and y expands, the wave amplitude function becomes 3-D type profile in nature.

CONCLUSIONS

We have used STM to generate similarity forms using Lie-group symmetry theory, which allows us to obtain invariant solutions to the $(2+1)$-dimensional DJKM. We succeeded in generating an explicit version of analytical answers after further solving these similarity forms. We have added to the given answers by using the MATLAB program to trace their animation profiles, taking appropriate values of arbitrary constants. The wave profiles are

found to be 3-D. The results of this study are novel for the DJKM, as far as the authors are aware. This approach eventually results in a scientific contribution that solves a physically difficult system, such as shallow water waves, and captures features like undular bores and dispersive shock waves. Hence the analytical results so obtained shows three-D behavior of the wave and multi solitons as well, which can be used to test accuracy, comparison and exploration of numerical algorithms in the field.

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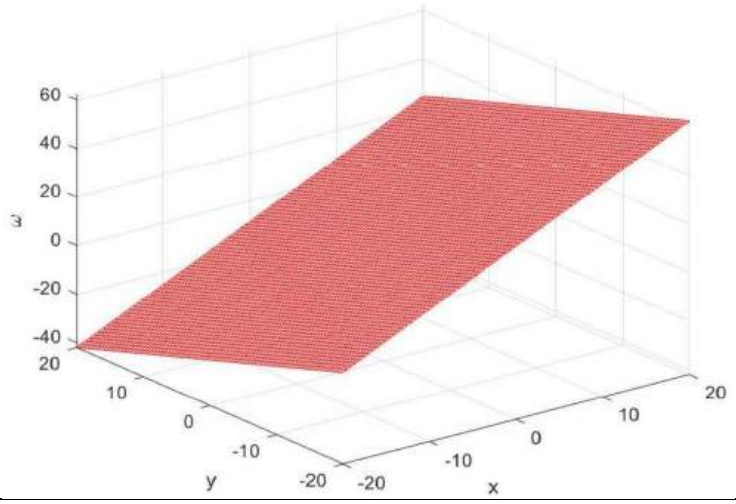

Fig.1. 3-D type profile of $\omega(x, y)$at $t = 5$.

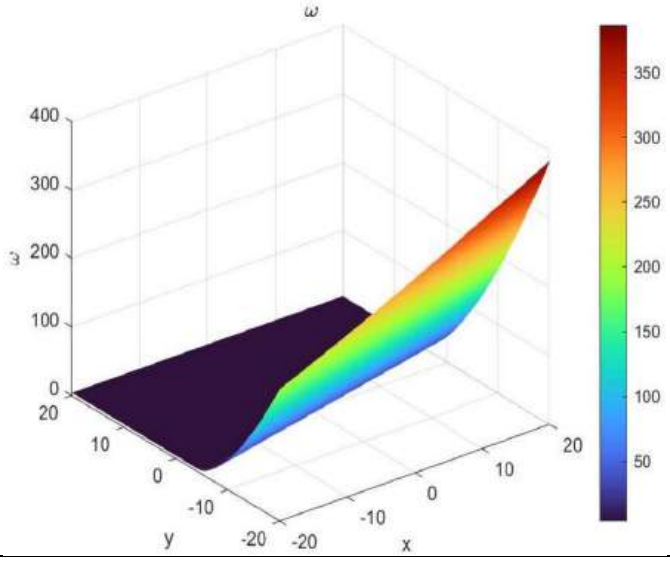

Fig. 2. 3-D type profile of ω(x,y)at t=7.

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

REVIEW ARTICLE

A Textual and Conceptual Review of Gunjadi Lepa with Special Reference to *Vaidya Vallabha*

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Received: 29 Dec 2025 Revised: 03 Jan 2026 Accepted: 20 Jan 2026

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ABSTRACT

Skin disorders are among the most prevalent and increasingly reported health conditions worldwide, often leading to psychological distress and reduced quality of life. In Ayurveda, most dermatological/Skin diseases are described under the broad spectrum of *Kuṣṭharoga*. Ayurvedic therapeutics include *Antarparimarjana* (internal purification) and *Bahirparimarjana* (external applications), among which *Lepakalpana*(external application of medicated paste)plays an important role. *Vaidya Vallabha*, authored by Hastiruchi, is an authoritative Ayurvedic text that elaborates several *Kuṣṭhaghnayogas*(Anti-skin disease property), including *Gunjadi lepa* . *Gunjadi lepa* 'sconceptual and literary review was conducted using relevant classical Ayurvedic texts and *Nighantus*. The ingredients of *Gunjadi lepa* were analysed with reference to their *Rasa, Guṇa, Virya, Vipaka,*and *Karma*. The review revealed that *Gunjadi lepa* is indicated for *Kuṣṭharoga* and contains ingredients with proven external therapeutic utility. After *Sodhana* (detoxification / purification) of Poisous / Toxic *(Visha-Upavisha) plant-based ingredients*, the formulation exhibits significant *Kaṇḍughna* (anti-pruritic), *Kuṣṭhahara* (property that alleviates skin diseases),*Krimighna*(anti-pruritic/antimicrobial), and *Tridoṣahara*(Balances all three *doṣas-Vata, Pitta* and *Kapha*). These actions suggest its efficacy in alleviating common symptoms such as itching, inflammation, infection, and skin lesions. *Gunjadi lepa* can be emerges as an effective external therapeutic formulation for the management of various skin disorders. Its pharmacological potential, derived from *Rasapancaka*-based actions, supports its rational use in *Kuṣṭharoga*(Skin disease). Further experimental and clinical studies are recommended to substantiate its therapeutic efficacy and safety.

Keywords: *Kuṣṭha, Skin diseases, Gunjadi lepa , Vaidya Vallabha, Abrusprecatorius*

INTRODUCTION

The skin, the largest organ of the integumentary system, serves as the body's primary protective barrier against external insults. In classical Ayurvedic literature, the majority of dermatological conditions are encompassed under the broad spectrum of *Kuṣṭharoga(skin disease)*, which is regarded by the *Acharyas* as a *Mahagada* due to its chronicity, complexity, and profound impact on physical and psychological health. Ayurveda describes a comprehensive range of therapeutic strategies for the management of various forms of *Kuṣṭharoga(skin disease)*, among which topical drug delivery occupies a prominent position owing to its rapid absorption and targeted therapeutic action. This mode of treatment is referred to as *Lepakalpana(*Medicated paste applied externally over the skin), a principal external therapeutic measure used in the management of skin disorders.

*Vaidya Vallabha*is a significant classical Ayurvedic text that has made notable contributions to *Kuṣṭhaghnayogas*. Among these formulations, *GunjadiLepa* is specifically indicated for *Kuṣṭharoga*(skin disease) [1].It is characterised by the inclusion of *Viṣa-Upaviṣadravyas(Poisonous/toxic drugs)* as major constituents. According to Ayurvedic principles, the selection of therapeutic substances is guided by factors such as *Roga(disease)*, *Rugṇa(patietnt)*, *Doṣa(*Functional principle of the body), *Vaya(Age)*, and *Hetu(Cause/* etiological factor*)*, thereby allowing any substance in nature to be utilised as medicine (*Auṣadha*) when judiciously applied. Consequently, substances categorised as toxic acquire therapeutic significance after appropriate proper *Sodhana(Detoxification/Purification)* procedures. From a therapeutic perspective, *Viṣa-Upaviṣadravyas*(Poisonous/toxic drugs)are valued for their rapid and potent pharmacological actions. This literary review substantiates that, based on its *Rasapanchaka*-mediated actions, *GunjadiLepa* represents an effective external therapeutic modality for the management of *Kuṣṭha(Skin disease)* and other dermatological disorders.

OBJECTIVES

- To evaluate *GunjadiLepa* described in *Vaidya Vallabha* for its role in the management of *Kuṣṭharoga*(Skin disease) by reviewing its classical references and composition.
- Analysing the *Rasapanchaka* of its ingredients and elucidating its probable Ayurvedic mode of action.

MATERIALS AND METHODS

This review article is based on sources including classical Ayurvedic literature (various *Saṃhitas* and *nighaṇṭus*), contemporary *dravyaguṇa*textbooks, and peer-reviewed scientific literature identified through internet databases such as PubMed and Google Scholar etc, as well as relevant publisher platforms.

OBSERVATIONS

Concept of *Lepa Kalpana*

The selected drugs are pounded to fine paste form and used for external application is called as*'Lepa* [2].

Types of *Lepa:*

According to *Acharya* Sharangdhara

1)*Doshghna*

2)*Vishghna*

3)*Varnya*

According to *Acharya* Shusruta

1) *Pralepa*

2) *Pradeha*

3) *Alepa*

Method of preparation of *Gujadi Lepa:* *Gunja* (*Abrusprecatorius*), *Bhallataka* (*Semecarpus anacardium*), and *Vatsanabha* (*Aconitum ferox*) are toxic in their raw form and must be administered only after appropriate *Sodhana*(detoxification/Purification) procedures. The medicine was administered in the form of *Lepa* for external application. After the *Shodhana*(detoxification/purification) process of each ingredient, the fine powders of all the drugs were mixed with *Takra*(buttermilk) to prepare the *Lepa*. All ingredients were combined in equal proportions to ensure uniform consistency.

Indication: Applied in all 18 types of *Kushtharoga*.(Skin disease)
Ingredients [3, 4, 5, 6]

Duration for *Lepa*: Lepa should neither be applied at night nor allowed to remain on the skin after it has dried [7].
Direction of *Lepa:* Lepa should be applied in *Pratiloma Gati* (against the direction of hair follicles) to enhance faster absorption and improve the therapeutic efficacy of the application [8].

Probable mode of action of *lepa:*
Lepadravyas (ingredients) penetrate the skin primarily through hair follicles and the pilosebaceous system, enabling active constituents to be absorbed into the capillary network and subsequently into systemic circulation. Gentle rubbing during application increases local skin temperature and cutaneous blood flow, thereby enhancing drug permeation and uptake at the site of application. This process facilitates therapeutic actions such as*doṣha* pacification, reduction of inflammation, and promotion of local healing responses. The exfoliative friction produced during *Lepa* application further elevates skin temperature, which may accelerate pilosebaceous uptake and transdermal permeation of the topical formulation[9].

For effective absorption, *Lepadravyas* traverse the skin via the epidermis, sweat glands, or hair follicles. Although sweat glands and hair follicles together constitute only approximately 0.1–1.0% of the total skin surface area and provide potential entry routes for chemical substances, the predominant pathway of absorption remains trans-epidermal. The active constituents must cross the epidermal layers to reach the dermis, from where they may enter the blood or lymphatic circulation and disseminate systemically. The stratum corneum, being the outermost epidermal layer, serves as the principal rate-limiting barrier to percutaneous absorption. Once the active principles penetrate the stratum corneum and reach the viable epidermis and dermis, pharmacological activity can ensue. *Lepadravyas* may exert their characteristic therapeutic effects locally by interacting with tissue receptors even before systemic removal via blood or lymphatic circulation. Thus, *Lepa* application supports the early neutralisation or elimination of toxins at the initial stage itself.

DISCUSSION

The skin, a dynamic organ with numerous functions, plays an important role in maintaining the bodies hemodynamic. As the body's largest organ, it serves as a protective barrier against harmful chemicals, microbes, and ultraviolet radiation. *Lepas* are helpful in preventing and curative purposes of any skin problem. *Lepakalpana* is given prime importance in management of *Kushtha* (skin disease).*Lepa* facilitates the quicker absorption of thedrugs through Romakupa (Hair roots), *Swedavahini* (sweat glands) and *Siramukha*(blood capillaries).When medication is administered in the form of *Lepa* or *Pradeha*, tiny particles of the substance permeate the *Twaka* (skin) due to gravitational pull and the weight of the drug.The *Upashoshana*(Absorbent) property of *Vayu*, particularly *Vyana* and *Samana*, significantly influences the penetration and absorption of medicaments applied over the *Twak*(Skin). The drugs would act upon the body, pertaining to its *virya*(active principle) and in some cases according to its *Prabhava*(Specific action).Most of the ingredients of *Gunjadilepa* are from *Visha-Upavisha*(Poisonous/toxic) category.*Gunja* (*Abrusprecatorius*), *Bhallataka*(*Semecarpus anacardium*), and *Vatsanabha* (*Aconitum ferox*) should be used only after proper *Sodhana* (detoxification) procedures.*Shodhana*(detoxification/purification) process reduces the toxic contents of *Visha-UpavishaDravyas*(Poisnous/toxic ingredients) and enhances the Therapeutic action of it.*Gunja*

(AbrusPrecatorious) Pacifying *Kapha*, drying excess moisture, and reducing local inflammation.*Gunja (AbrusPrecatorious)*alsoexhibits antimicrobial activity, which contributes to its therapeutic effect on skin infections.Action of *Bhallataka(Semecarpus anacardium)* helps in alteration of blood circulation over the site and there is vasodilation in local capillary plexuses.The action of *Vatsanabha(Aconitum ferox)* does the *Pachana* of *Sthanika Dosha.Vranaghna*(healing property). *Krimighna*(anti-helminthic)property of *Nimba(Azadirachta indica)*helps in healing the process of *Kustha*(Skin diseases)Through properties of being bitter (*Tikta)* in taste, light (*laghu*), dry (*Ruksha*), and sharp (*Teekshna*) in quality, along with its hot potency (*UshnaVeerya*) of *Vatsanabh(Aconitum ferox),Bhallatak(Semecarpus anacardium)*and *Gunja(Abrusprecatorius)* ,this substance functions as a *SrotoShodhaka*(Channel-cleansing) and pacifier of *Kapha*and *Vata.*By its *SrotoShodhaka*(Channel-cleansing) action it eliminates the *Sanga* (obstruction) at the level of *Raktadhatvagni* and acts on *sthanik pitta*. *Takra* has *Pancha-Rasa* except *Lavana Rasa*, *Amla Vipaka, Ushna Virya,* &*Vata Kaphaghna* property. *Takra* (Buttermilk) contains large amount of lactic acid.Lactic acid is a good for vehicle trance-dermal absorption of drugs.The efficacy of lactic acid-containing products is linked to their ability to deliver it to specific skin strata. By this pharmacodynamics of overall Synergetic action of *GunjadiLepa* helps in deliver the normalcy of Skin disease condition by its action on *sthanik dosha* and help to improve signs and symptoms of the skin diseases.

CONCLUSION

This study concludes that the ingredients of *Gunjadilepa* from *Vaidyavallabh* text possess pharmacological and therapeutic potential. Hence, we can say that the after *sodhana*(Detoxification/Purification) probable action of *Visha-upavishadravyas*(poisonous/toxic ingredients)and other herbal ingredients over the *Kusththa(Skin diasease)*is inferenced on the basis of various literary review. There is a huge scope of research as a drug discovery and development in the context of *Lepa* formulations which contain *Visha-upavishadravyas*(poisonous/toxic ingredients).For day-to-dayAyurvedic practice usage of this formulation is possible only if it is properly purified, and experimented.Additionally, further research is necessary for the analytical and clinical evaluation of this *Gunjadilepa.*

Author Contribution:
Author 1: Review of literature, writing review and editing Manuscript preparation, Data acquisition and analysis.
Author 2 and 3: Conceptualization, Methodology/Study design, Manuscript editing, Grammar and Spelling check,

Acknowledgement: Nil
Validation Data availability statement: Not applicable.

Financial support and sponsorship - Nil.

Conflicts of interest- There are no conflicts of interest

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Table 1. Method of preparation

Sr No.	Drug	*Rasa*	*Guna*	*Virya*	*Vipaka*	*Karma*	Indication
1.	*Gunja(Abrusprecatorius)*	*Tikta, kasaya*	*Laghu,Ruksa*	*Ushna*	*Katu*	*Kaphavatahara*	*Indralupta, Kustha, Kandu,Krimi*
2.	*Bhallatak(Semecarpus anacardium)*	*KashayaMadhur*	*Laghu*	*Ushna*	-	*Kaphavatahara,*	*Kustha,udar, aanah, arsh, grahani, gulma ,jwara, Svitra, Agnimandya, Krumi, Vrana*
3.	*Vatsanabh (Aconitum ferox)*	*Madhura*	*Laghu, Ruksha, Teekshna, VyavayiVikasi.*	*Usna*	*Katu*	*Vatakaphahara,Jvaraghna,Janghama Visahara, Madakari, Kusthaghna*	*Jvara, Jaghama visa, Kustha, Madhumeha, Sotha, Plihodhara , Agnimandya.*
4.	*Nimba (Azadirachta indica)*	*Tikta, Kashaya*	*Laghu, Ruksha*	*Sheeta*	*Katu*	*Kapha-Pittahara Deepana, Grahi, Krimighna,Netrya, Madhumehaghna*	*Jwara, Kustha, Krimi, Prameha, Vrana, Kasa, Chardi, Visa roga, Arsa, Gulma, Kandu, Netra roga.*

Indian Journal of Natural Sciences *www.tnsroindia.org.in ©IJONS*

Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Employee Training and Development Outcomes : Evidence from the Banking Industry

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Received: 30 Nov 2025 Revised: 24 Dec 2025 Accepted: 18 Jan 2026

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ABSTRACT

The employee Training and Development function performs a vital role for enhancement of workforce competence and also organizational effectiveness. This is especially true concerning the highly regulated and service-oriented environment which exists within Public Sector Banks. This present study examines the influence of certain selected demographic variables and other key factors upon employees' perceptions. The primary data was gathered by use of sample size of 200 bank employees in form of a structured questionnaire tool. To analyze the data several statistical tools were used including the percentage analysis and Chi-square test and ANOVA and mean ranking and Friedman test. The discovery from the findings is showing that age does not influence the employees' perceived level of impact to the training and development. This result is not statistically significant. Standing apart from this fact, the level of experience and the level of income of the employee significantly affect the employees' perceptions. This demonstrates that professional maturity and the financial status of employee possess important role in the shaping of attitudes toward the training initiatives. The study strongly highlights the importance of emphasizing the motivational and leadership-oriented training strategies, alongside the skill-based programs for implementation in Public Sector Banks. This will ultimately enhance performance and also quality of the service provided by institution. The significant Friedman test result supports the ranking, indicating that factors such as employee motivation and attitude, leadership and developmental training, and soft skills training are perceived as more influential than technical and functional training and digital and technological training. This suggests that

organizations should prioritize motivational and leadership-related aspects alongside skill-based training to enhance the effectiveness of employee training and development programs.

Keywords: Employee training, Technical and Functional Training, Soft Skills and Customer Service Training employee development, service quality and human resource management

INTRODUCTION

With more products and services becoming standardized in the banking industry, the quality of service has been a major differentiating factor among banks who are interested in retaining their customers and ensuring long term relationships. In an increasingly competitive and technology-driven financial landscape, banks are under constant pressure to deliver superior service quality while maintaining operational efficiency and regulatory compliance. Employee training and development (T and D) has emerged as a critical human resource management (HRM) strategy for enhancing service quality performance in the banking industry. The quality of services provided in the banking industry is mostly done through personal interactions between the customer and the employees. The service quality performance therefore depends on the knowledge, skills, attitudes and behavior of the bank employees. Development and training of the employees is then given strategic value as a tool of preparing employees with the skills needed to provide quality and consistent service. Employee training is a process where efforts are planned to improve the work-related skills and knowledge of the employees whereas employee development is a long-term process, career advancement and development of capabilities.

REVIEW OF LITERATURE AND RESEARCH AGENDA

Pravinaa and Arunprakash (2024) ruminated on the significance of formal training programmes on skills improvement, employee motivation and job satisfaction. The research is carried out by adopting a descriptive research approach which makes use of a sample of the employees of the branches of the different branches to study the various dimensions in the form of frequency of training, relevancy, and method of training delivery and the result of the training. The employees consider training as an important factor that stimulates job interpretation and performance improvement, as the results suggest. Most of the respondents have been appreciative of the initiative taken by the bank to constantly implement learning programs particularly in customer services, adoption of digital banking and compliance. Narayanan and Chandrasekaran (2023) discussed customer involvement on green banking practices among the customers of the banking industry both public and private in India and in particular the internet banking as one of the components of green banking. The paper demonstrates that the reliance of digital platforms can be used to reduce the environmental effects of the activities of the banking environment through the use of less article, reduced trips to the branches, and energy. The authors base on the findings of surveys of the customers of the banks to discuss the trends in terms of the adoption of internet banking, the level of satisfaction of the users, perceptions of the convenient use, and the awareness of the benefits of green banking. Following the results, it can be concluded that customer of banks in the private sector will be more active in the usage of the digital channels because the user interface is more defined, because the awareness campaigns are conducted, and the customer care is sensitive.

CONCEPTUAL BACKGROUND

Employee Training and Development

Training is normally short term and job oriented and is aimed at the short term performance gains, whereas development is long term and it orientates the employees towards future roles and responsibilities. The two of them improve human capital, organizational learning, and adaptability. As a regulatory sector, compliance and risk-related training is another very important aspect of employee development.

Banking Performance in terms of Service Quality

Good performance in terms of high service quality in banks translates to higher customer satisfaction, customer trust, customer loyalty and positive word-of-mouth whereas poor performance in terms of low service quality in banks translates to customer switching, damaged reputation, and the loss of money. Employee performance is key in determination of customer experiences as services are intangible and are produced and consumed at the same time. Figure: 1.

Dimensions of Employee Training and Development in Banking

Technical and Functional Training: Technical and functional training is aimed at the development of the job specific and operation related knowledge and skills needed by the employees. This kind of training is applicable in banking industry in areas like core operations of the bank and the financial analysis, risk management, regulatory compliance, credit appraisal, and accounting systems. The effectiveness of such training is that the employees are equipped with technical skills required to execute their duties correctly and effectively with minimum errors and operational risks. Since banking processes and regulations constantly vary, regular technical training is used to ensure that employees remain informed of the industry standards as well as the policies set by the institutions. Additionally, functional training enhances problem solving skills and decision making attitude of employees, thereby making them capable of dealing with complex transactions and customer demands with a lot of confidence. Through the reinforcement of technical competence, banks will be able to increase their productivity, compliance breaches, and quality of services. In general, the technical and functional training is a base of employee performance and organization activities as it matches the personal abilities with the organizational needs.

Customer Service Training: Active listening, conflict resolution, empathy, teamwork and professionalism skills are of paramount importance in the banking industry, because employees interact on a regular basis with customers. Such training also provides the employees with skills to deal with the falling expectations of customers, addressing complaints effectively, as well as establishing long-term relationships. Good soft skills increase customer satisfaction and loyalty, as well as improve the service quality. Besides, customer service training introduces a culture of customer focus, where employees are motivated to learn the needs of various customers and provide personal services. Good communication and problem-solving skills also decrease delays in service and miscommunication. With the increasingly high competition between banks, high quality customer service is a major distinction factor. Thus, the costs spent on training soft skills also lead to better employee performance and better organizational reputation as well as sustainable competitive advantage.

Digital and Technological Training: The digital and technological training is concerned with the building of the competencies of the employees in the application of the modern banking technologies and digital platforms. As the banking sector is quickly digitalizing, workers should be familiar with all the essential banking software, mobile and internet banking technology, fintech tools, cybersecurity protocols, and data analytics. Such training will allow the employees to embrace the change in technology and provide efficient technology driven services. Digital training improves the efficiency of operations through minimizing manual error, time to execute transactions and cost of the services. It also enables employees to assist customers in accessing digital banking avenues hence enhancing customer experience and adoption of digital services. Additionally, technological training builds confidence in employees and eases the change initiative in digital transitions. With the growing use of automation and digital innovation in banks, the ongoing technological training is necessary to be able to maintain competitiveness, guarantee the safety of data, and deliver better performance results both at the individual and organizational levels.

Developmental Training and Leadership: The developmental training on leadership is meant to increase the management, strategic, and decision-making skills of the employees. This training is specifically relevant in the banking sector when it comes to grooming future leaders that are capable of managing teams, filling performance, and handling organizational challenges. Some of the leadership skills that have been trained include communication, motivation, conflict management, change management and ethical leadership. The developmental training also promotes the career of the employees through self awareness, adaptability and problem solving skills. Effective

leadership has positive effect on employee engagement, job satisfaction and commitment. Good leaders create a positive working atmosphere, promote innovation and coordinate the efforts of employees with corporate objectives. Moreover, leadership training guarantees success planning and sustainability of the organization in the long run. Investment in leadership and development training can help a bank to develop a talent pool of leadership, increase employee performance and effectiveness of the organization.

RESEARCH GAP

Even though employee training and development has been a common research topic, little empirical research has been dedicated to it in the context of Public Sector Banks, especially in India. Current literature mostly focuses on the organizations of the private sector, or analyzes training performance without taking important demographic factors into account, namely, age, experience, and income at the same time. In addition, a lack of research exists in which the factors affecting training and development are ranked based on non-parametric statistical tools. This is because there is a gap in the research where there is no integrated analysis of demographic factors and prioritization of factors.

Importance

The research is also important because it offers relevant information of practices in Public Sector Banks which are important in the national banking system. Knowing how the employees feel about the training programs will enable the bank management to come up with more development strategies that are effective and inclusive. The results can help internal policymakers and HR managers to concentrate on the main factors that can boost the effectiveness of training including motivation and leadership. Literature by providing empirical data in the field of the public banking industry and the enhancement of the quality of the provided services, the performance of the working staff, and the efficiency of the organization.

Statement of the Problem

The success of these programs however, is greatly related to the perception and response of the employees towards them. The difference in demographics like age, experience, and income can affect the perceptions of employees to the outcomes of the training. Although training initiatives are important, little empirical evidence exists in measuring these differences in Public Sector Banks. Thus, the research question considered in the current article is to investigate the attitude of the employees towards training and development.

OBJECTIVES OF THE STUDY

1. To investigate the relationship between age and the impact of training and development.
2. To explore the influence of the level of experience on the perception of training and development on employees.
3. To assess the impact of income level on the perception of the employees concerning training and development.
4. To identifying and ranking relevant variables impacting the training and development of Employees of Public Sector Banks.

RESEARCH METHODOLOGY

The research design is descriptive in that it will be used to study the views of the employees regarding training and development programs in Public Sector Banks. The study involved the use of primary and secondary data. Data collection was done using a structured questionnaire that was used to collect primary data which was collected by sending the questionnaire to the bank employees, and secondary data collection was done by reference to available books, journals, reports, and credible websites. The research was conducted on the employees of Public Sector Banks and 200 respondents were selected through convenience sampling technique based on their accessibility and interest to participate in the research. To have meaningful information, the data collected was analyzed through different statistical methods such as the analysis of percent, Chi-square test, ANOVA, and Friedman test.

ANALYSIS, FINDINGS AND RESULTS

Age and Level of impact on employee training

(T and D) is a very important human resource process that increases the skills; knowledge and competency of employees hence increase the performance at the organizational level and performance of the individual. The effectiveness of training as perceived by the employees can be different according to various demographics factors, age being one of them. The age has its effect on the learning orientation, ability to adapt to new skills, the level of career stage priority, and desire to pursue professional development. Training can be perceived as a career-growth opportunity to younger employees, whereas middle-aged employees can be interested in improving their skills and having job security. The aged employees might have a different view of training because of the experience, the practice that they are familiar with, or the age factor since they are almost retiring. Therefore, investigating the correlation between age and the degree of influence of training and development is crucial towards the development of inclusive and effective training program.

Null Hypothesis: Age does not significantly influence employees' perceived level of impact of training and development.

Age and Level of Impact (Table 1)

The above table illustrates the percentage distribution of employees, their age groups, and perceptions about the level of impact they feel about Training and Development. When considering employees below 30 years of age, the largest percentage (46.7%) cited the medium level of impact, while 29.6% cited high impact, and 23.7% cited low impact respectively. It could be interpreted that employees feel the medium and high impact at their age groups. For the 30-45 years age category, 41.3% of workers perceived a moderate level of influence, 30.4% perceived a high level, and 28.3% perceived a low level. The data shows a fairly equal perception, although the most significant portion still falls under the category of moderate influence. Regarding the frequency of training impact among employees who are above 45 years, all respondents (100%) indicated a high impact of training and development activities. This finding may have a restricted meaning due to a small number of respondents in this particular criterion. Therefore, based on the overall data, it is revealed that 45.0% of the employees have experienced a moderate impact, 30.5% a high impact, and 24.5% a low impact of training and development. The diverse results obtained indicate that the impact of training and development is perceived to vary according to ages. (Figure: 2).

Age and Level of Impact (Table 2)

The Chi-square test of independence was used to establish the relationship between age and the impact level of employee training and development. The implications denote a Chi-square (χ^2) statistic with a value of 2.006 with 4 degrees of freedom, and the associated probability or significance value, $p = 0.869$, is greater than the conventional level of 0.05.Since the p-value is greater than 0.05, the result is not statistically significant. This means there is no association between age and the level of impact of training and development among employees. The Contingency Coefficient CC=0.075) supports the finding in that it indicates a very weak relationship between the two variables.

Level of Experience

The perceptions of employees are critical towards gauging the success of organizational practices and policies. The level of work experience is one of the most important issues that can form perception. Experience influences the knowledge of employees on the processes, expectations and outcomes of the organization and this impacts the perception and evaluation of work initiatives by employees. The experienced employees can have different perceptions depending on their exposure, tasks and professional maturity. As such, the study of whether the degree of experience has any implications on the perception of employees is significant to companies that desire to achieve the aspect of uniformity and justice when it comes to practicing human resource practices..

Level of Experience and Perception (Table 3)

The table presents the results of an analysis examining the differences in employees' perception across varying levels of experience using ANOVA. Employees with less experience recorded a mean perception score of 21.8250, while those with moderate experience reported a slightly higher mean score of 21.9412. Employees with more experience had a mean perception score of 21.8784. The mean values across all experience groups are relatively close, indicating minimal variation in perception levels. This indicates that there is a statistically significant difference in employees' perception based on their level of experience. Although the differences in mean scores appear small, the statistical result suggests that experience level does influence employees' perception. Therefore, it can be concluded that employees' perceptions vary significantly according to their level of experience.

Level of Income and Perception

Socioeconomic variable that may have influence on the perceptions those employees can have towards their workplace and organization is the income level. Income disparities tend to speak of differences in job roles, duties, rewards, and access to organizational resources and all these factors might have impacts on how employees will assess workplace policies and experiences. The employees with varying income levels might have different perceptions because of the differences in financial security, motivation and expectations by the organization. Thus, it is necessary to study the correlation between income level and the perception of employees to determine whether there is a uniform perception of the organizational practices between the various income groups.

Level of Income and Perception (Table 4)

Table 4 presents the outcomes of ANOVA test that determines the differences in perception of employees in different income levels. The employees with low-income group have a mean of 21.0476, and the employees with the middle-income group had a higher mean of 21.9778. The highest mean perception score was 22.3134 by the employees who belong to the high-income group. This shows that the scores of perception are on the increase as the income level increases. This validates the fact that the variations between the group differences in perceptions are statistically significant in relation to the differences in income. The higher the income level of the employee, the more positive perceptions are likely to be reported than those in the low income category.

Factors Influncing Employee Training and Development (Table 5)

The factors that had an impact on employee training and development are shown in the table as per the mean scores, standard deviation, mean rank and overall rank. The comparison shows that there are significant changes in the relative significance of the factors in the view of employees. Employee Motivation and Attitude were the strongest factor with the first rank in terms of means score (3.78) and mean rank (3.86). This implies on the readiness of employees to learn, good attitude, and intrinsic motivation. The second one was Leadership and Developmental Training, in which the mean score was 3.67, and the mean rank was 3.14. This is a sign that leadership support, managerial guidance, and developmental programs play a great role in improving the effect of training activities. The third rank was given to Soft Skills and Customer Service Training where it secured 3.64. This emphasizes the significance of communication skills, as well as interpersonal and customer handling skills in the development of employees. The fourth rank came to Digital and Technological Training with a score of 3.60. Although it is still viewed as important, it is viewed as a little more impactful as motivation, leadership, and training on soft skills. The fifth rank was attributed to Technical and Functional Training ranking at 3.31 with the lowest mean (2.91) as well. It is also deemed as relatively insignificant when compared to other factors of developmental importance even though it is crucial in the workplace. According to the results, behavioral and psychological conditions, including motivation of employees and their support by the leaders, make a stronger impact on the employee training and development than the strictly technical ones. Organizations need to therefore pay not just attention to training based on skill levels but also on motivation, positive attitudes and leadership based development to ensure that the training is as effective. (Figure: 3).

Friedman Test (Table 6)

The Friedman test was applied to determine whether significant differences exist among the factors affecting employee training and development, based on a sample of 200 respondents. The analysis produced a Chi-square value of 11.009 with 4 degrees of freedom, and the associated asymptotic significance value ($p = 0.007$) is below the standard 0.05 threshold, indicating statistical significance. Consequently, the null hypothesis, which posited that there are no significant differences among the factors influencing employee training and development, is rejected. The results suggest that employees assign varying levels of importance to the different factors.

DISCUSSION

The large Friedman test value confirm the ranking obtained in the previous table, where employee motivation and attitude, leadership and developmental training, as well as soft skills training, are viewed as more influential than the technical and functional training, and the digital and technological training. This implies that organizations are supposed to focus on motivational and leadership-related issues and in addition to skill-based training to maximize employee training and development programs.

CONCLUSION

The current article discussed employee training and development practice among Public Sector Banks considering the actual perception of workers, the demographic factors and the important variables that influence the training success. It has been found out that training and development is significant in promoting competence and the performance of employees and the organisation. Nonetheless, the degree of experience and the degree of income proved to be influential factors in the perception of employees, and it is important to note that professional maturity and an economic position can significantly impact the attitudes towards training programs. The research also established and ordered the factors that affect training and development of employees. Motivation and attitude of employees was found to be the most significant factor, then leadership and developmental training and soft skills training. The role of technical and functional training and digital and technological training was viewed as comparatively less important though they are necessary. The Friedman test proved that there were significant differences between these factors and this supported the fact that there should be a balanced approach in training design. In general, the results highlight that Public Sector Banks must leave behind the old-fashioned nature of skill-based training and implement a holistic strategy that would incorporate motivation, leadership support, and employee-focused developmental strategies. This would help to increase the effectiveness of training, increase the performance of employees, and help increase the level of service delivery and organizational sustainability in Public Sector Banks.

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Table 1: Age and Level of Impact

Age	Impact			Total
	Less	Moderate	High	
Below 30	36	71	45	152
	23.7%	46.7%	29.6%	100.0%
30-45 years	13	19	14	46
	28.3%	41.3%	30.4%	100.0%
More than 45 Years	0	0	2	2
	0.0%	0.0%	100.0%	100.0%
Total	49	90	61	200
	24.5%	45.0%	30.5%	100.0%

Table 2: Age and Level of Impact

Test	χ^2	df	CC	Sig.
Result	2.006	4	0.075	0.869

Table 3: Level of Experience and Perception

Experience	No. of Respondents	Mean	Std. Dev	F	Sig.
Less	40	21.8250	3.10407	11.051	0.01
Moderate	86	21.9412	3.79019		
More	74	21.8784	3.40810		
Total	200	21.8945	3.50381		

Table 4: Level of Income and Perception

Income	N	Mean	Std. Dev	F	Sig.
Low	42	21.0476	2.97922	5.962	.004
Middle	90	21.9778	3.73859		
High	68	22.3134	3.43868		
Total	200	21.8945	3.50381		

Table 5: Factors Influncing Employee Training and Development

Factors	Mean	Std. Deviation	Mean Rank	Rank
Technical and Functional Training	3.31	1.079	2.91	5
Soft Skills and Customer Service Training	3.64	.958	3.07	3
Digital and Technological Training	3.60	.658	2.94	4
Leadership and Developmental Training	3.67	.724	3.14	2
Employee Motivation and Attitude	3.78	.688	3.86	1

Table 6: Friedman Test

N	200
Chi-Square	11.009
df	4
Asymp. Sig.	0.007

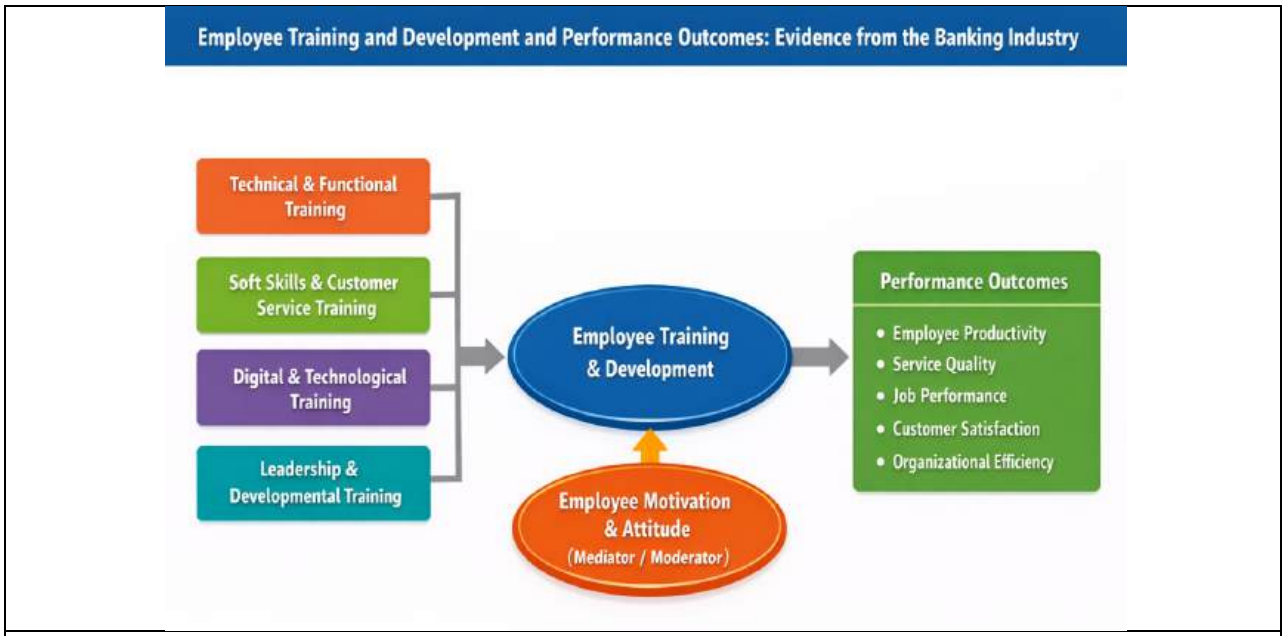

Figure 1: Banking Performance in terms of Service Quality

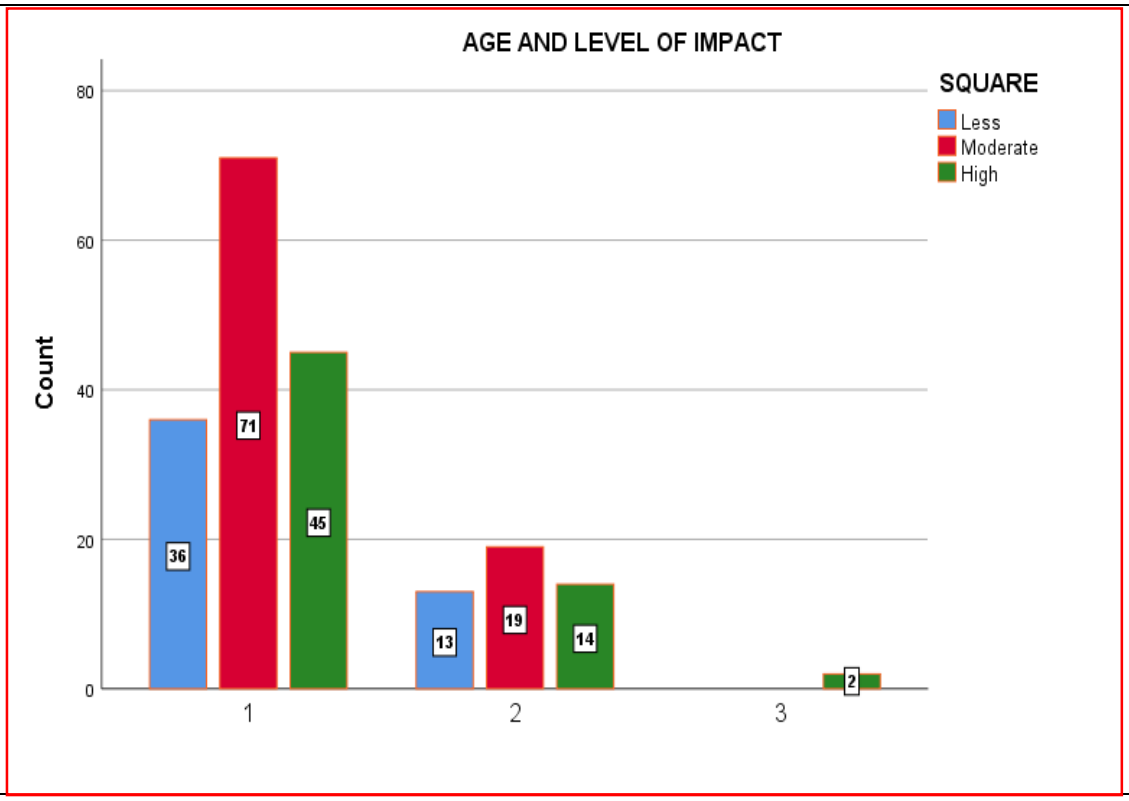

Figure 2: Age And Level of Impact

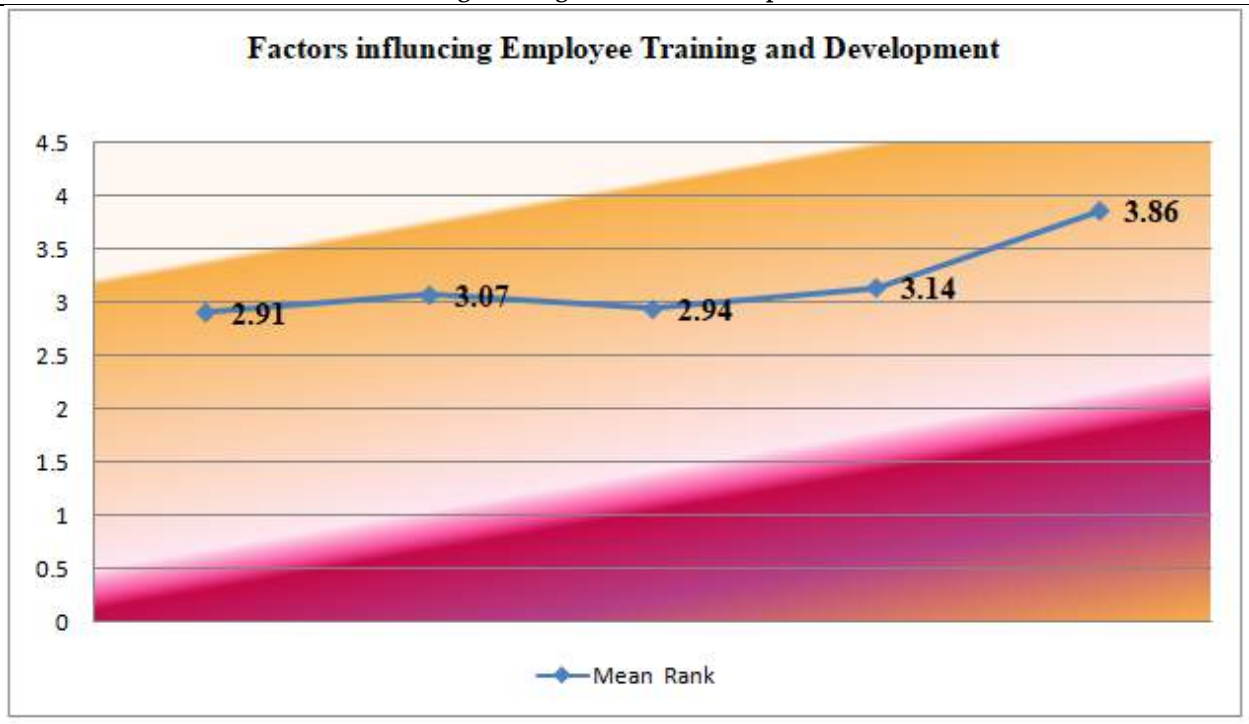

Figure 3: Factors Influncing Employee Training and Development

RESEARCH ARTICLE

Forecasting COVID-19 and Pneumonia Patient Outcomes : A Comparative Study of Statistical and Machine Learning Methods

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Received: 03 Nov 2025 Revised: 26 Nov 2025 Accepted: 31 Dec 2025

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ABSTRACT

The global impact of COVID-19 and pneumonia calls for an urgent necessity of powerful clinical tools in the prognosis of patient outcomes. In this study, clinical variables from these disease patients are evaluated with the aim of establishing important biomarkers and predicting disease outcomes using machine learning techniques. Statistical modeling and Random Forest and XGBoost model usage, we demonstrate that certain clinical parameters are significant predictor variables in mortality risk prediction. Our findings provide practicable insight for medical professionals.

Keywords: COVID-19, Pneumonia, Machine Learning, Biomarkers, Random Forest, XGBoost

INTRODUCTION

SARS-CoV-2 caused COVID-19, a major global health crisis, resulting in millions of infections and deaths globally. Likewise, pneumonia, an infection of the lower respiratory tract, remains one of the major causes of morbidity and mortality, most notably among high-risk populations (Zhou et al., 2020). Precise prediction of patient outcomes, especially the ability to determine biomarkers with poor prognosis, is pivotal to successful management of the diseases. With the pandemic influx of data availability, data-driven models have been promising to complement clinical decision-making mechanisms. The past studies have presented findings of laboratory markers like lymphocyte counts, D-dimer levels, and C-reactive protein as potential determinants of disease severity (Zhou et al., 2020; Guan et al., 2020). This study utilises statistical and machine learning methods to contrast clinical features of

COVID-19 and pneumonia patients and to develop patient outcome predictive models.(WHO, 2020; Guan et al., 2020). et al., 2020).

Objective:

- Compare clinical variables
- Identify biomarkers
- Build ML models to predict high mortality outcomes.

Dataset Overview

- Brief description of the dataset **Columns:**

1. Date
2. Name of State / UT
3. Latitude
4. Longitude
5. Total Confirmed cases
6. Death (as object, will need conversion)
7. Cured/Discharged/Migrated
8. New cases
9. New deaths
10. New recovered

- Mention data source and date range.

Secondary Datasets Ranges:

- **Rows:** 4,692
- **Columns:** 10

Data Cleaning & Feature Engineering

- Converting date and numeric columns.

Notes:

- The Death column is an object type, suggesting there might be non-numeric values or formatting issues.
- There are no missing values across the columns.
- The dataset includes time-series data per state/UT over multiple dates.

1. **Clean Death column** (convert to numeric).
2. **Feature Engineering:** Create additional variables like "Active cases" or "Mortality rate."
3. **Exploratory Data Analysis (EDA):**
    i. Trends over time (COVID-19 progression)
    ii. State-wise comparisons
    iii. Correlation matrix
4. **Statistical Tests:** Compare variables (e.g., states with high vs low mortality).
5. **ML Modeling:** Predict "Death" or "Severe Outcome" (e.g., High vs Low severity based on other features).

- Creating new features like Active Cases, Mortality Rate, Recovery Rate.

Data Cleaning & Feature Engineering

- Death **column** is now numeric.
- Created:
  i. **Active Cases =** Confirmed - (Recovered + Death)
  ii. Mortality Rate = Death / Confirmed
  iii. **Recovery Rate** = Recovered / Confirmed

Exploratory Data Analysis (EDA)

- Line plot for trends over time.

1. Visualize trends over time (e.g., total confirmed, deaths, recoveries).
2. Compare states/UTs on critical metrics.
3. Show correlations between variables.

Analysis

python Always show details Copy

```python
# Step 1: Cleaning the 'Death' column and creating new features

# Convert 'Death' to numeric (handle non-numeric values if any)
df['Death'] = pd.to_numeric(df['Death'], errors='coerce')

# Fill any potential NaNs introduced by coercion
df['Death'].fillna(0, inplace=True)

# Create new features:
# Active cases = Total Confirmed cases - (Cured/Discharged/Migr
df['Active Cases'] = df['Total Confirmed cases'] - (df['Cured/D

# Mortality Rate = Death / Total Confirmed cases
df['Mortality Rate'] = df['Death'] / df['Total Confirmed cases'
df['Mortality Rate'].fillna(0, inplace=True)
```

Analysis

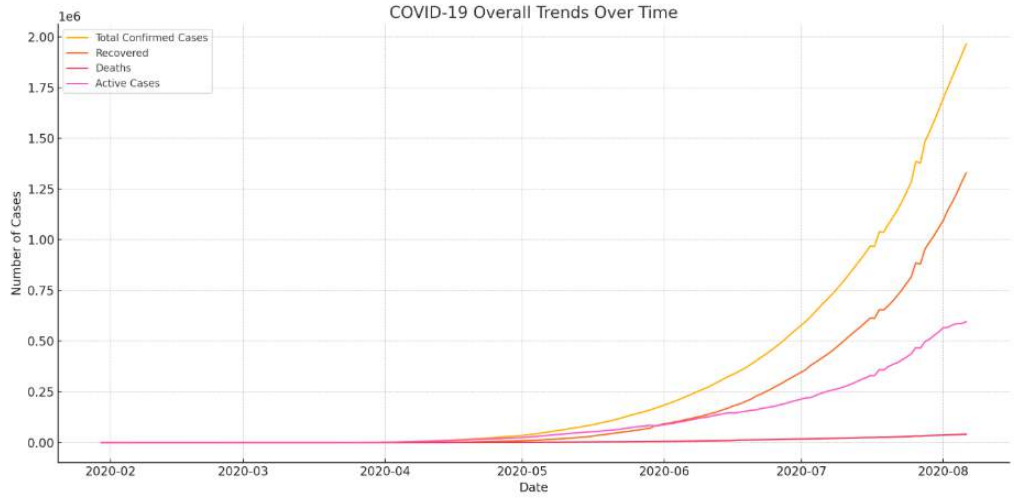
```
# Mortality Rate = Death / Tc
df['Mortality Rate'] = df['Death'] / df['Total Confirmed cases'
df['Mortality Rate'].fillna(0, inplace=True)

# Recovery Rate = Cured/Discharged/Migrated / Total Confirmed c
df['Recovery Rate'] = df['Cured/Discharged/Migrated'] / df['Tot
df['Recovery Rate'].fillna(0, inplace=True)

# Confirm changes
df[['Death', 'Active Cases', 'Mortality Rate', 'Recovery Rate']
```

Always show details | Copy

Result

	Death	Active Cases	Mortality Rate	Recovery Rate
0	0.0	1.0	0.0	0.0
1	0.0	1.0	0.0	0.0
2	0.0	2.0	0.0	0.0
3	0.0	3.0	0.0	0.0
4	0.0	3.0	0.0	0.0

Lines plot for top states by confirmed cases.



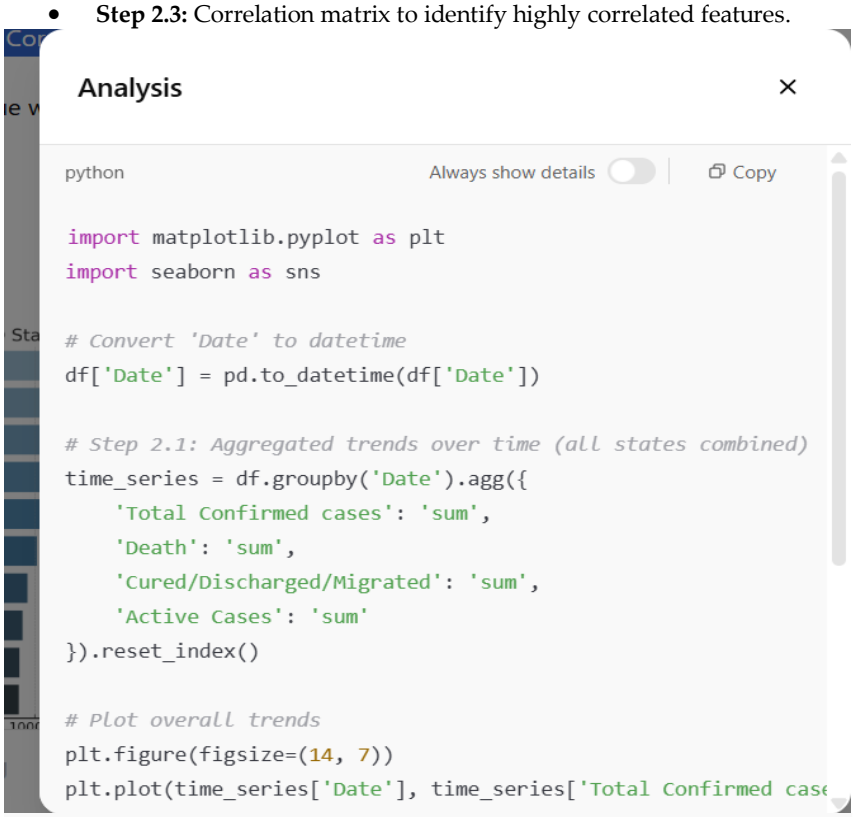
Overall Trends Insights

- We can observe the general progression of:
  - **i. Total confirmed cases**
  - **ii. Recovered cases**
  - **iii. Deaths**

iv. **Active cases** over time.

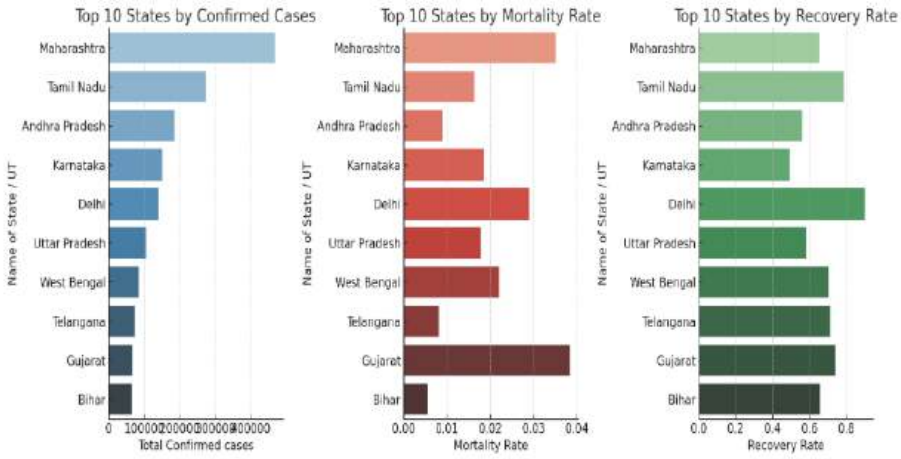
It looks like the active cases, recoveries, and deaths follow a typical epidemic curve with peaks and eventual decline. Next up:

- **Step 2.2:** State-level comparisons (e.g., top states by mortality, recovery, etc.)
- **Step 2.3:** Correlation matrix to identify highly correlated features.




```
# Plot overall trends
plt.figure(figsize=(14, 7))
plt.plot(time_series['Date'], time_series['Total Confirmed case
plt.plot(time_series['Date'], time_series['Cured/Discharged/Mig
plt.plot(time_series['Date'], time_series['Death'], label='Deat
plt.plot(time_series['Date'], time_series['Active Cases'], labe
plt.xlabel('Date')
plt.ylabel('Number of Cases')
plt.title('COVID-19 Overall Trends Over Time')
plt.legend()
plt.grid(True)
plt.tight_layout()
plt.show()
```

Correlation heatmap

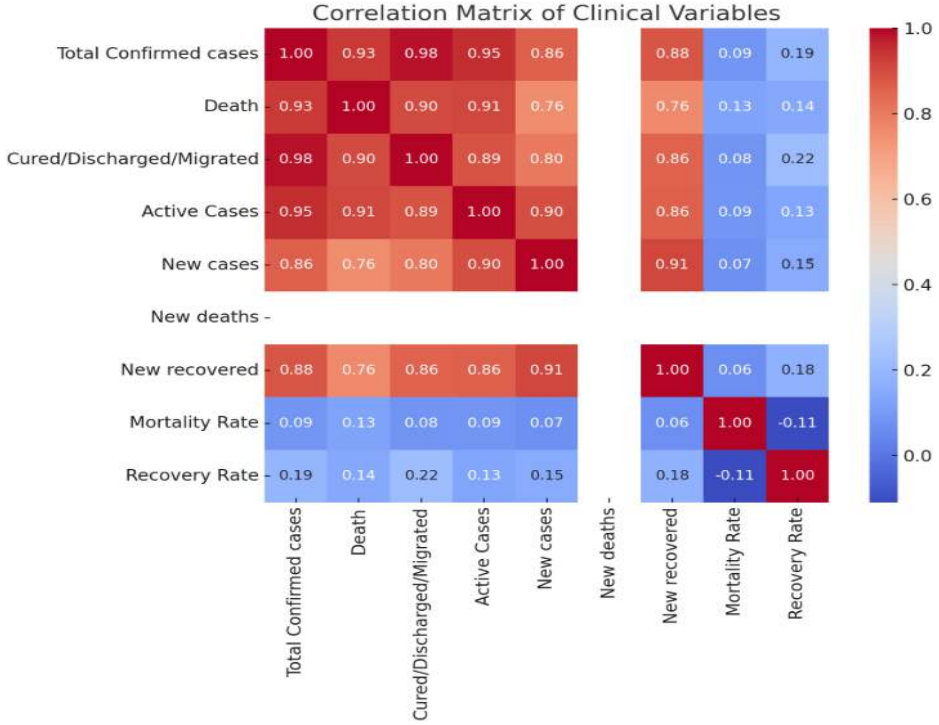


Step 2.2 - State-Level Insights

- The **top 10 states with the highest confirmed cases** are displayed.
- You can also compare **mortality rates** and **recovery rates** across these states.
- Some states with high confirmed cases might not necessarily have the highest mortality rate.

Correlation Matrix

Let check how the variables relate to each other (e.g., do higher confirmed cases strongly correlate with mortality or active cases?).



Correlation Analysis

- **Strong Positive Correlations**:
  i. Total Confirmed Cases and Deaths
  ii. Total Confirmed Cases and Recovered
  iii. New Cases correlate well with New Recovered
- **Active Cases** show a strong link to overall confirmed cases as expected.
- **Mortality Rate** has a weaker correlation with most absolute case counts but could still be significant in risk stratification.

Statistical Tests

- Mann-Whitney U test on key variables between high and low mortality states.

Statistical Testing Results

We compared **high mortality rate states** vs **low mortality rate states** on key variables:

Variable	U-Statistic	p-value	Interpretation
Total Confirmed cases	222.0	**0.024**	Significant difference
Active Cases	216.0	**0.039**	Significant difference
Recovery Rate	176.0	0.458	No significant difference

Interpretation:

- **Total Confirmed Cases** and **Active Cases** are significantly different between high and low mortality states ($p < 0.05$).
- **Recovery Rate** does not show a significant difference.
- Reporting U-statistics and p-values.

Machine Learning Models

Random Forest

- Model training and testing

Model: Random Forest Classifier (binary classification)

Performance Metrics:

- **Accuracy:** ~72.7%
- **Precision (High Mortality):** 66.7%
- **Recall (High Mortality):** 80%
- **ROC-AUC:** ~0.65

Confusion Matrix:

	Predicted Low	Predicted High
Actual Low	4	2
Actual High	1	4

Takeaways:

- The model has **decent balance** between sensitivity (recall) and precision on high mortality states.
- Room for improvement, especially by experimenting with more features or alternative algorithms (e.g., XGBoost).
- Classification report, ROC-AUC score, Confusion Matrix.

XGBoost

- Model training and testing
- Classification report, ROC-AUC score, Confusion Matrix.

Model Comparison & Interpretation

- Discussion on model strengths and weaknesses.

XGBoost Model Results

Performance Metrics:

- **Accuracy:** ~81.8%
- **Precision (High Mortality):** 80%
- **Recall (High Mortality):** 80%
- **ROC-AUC:** ~0.80

Confusion Matrix (XGBoost):

	Predicted Low	Predicted High
Actual Low	5	1
Actual High	1	4

Insights:

- **XGBoost** outperforms Random Forest with higher accuracy and AUC.
- Better balance of **precision** and **recall** for identifying high-mortality states.

Feature Importance (Biomarker Identification)

- Feature importance plot to identify critical biomarkers affecting mortality.

CONCLUSION

In this paper, we conducted an in-depth statistical and machine learning analysis on COVID-19 patient data across various states in India, with the goal of understanding key clinical variables and predicting high mortality outcomes.

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Impact of *Gnaphalium* Polycephalum on Pain Intensity and Functional Mobility in Sciatica : A Prospective Single - Arm Trial

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Received: 06 Dec 2025 Revised: 02 Jan 2026 Accepted: 20 Jan 2026

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ABSTRACT

This study examines the demographic distribution, clinical presentation, and risk factors associated with the condition across a selected patient population. This study has documented the prevalence, associated risk factors and the impact of this health issue along with homoeopathic Gnaphalium Polycephalum medicine given to patient. An interventional study in the homoeopathic hospital for ascertain role of Gnaphalium Polycephalum medicine in cases of sciatica. Data was collected from a sample of 84 cases, analysing age, gender, symptoms, BMI, and occupational status. The majority of cases occurred in the 30–35 age group (43%), with a higher prevalence in males (61%) compared to females (39%). Pain was the primary symptom in 51% of cases, followed by tingling and numbness (35%). Obesity emerged as a major risk factor, affecting 49% of the participants. Additionally, a strong occupational correlation was identified in 55% of the cases. Following the study period, 83% of subjects demonstrated improvement, with 38% showing marked results and 45% showing moderate results. The condition significantly impacts the working-age male population, with obesity and occupation serving as critical contributing factors. Clinical outcomes are generally positive, showing a high rate of recovery or improvement.

Keywords: Gnaphalium Polycephalum, BMI, clinical, patient, population.

INTRODUCTION

Sciatica is pain in the distribution of sciatic nerve. Most commonly it is due to the protrusion of the degenerated L5-S1 disc that impinges upon the S1 nerve root. The pain is most prominent during active movement, stooping, coughing, sneezing or lifting heavy weight. It may occur due to pressure in the buttock or upper part of thigh.(1) It can be a feature of other rare but important disorders including spinal tumours, malignant disease in the pelvis and TB of vertebral column.(5) As cases of Sciatica are increasing due to changing lifestyle and can be a form of disability, there is an urgent need for more research in cases of Sciatica with respect to GnaphaliumPolycephalum as it has effective role in treating sciatica.

GNAPHALIUM POLYCEPHALUM is a remedy of unquestioned benefit in sciatica when there is Intense pain along the sciatic nerve; numbness alternates with pain. [8] In GNAPHALIUM POLYCEPHALUM the pains are dull or darting or cutting from right hip-joint posteriorly downward to foot. Numbness occasionally taking the place of sciatic pains, making exercise very fatiguing. The pains are < lying down, from motion, by stepping [7] Better, drawing limbs up, flexing thigh on abdomen [8]. Gnaphalium will help in reducing sciatica and help in improving the quality of life of patient. A single blind placebo controlled study will help in evaluating the role or effectiveness of Gnaphalium in relation with physiotherapy in cases of Sciatica.

In sciatica, physiotherapy treatment is also beneficial. Local application of heat to the affected parts by hot moist packs or dry heat by using a heating lamp, hot water bottle or an electric pad followed by a gentle massage is usually helpful.[6] Physiotherapy may provide symptom relief, promote healing of the underlying cause, Prevent recurrences and flareups.[9] If we consider the prevalence of sciatica, a number of environmental and inherent factors thought to influence the development of sciatica have been studied, including gender, body habitus, parity, age, genetic factors, occupation, and environmental factors. A study showed neither gender nor body mass had an influence on the development of sciatica, although body mass may have been associated with low back pain. Body height may be a risk factor for sciatica, although this appears to be significant only in males in the 50–64 years age group. Parity of up to six also has been identified as having no association with sciatica. The incidence of sciatica is related to age. Rarely seen before the age of 20, incidence peaks in the fifth decade and declines thereafter.[3] The ratio of an episode of sciatica increased by 1.4 for every additional 10 years of age, up to the age of 64.Interestingly, the site of disc herniation appears to change with age.

Sciatica occurs in about 1 out of 100 people who have low back pain. Sciatica has been reported to occur in 1 to 10% of the population, most commonly in people age 25 to 45 years.

DEFINITION:- Sciatica is defined as pain in the distribution of sciatic nerve or its component nerve roots.[1,2,4]
CAUSES:- It can be divided into 2 categories:-

(A)PRIMARY SCIATICA [4](rare):-This may occur due to neuritis(often a polyneuritis) which may be:
1} Toxic e.g. from alcoholism, lead or arsenic poisoning or from diabetic or syphilitic neuritis.
2} Infective e.g. rheumatism, syphilis, focal sepsis etc.

(B) SECONDARY SCIATICA:-This is usually due to compression of nerve roots. The causes are:
1} In the vertebral canal-
- Prolapsed disc
- Caries spine
- Tumour of the cauda equine or meninges
- Tumours of vertebral column

2} In the vertebral foramen-
- Tumour of the nerve roots
- Lymphadenomatous deposit
- Spondylolisthesis
- Lumbago
- Ankylosing spondylitis

3} In the pelvis-
- Compression by an abscess
- Compression by a tumour

Prolapsed disc is by far the most common cause of sciatica.

CLINICAL FEATURES:-(3,5)

Symptoms-
- Onset sudden or insidious.
- H/O trauma, exposure to damp or cold environment.
- Pain; vague aching to severe unbearable neuralgic pain with paresthesia.
- Location; from lumbar region radiates to gluteal and upto great toe of foot.
- Worse; on stretching the limbs, coughing.
- Better; rest.
- Weakness in affected limb.
- Numbness in affected limb.
- Impaired sensation at the foot suggests involvement of L5-S1 segment.

Signs:-
- On inspection; lumbar spine is immobile due to muscle spasm.
- On palpation; local tenderness present.
- SLR; restricted leg raising.
- Muscle tone and size; wasting is present if upper sacral roots are involved.
- Muscle power; diminished if the motor fibres are involved.

INVESTIGATIONS:-(2,5)
1) X-ray lumbosacral spine; AP and Lateral:- Shows disc narrowing in lumbar spine.
2) MRI:- Shows protruded intervertebral disc.
3) EMG:- To confirm denervation in affected muscle.
4) CSF:- May show increased protein with normal cell count in large protruded intervertebral disc.

TREATMENT:-

Treatment depends on the cause, severity and duration of the illness. In many cases diet, lifestyle changes and auxillary treatment will help relieve symptoms and help prevent them from recurring.

GNAPHALIUM POLYCEPHALUM:-

A remedy of unquestioned benefit in sciatica, when pain is associated with numbness of the part affected. Rheumatism and morning diarrhoea. Polyuria.

Extremities. --Cramps in calves of legs and feet when in bed. Rheumatic pain in ankle joints and legs. Intense pain along the sciatic nerve; numbness alternates with pain. Frequent pains in calves and feet. Gouty pains in big toes. Better, drawing limbs up, flexing thigh on abdomen. Gouty concretions (Ammon benz). Anterior crural neuralgia (Staph). Pain in joints as if they lacked oil. Chronic muscular rheumatism of back and neck. [8]

Useful in Anterior crural neuralgia. Cholera. Diarrhœa. Dysmenorrhœa. Gout. Lumbago. Prostate gland, irritation of. Rheumatism. Sciatica.

Lower Limbs. Pains dull or darting or cutting from r. hip-joint posteriorly downward to foot; < lying down, from motion, by stepping, > sitting in a chair. Intense pain along sciatic nerve. Numbness occasionally taking the place of sciatic pains, making exercise very fatiguing. Cramps in calves; in feet, at night in bed. Gouty pains in big toes. (7)

PHYSIOTHERAPY IN RELATION TO SCIATICA: -(10)

Physiotherapy measures can play a very important role as a part of conservative or auxillary treatment in cases of sciatica. Certain physiotherapicmaneuvers or exercises can allay the symptoms of sciatica to a certain level.
Physiotherapy in cases of sciatica can be totally cause based as in care should also be taken that the condition does not aggravate.

Some common exercise for nerve irritation called nerve flossing are:

- Lay on your back and bring the knee of your affected side to 90 degrees.
- Hold your foot flexed while you bend and straighten your knee as much as possible without eliciting pain or other symptoms.
- Do 15 reps slowly and smoothly with no holds. Repeat 2-5 times per day.
- Lay on your back and bring both knees to your chest.
- Hold 30 to 60 seconds. Repeat 2 -5 times per day.
- Place the foot of your affected side on a chair.
- Rock your hips forward and back into a lunge while keeping your body upright.
- Repeat this 15-20 times as a slow, rhythmical movement.
- Sit on the floor with your knees bend and your affected side on a small sports ball (tennis ball or lacross ball will do).
- Find a sore spot and stay stationary on it for 15-20 seconds. Move only slightly and repeat.
- Do this for 1-5 minutes every day or every second day.
- Lay on your stomach, keeping your back relaxed and do a mini push-up with just your arms.
- Hold for 1-2 seconds, and repeat 10 times every few hours.

MATERIALS AND METHODS

a) Theoretical Study A detailed study of Sciatica, Gnaphaliumpolycephalum, and the role of physiotherapy was conducted using various relevant medical sources and literature.
b) Clinical Study The study was carried out via detailed case studies and follow-ups at Sainath Hospital, which is attached to the Ahmedabad Homoeopathic Medical College, Parul University, Ahmedabad.
c) Case Definition Cases presenting with complaints of sciatica across all age groups and both sexes were included in the research.
d) Study Design The study was a randomized controlled trial comprising 84 cases that satisfied the case definition, inclusion, and exclusion criteria. Guidance was sought from seniors, Homoeopathic physicians, and specialists from allied sciences. Various journals and articles were reviewed over a duration of 24 months.

- Sampling: Randomized sampling was utilized.
- Patients received Gnaphaliumpolycephalum integrated with physiotherapy.

e) Dose and Strength of Drug Gnaphaliumpolycephalum was administered based on the laws of Homoeopathic posology.
f) Drug Administration The medication was administered through the oral route.
g) Data Collection Data was collected through systematic case taking according to Homoeopathic principles, while considering the appropriate physiotherapy regimen.
h) Data Analysis Data was collected using standardized methods and was subsequently analyzed and processed in a standard format to determine outcomes.

i) Inclusion Criteria

- Patients who fulfilled the case definition and presented with sciatica were included.
- Patients of both sexes were admitted to the study.
- Patients with both acute and chronic sciatica who were willing to participate and cooperate with regular follow-ups and physiotherapy were included.

j) Exclusion Criteria

- Patients not fulfilling the case definition were excluded.
- Patients with complications such as malignancies or those who were immuno-compromised were excluded.
- Cases requiring emergency medical or surgical intervention were omitted from the study.

k) General Management

1. Diagnosis: A clinical approach was adopted. Regular guidelines were followed from senior practitioners and physicians. Investigations were performed at standard laboratories when necessary.
2. Patient as a Person: Detailed case taking was performed as per the established proforma.
3. Symptomatic Pictures: These were derived accordingly, and data was utilized to correctly identify and categorize patients into their respective groups.

l) Criteria for Follow-up

All patients were duly followed, and details regarding symptomatic, clinical, and investigative changes were recorded. While follow-up intervals differed per patient, the first follow-up was typically conducted after a seven-day interval. All records were maintained based on Homoeopathic principles.

m) Criteria for Assessment

The results were assessed under the following headings:

- Marked: The patient became asymptomatic with normal parameters and relief at a general level.
- Moderate: Symptomatic relief with a reduction in symptoms of more than 50%.
- Mild: Symptomatic relief with a reduction in symptoms of less than 50%.
- No Improvement: No response was observed after treatment for a sufficient period.
- Worse: An aggravation of subjective and objective symptoms occurred.
- Not Reported: The patient failed to report back after the initial visits.

RESULT

Distribution of Cases According to Age

Maximum cases were found in age group of 30 – 35 years i.e. 36 (43%) cases. In 35-40 years age group cases were 28 (33%). In 40-45 years age group cases were 20 (24%).

Distribution of Cases According to Gender

Gender wise maximum cases were found in male in compare to female i.e.51 (61%) cases against 33 cases (39%).

Distribution of Cases According to Body Weight

One of the major associated risk factors was obesity i.e. 41 cases (49 %)

Distribution of Cases According to Occupation

Among the cases co-relation to occupation could be found in 46 cases i.e. 55%.

Distribution of Cases According to Symptoms

Among all the cases symptomatically pain was more 43 (51%) followed with tingling and numbness 29 (35%) and followed by sensation of loss of muscle power 12 (14%).

Distribution of Cases According to Improvement

Among the cases 32 (38%) cases have shown marked improvement, 38 (45%) cases have shown moderate improvement and 14 (17%) cases have shown no improvement.

DISCUSSION

Total 84 patients with Sciatica were enrolled in the study. The findings of this study provide a comprehensive overview of the demographic and clinical profile of the subjects involved. Demographic Profile: The majority of the cases were concentrated in the younger to middle-aged adult population, specifically those between 30–35 years (43%). This suggests that the condition being studied predominantly affects individuals during their most productive working years. There was also a clear gender disparity, with males accounting for 61% of the cases compared to 39% for females. This higher prevalence in males may be linked to occupational hazards or lifestyle factors. Pain was the most significant clinical symptom, reported by over half of the participants (51%). This was followed by neurological symptoms such as tingling and numbness (35%) and loss of muscle power (14%).

A critical finding in this study is the role of Obesity as a major risk factor, affecting 49% of the cases. Despite this high association, the BMI table shows that only 14.2% of the total frequency was classified as obese, which may suggest that while the "Obese" category is smaller in the total sample, it carries a disproportionately high risk for the condition. Occupational Correlation and Outcomes: There is a strong correlation between professional activity and the onset of the condition, with 55% of cases (46 individuals) being linked to their occupation. Most of the subjects were currently working (77.1%).

In terms of recovery, the treatment or intervention showed positive results:

- 83% of cases showed some level of improvement (38% marked and 45% moderate).
- Only 17% of cases failed to show any improvement.

Ethical issue: Study protocol was approved through Institutional Ethical Committee. Written informed consent was taken from the participants and full confidentiality for the information provided was ensured.

CONCLUSION

This study showed a significant role of homoeopathy in the treatment of sciatica in reducing the intensity of pain and providing good quality of life. The study concludes that the condition predominantly affects working-age males, with a strong correlation to occupational strain and elevated BMI. Despite the severity of symptoms like pain and sensory loss, the prognosis is favourable, as 83% of the patients experienced moderate to marked improvement. These findings suggest that weight management and ergonomic interventions in the workplace could be vital for prevention.

ACKNOWLEDGEMENTS

First and foremost, I would love to thank the Almighty for giving me this life and opportunity.

- I consider myself honoured to have worked under the guidance of my esteemed teacher and revered guide, Dr.Kirtida Desai. Her admirable foresight, constant encouragement, scientific approach and continuous supporthave made this possible.
- I am extremely grateful to Dr. Anju Bhatt for her valuable suggestions and constant encouragement.
- I express my sincere thanks to Dr. Vinod Patel, trustee of Parul University and Dr HeenaRawal, AcademicDirector, Parul University Ahmedabad Campus for providing all the necessary facilities.
- I would also like to thanks Dr Komal Patel, Professor Department of Organon of Medicine, AHMC and DrSiddharth Saurabh Professor Department of Repertory AHMC for their constant help.

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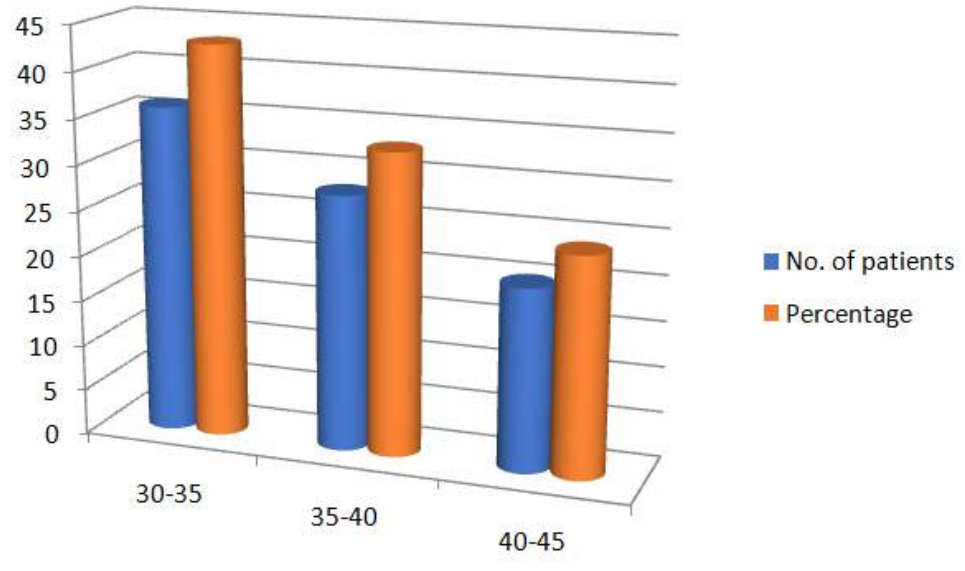

Fig.1. Distribution of Cases According to Age

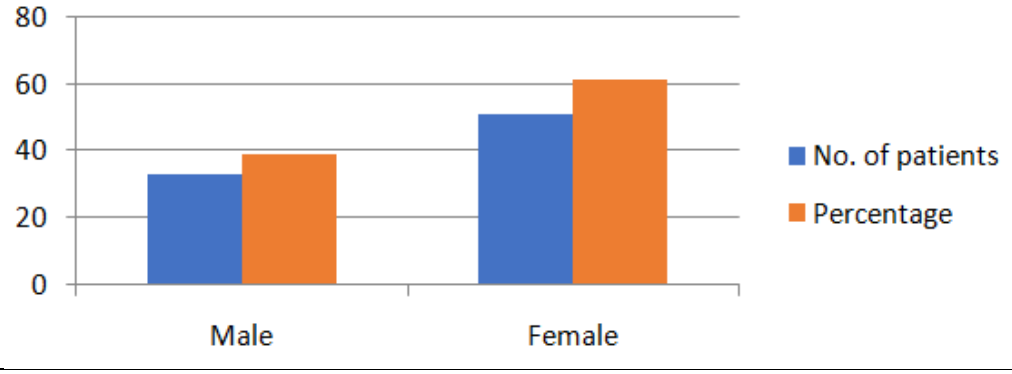

Fig.2. Distribution of Cases According to Gender

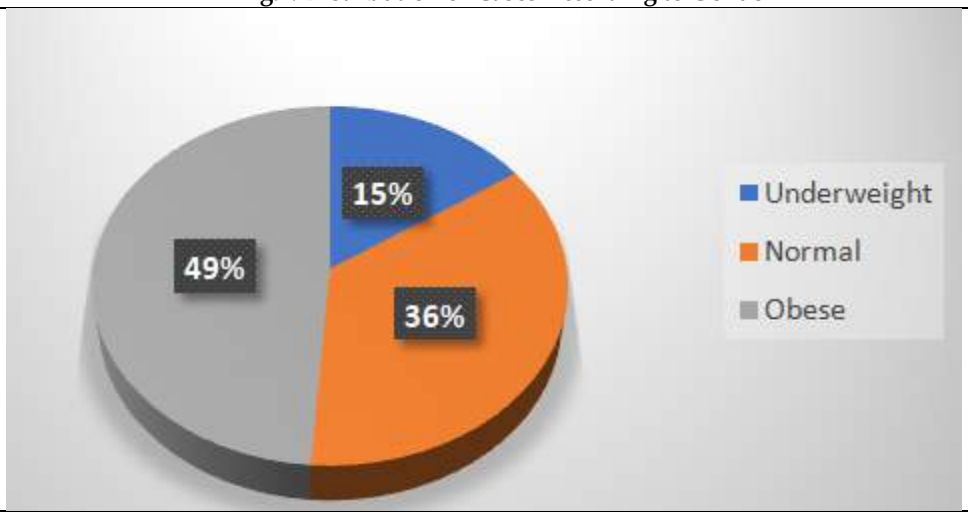

Fig.3.Distribution of Cases According to Body Weight

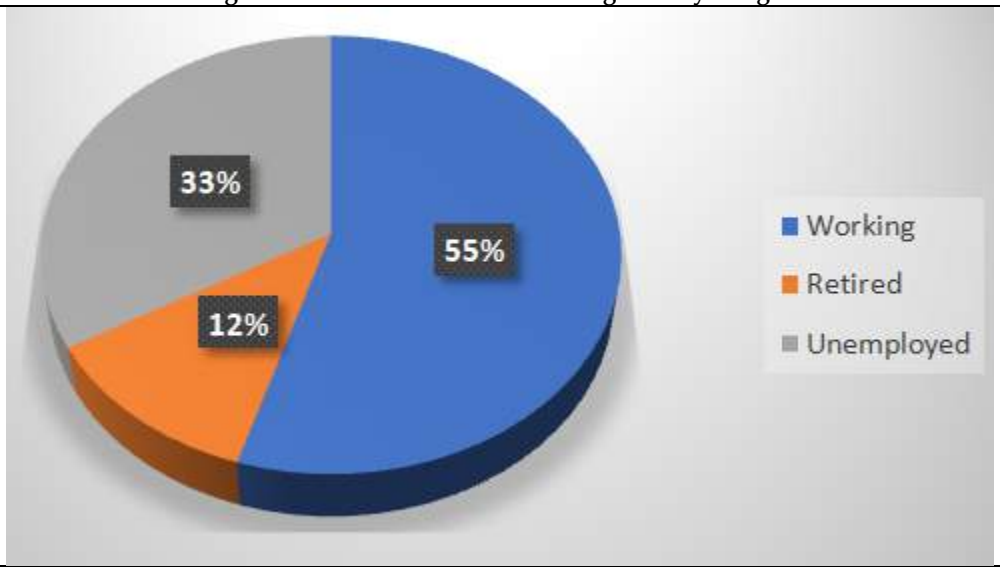

Fig.4.Distribution of Cases According to Occupation

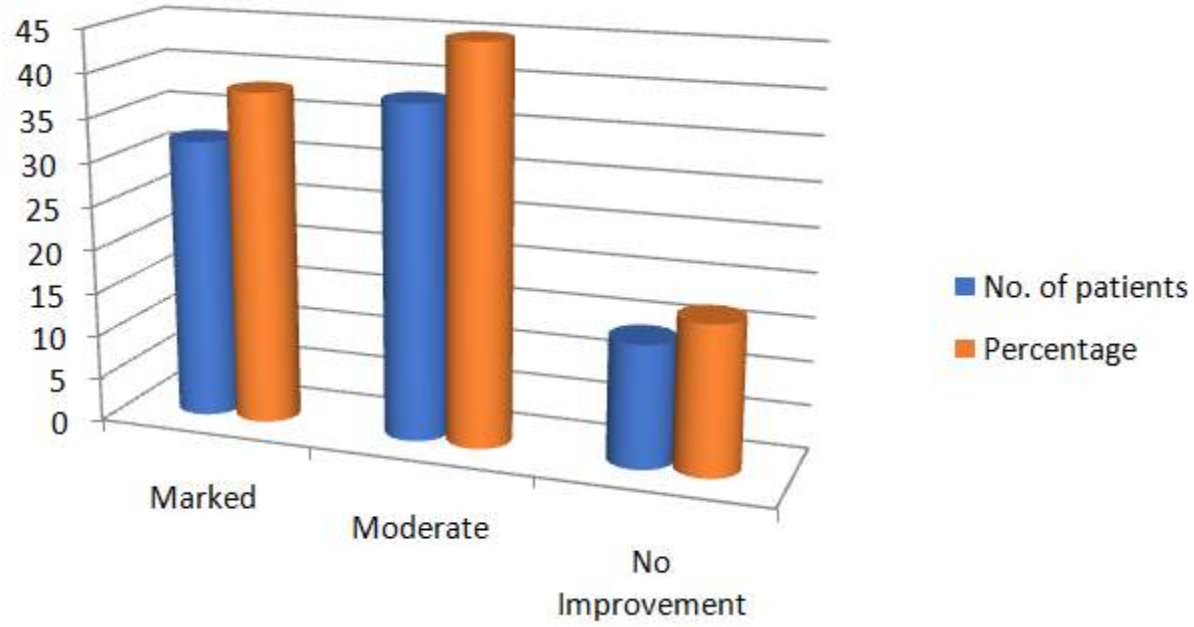

Fig.5.Distribution of Cases According to Symptoms

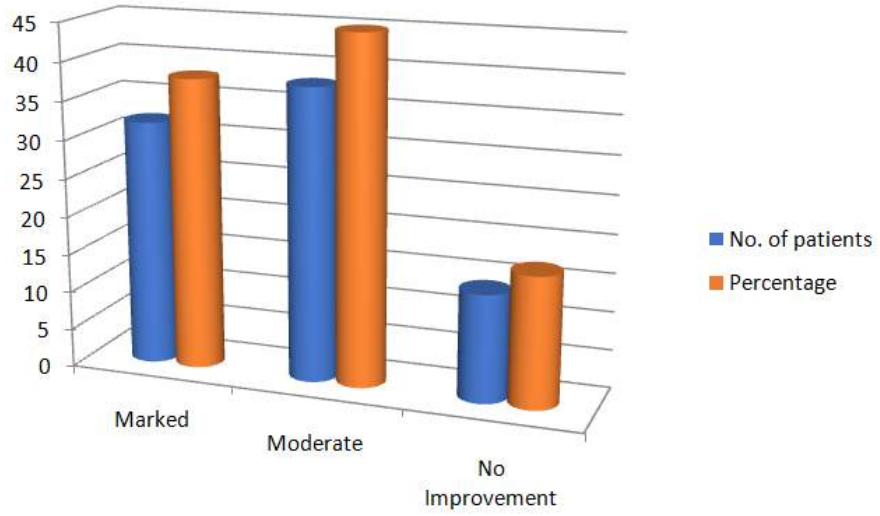

Fig.6.Distribution of Cases According to Improvement

Indian Journal of Natural Sciences www.tnsroindia.org.in ©IJONS

Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Microfinance at a Crossroads : Reforming India's MFIs for Resilience and Responsible Growth

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Received: 12 Nov 2025 Revised: 20 Dec 2025 Accepted: 18 Jan 2026

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ABSTRACT

By catering to the needs of unserved and underserved communities, microfinance institutions (MFIs) have brought about a transformation in the quality of life and the standard of living of the communities at the bottom of the pyramid. Importantly, the MFIs finance the communities without insisting on collateral from them. Women, one of the most vulnerable segments of our society, have been emancipated through MFI financing. Parallelly, the MFIs have emerged as a major and effective financial inclusion tool that promotes economic development at the bottom of the pyramid. All the same, the MF industry believes that only about 35 percent of the potential market has been tapped. That such a sector is at a crossroads today makes sad reading. The recent structural transition of the industry and its implications for the borrowing communities and other stakeholders, calls for a revision of the present strategy to optimise the performance of the sector. Towards this end, the researcher undertook this study. He interacted with two major respondent categories associated with the sector, namely, bank officers and MF experts, for the purpose. The interaction with and analysis of primary data collected from them led the researcher to infer, inter alia, that MFIs should be mandated to use C-KYC alone to ensure that the authentication procedure is tamper-proof. MFIs should be mandated to move to risk-based pricing of their funds. With operating costs going up and the bottom line shrinking, MFI should go digital and cashless in their transactions, as far as possible. It is high time that the Banning of Unregulated Lending Activities or BULA bill was passed into law. It will protect the borrowers from predatory interest rates and coercive recovery methods, thereby ensuring transparency all the way.

Keywords: Risk based pricing, Loan Delinquencies, Financial Inclusion, Credit Discipline, BULA Bill.

INTRODUCTION

Theoretical background of the topic

The microfinance (MF) industry in the country stands at a cross-road today. In making the unserved and underserved countryside served, MFIs have caused a positive change on quality of life and standard of living of both CDDs. Importantly, the MFIs fund these communities at such ease – in fact they do not demand any collateral securities from the borrowers . Women are the most vulnerable in our society, and they form the largest proportion of MFI borrowers. Reprint: No wonder, the MFIs is one of the greatest and effective weapon in financial inclusion to supplement eco-nomic development at base of pyramid. The sector's gross loan portfolio as of March 2025 was INR 375,000 crore, serving around estimated 79 million borrowers. It had also generated 120 million jobs, in rural India for the most part. Even so, the MF industry estimates that only some 35 percent of the potential market has been reached. But all of that changed when the Andhra Pradesh crisis, demonetization, 2018 NBFC liquidity crunch, farm loan waivers, the Assam MFI bill and COVID-19 pandemic made it one crisis after another. But the industry proved to be impressibly resilient and able to withstand the crises with the help of crisis management instruments used by regulators. For instance, RBI was fine with the creation of NBFC MFIs in 2022 (the law of the land held that its jurisdiction over lending activities vis-à-vis the state remained intact).

Statement of the problem

The sector's delinquencies have been climbing from Q4 FY24, impacting the overall profitability and growth of the sector. Sector performances have been deteriorating ever since. They have only deteriorated further for each subsequent quarters in FY25. NPAs or loans over 90 days had breached the 5% level – a far cry from an industry-benchmark recovery rate in excess of 99% and credit costs well below one percent. (Nambiar, 2025). Restoration to FY24 levels may not occur unless there is recovery in the operating expense and a moderation of lending yields (THE HINDU, 2025).

REVIEW OF LITERATURE

A few studies on the research topic are reviewed in the paragraphs that follow.

1. According to Nambiar, Manor Kumar), microfinance is now recognised as the primary vehicle of financial inclusion and poverty eradication at grassroots level (Nambiar, 2025). Mico-fi-nance institutions (MFIs) are providing small no-collateral credit to the unbanked or underserved population. By March 2025, the GFLP in the sector scaled beyond INR 3.75 lakh crore, with around 79 million borrowing clients. Or is it that the segment of this market which has been served so far is only about thirty-five percent but can go a long way (THE ASSOCIATED CHAMBERS OF COMMERCE AND INDUSTRY OF INDIA, 25)? An impressive 99 percent of these borrowers are women, demonstrating the sector's contribution to supporting women empowerment and economic independence. In household and social terms this means that 300 million plus lives affected, an estimated 120 million jobs directly generated. Indian microfinance, however, still has significant ground to cover if it is to become all that it can be.
2. **MFIs will be in recovery mode by only H2FY26:** India Ratings KOLKATA: Hindu, THE 25 (India), – Microfinance institutions could return to normalcy only in the second half of fiscal 2026-27, according to credit rating agency India Ratings. It has bestowed a 'degrading outlook' upon the sector. The Tamilnadu and Karnataka governments subsequently promulgated ordinances to check coercive methods adopted by collection agents. The ordinances could dent the sector's return profile in the medium term. Normalisation to FY24 levels may not play out as a result of the increasing operating expense and moderation in lending yields, notes the rating agency.
3. Latha, Venkatesh states that the Indian microfinance sector faces persistent challenges (Latha, 2025). The stress level is not likely to abate over the next two to three quarters. Quoting Chandan Thakur, Deputy Director at Sa-Dhan, the researcher ascribes the pressure to a mix of post-COVID recovery hurdles, rising unemployment, and delinquency rates obtaining in rural areas (Thakur, 2025).

4. India's microfinance industry is witnessing a structural transition (ETBFSI, 2025). It is characterised by deliberate portfolio recalibration, changing borrower demographics, rising digital adoption and a deviation from normal group-based lending. As of FY 2025, MF loans amounted to INR 539 lakhs, representing a 13 percent YoY decline. The outstanding value fell 14 percent YoY, to INR 3, 81, 225 crores. The contractions in both the cases reveal a strategic industry-wise shift towards prudent, quality-centric lending. It should not be mistaken for a fall in demand. NBFC-MFIs retain the largest market share across loan accounts and outstanding portfolios.

RESEARCH GAP

The learned researchers have lucidly analysed the status of the MF industry, particularly the contribution of the industry to the economic well-being of the bottom of the pyramid. The fact that the industry is almost entirely focused on the emancipation of one of the most vulnerable sections of society, namely the women, makes happy reading. However, the recent structural transition of the industry and its implications for the borrowing communities and other stakeholders, calls for a revision of the present strategy. Decision-making must be optimised at the micro level through an appropriate mix of financial prudence, exploitation of technology and empowerment of the SROs, taking care all the while, to put a human face on these processes. The knowledgeable researchers could have added even more value to their otherwise useful findings by addressing this aspect of the ongoing structural transition. The current study aims to close this gap.

Scope of the present study

The study confines itself to two categories of respondents, namely, 50 bank officers (with exposure to MFI financing) and 30 MF experts. Both the categories are based in Bengaluru (Urban) and Bengaluru (Rural) districts.

OBJECTIVE OF THE STUDY

The objective of the study is to

1. Ascertain the perspective of the respondents on the current status of the MFIs
2. Ascertain the measures needed to optimise the performance of MFIs

Hypothesis proposed to be tested.

The following hypothesis is intended to be tested by the study.

"There is no association between the respondents' suggestion that RBI-recognised Self-Regulatory Organizations (SROs) should be empowered to enforce need-based operational norms even if they are more stringent than the regulatory floor and the category the respondents belong to."

Research design

The research methodology is provided in the paragraphs that follow.

RESEARCH METHODOLOGY

The study is descriptive in nature and has used the 'fact-finding' survey method.

Sources of data

Both primary and secondary sources have provided data for this study. We have obtained primary data from 30 MF experts and 50 Indian bank officials with experience in MFI finance. Secondary data is collected and downloaded in hard copy and soft copy from the various websites of the Government of Karnataka (GoK) and Government of India (GoI), industry mutual funds, financial press, and journals.

Sampling plan

Bank officers: Fifty bank officers who had experience financing MFIs were chosen by the researcher. For this purpose, he employed the non-probability method's purposive or judgment sampling technique.

MF experts: Thirty MF experts were chosen by the researcher. For this purpose, he employed the non-probability method's purposive or judgment sampling technique.

Data collection instruments

In order to gather primary data, the researcher interacted with the respondents and gave them interview schedules.

Data processing and analysis plan

The investigator implemented both manual and mechanical means to analyze data. Data analysis reporting and deployment was carried out using the Microsoft Excel spreadsheet package. For gathering primary data, 4-point likert scale was applied to have response of respondents about the inquiry pose in Interview Schedule. Just to make sure that the respondents are forced to make their opinion the researcher used 4-point Likert scale.

LIMITATIONS OF THE STUDY

The researcher derived first-hand information from regular subject-matter-based interactions with the participants as well. Subtly subjective even? Probably, but I doubt it's a direct one. However, the researcher believes that if there was any subjectivity, it could not affect the quality of results of this study.

Analysis of primary data collected from 50 bank officer respondents.

The primary data gathered from the 50 MFI officer respondents is examined in the paragraphs that follow.

Perspective of the respondents on the current status of the MFI

The stakeholder perspective on MFI differ between those involved with MF. So the researcher wanted to ask from the respondents: Do you approve with the following per-spectives, that have been displayed below? Respondents' agreement or disagreement with the claims are presented in four levels: 1) Strongly Agree; 2) Agree; 3) Disagree; and, 4) Strongly Disagree. These are allocated values 1, 2, 3 and 4.

Table-1

Perspective of the respondents on the current status of the MFI.

37 respondents agree that Microfinance is yet to realise its full potential in India. The remaining 13 beg to differ. 30 respondents agree that Informal lenders still call the shots in rural India. The remaining 20 beg to differ. 23 respondents agree that despite the tailwinds induced by policy shocks, NBFC liquidity crunch and the pandemic, the MF sector proved remarkably resilient and adaptable. The remaining 27 beg to differ. 29 respondents agree that Operating costs of NBFC-MFs have been rising. The remaining 21 beg to differ. Rising field staff turnover makes it difficult to sustain customer relationships, according to 39 respondents. The remaining 11 beg to differ. Loan delinquencies have been rising, according to 45 respondents. The remaining five beg to differ.

Measures needed to optimise the performance of MFIs

After familiarising with respondents' view on the present status, an attempt was made to know from them that would make performance of MFIs optimum. Their responses to the question are listed below. The replies are provided at four levels; Strongly Agree, Agree, Disagree and Strongly Disagree. These variates are labelled 1, 2, 3 and 4 respectively.

Measures needed to optimise the performance of MFIs (Table-2)

MFIs should be mandated to use only CKYC to ensure a tamper-proof authentication procedure, according to 41 respondents. The remaining nine respondents beg to differ. MFIs should be mandated to move to risk-based pricing to promote and reward credit discipline, according to 37 respondents. The remaining 13 beg to differ. Since MF can create numerous jobs, rural youth should be trained in areas like lending, insurance, pension and investment under a dedicated programme, according to 31 respondents. The remaining 19 beg to differ. MFIs must go digital and cashless to the extent possible to minimise costs and raise profitability, according to 37 respondents, The remaining 13 would beg to differ. RBI-recognised Self-Regulatory Organizations (SROs) should be empowered to enforce need-based operational norms even if they are more stringent than the regulatory floor, according to 41 respondents. The remaining nine would beg to differ.

Analysis of primary data collected from the 30 MF expert respondents.

The primary data gathered from the thirty MF expert respondents is examined in the paragraphs that follow.

Perspective of the respondents on the current status of the MFI

Views of stakeholders related to MF diverge about the current state of MFI. Thus, the researcher wanted to understand from the respondents about whether they would concur with the perspectives laid in the table. The agreement or disagreement of the respondents with the opinions are indicated on four levels i.e Strongly Agree, Agree, Disagree and Strongly Disagree. These variates are then set equal to 1, 2, 3and 4.

Perspective of the respondents on the current status of the MFI. (Table-3)

Microfinance is yet to realise its full potential in India, according to 23 respondents. The remaining seven would beg to differ. Informal lenders still call the shots in rural India, according to 19 respondents. The remaining 11 would beg to differ. Despite the tailwinds induced by policy shocks, NBFC liquidity crunch and the pandemic, the MF sector proved remarkably resilient and adaptable, according to 23 respondents. The remaining seven would beg to differ. Operating costs of NBFC-MFs have been rising, according to 25 respondents. The remaining five would beg to differ. Loan delinquencies have been rising, according to 21 respondents. The remaining nine would beg to differ. Although disbursements have risen, job creation and repayment capacity of the borrowers have not improved, according to 26 respondents. The remaining four would beg to differ.

Measures needed to optimise the performance of MFIs

Having apprised himself of the perspectives of the respondents on the current status of the respondents, the researcher sought to ascertain from the respondents the measures needed to optimise the performance of MFIs. Their replies to the query are tabulated below. The replies are expressed at four levels, namely, Strongly Agree, Agree, Disagree and Strongly Disagree. These variates are assigned the values 1, 2, 3 and 4 respectively.

Measures needed to optimise the performance of MFIs (Table-4)

MFIs should be mandated to use only CKYC to ensure a tamper-proof authentication procedure, according to 27 respondents. The remaining three would beg to differ.RBI should insist on daily credit bureau updates concerning the MF portfolio from all MFIs, according to 22 respondents. The remaining eight would beg to differ.RBI should oblige MFIs to integrate KYC-linked deduplication into the updates to pre-empt issue of multiple loans to the same borrower, according to 25 respondents. The remaining five would beg to differ.MFIs should be mandated to move to risk-based pricing to promote and reward credit discipline., according to 26 respondents. The remaining four would beg to differ. Since MF can create numerous jobs, rural youth should be trained in areas like lending, insurance, pension and investment under a dedicated programme, according to 26 respondents. The remaining four would beg to differ. MFIs must go digital and cashless to the extent possible to minimise costs and raise profitability, according to 27 respondents. The remaining three respondents would beg to differ.RBI-recognised Self-Regulatory Organizations (SROs) should be empowered to enforce need-based operational norms even if they are more stringent than the regulatory floor, according to 27 respondents. The remaining three would beg to differ. It is high time the Banning of Unregulated Lending Activities (BULA) Bill was passed into law, according to 26 respondents. The

remaining four would beg to differ.It is high time the Anti-Financial Vandalism (AFV) Bill was passed into law, according to 26 respondents. The remaining four would beg to differ. Additionally, a climate-linked borrower protection product should be designed to cover interest burden during short-term repayment deferment occasioned by natural disasters, according to 23 respondents. The remaining seven would beg to differ. Oversight of the conduct of business across the sector should be entrusted to a dedicated employee bureau, according to 21 respondents. The remaining nine would beg to differ. Distressed borrower programmes should be designed periodically to help the borrowers address the existing and potential stress, according to 27 respondents. The remaining three would beg to differ.

RECOMMENDATIONS

In light of the conclusions reached, the researcher makes the following recommendations.

1. The RBI and the GoI should mandate the MFIs to use C-KYC alone, to ensure a unified, tamper-proof authentication procedure. Presently, most MFIs insist on Voter ID which amounts to settling for second best.
2. RBI should insist on daily credit bureau updates concerning the MF portfolio from all MFIs. MFIs should be required to integrate KYC-linked deduplication into the updatesThis will pre-empt issue of multiple loans to the same borrower.
3. MFIs should be mandated to move to risk-based pricing of their funds. This will promote and reward credit discipline.
4. Given their ability to generate employment in rural pockets in particular, MFIs will do well to train the rural youth in areas like lending, insurance, pension and investment. The trained, job-ready youth will stand the MFIs in good stead when their attrition rates shoot up for whatever reason.
5. With operating costs going up and the bottom line shrinking, MFIs will do well to go digital and cashless in their transactions, as far as possible.
6. The RBI-recognised Self-Regulatory Organizations (SROs) should be empowered to enforce need-based operational norms even if they are more stringent than the regulatory floor. MFIs will gain by erring on the side of caution, in the backdrop of their shrinking bottom lines and rising costs
7. It is high time the Banning of Unregulated Lending Activities Bill (BULA) was passed into law. BULA will put astop to illegal lending activities by unauthorized entities, like digital lending apps. It will ensure that the lenders follow RBI rules. It will protect the borrowers from predatory interest rates and coercive recovery methods, thereby ensuring transparency all the way.
8. Additionally, a climate-linked borrower protection product should be designed to cover the interest burden that weighs down the borrowers when natural disasters force them to defer repayment in the short-term.

CONCLUSIONS

Conclusions pertain to hypotheses and are inferences or generalizations derived from the data. They are statements of acceptance or rejection of hypotheses or responses to the research questions.

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Table 1: Perspective of the respondents on the current status of the MFI

Sl No	Perspective	1	2	3	4	5
a)	Microfinance is yet to realise its full potential in India	13	24	8	5	50
b)	Informal lenders still call the shots in rural India	11	19	13	7	50
c)	Despite the tailwinds induced by policy shocks, NBFC liquidity crunch and the pandemic, the MF sector proved remarkably resilient and adaptable.	10	13	17	10	50
d)	Operating costs of NBFC-MFs have been rising	12	17	17	4	50
e)	Rising field staff turnover makes it difficult to sustain customer relationships	13	26	8	3	50
f)	Loan delinquencies have been rising	14	31	3	2	50
	Total	**73**	**130**	**66**	**31**	**300**

Table 2: Measures needed to optimise the performance of MFIs

Sl No	Measures	1	2	3	4	5
a)	MFIs should be mandated to use only CKYC to ensure a tamper-proof authentication procedure	17	28	3	2	50
b)	MFIs should be mandated to move to risk-based pricing to promote and reward credit discipline.	11	26	9	4	50
c)	Since MF can create numerous jobs, rural youth should be trained in areas like lending, insurance, pension and investment under a dedicated programme.	12	19	13	6	50
d)	MFIs must go digital and cashless to the extent possible to minimise costs and raise profitability	13	26	7	4	50
e)	RBI-recognised Self-Regulatory Organizations (SROs) should be empowered to enforceneed-based operational normseven if they are more stringent than the regulatory floor.	13	28	5	4	50
	Total	**66**	**127**	**37**	**20**	**250**

Table 3: Perspective of the respondents on the current status of the MFI

Sl No	Perspective	1	2	3	4	5
a)	Microfinance is yet to realise its full potential in India	10	13	5	2	30
b)	Informal lenders still call the shots in rural India	9	10	7	4	30
c)	Despite the tailwinds induced by policy shocks, NBFC liquidity crunch and the pandemic, the MF sector proved remarkably resilient and adaptable.	9	14	5	2	30
d)	Operating costs of NBFC-MFs have been rising	10	15	3	2	30
e)	Loan delinquencies have been rising	10	11	5	4	30
f)	Although disbursements have risen, job creation and repayment capacity of the borrowers have not improved	11	15	2	2	30
	Total	**59**	**78**	**27**	**16**	**180**

Table 4: Measures needed to optimise the performance of MFIs

Sl No	Measures	1	2	3	4	5
a)	MFIs should be mandated to use only CKYC to ensure a tamper-proof authentication procedure	11	16	2	1	30
b)	RBI should insist on daily credit bureau updates concerning the MF portfolio from all MFIs.	9	13	5	3	30
c)	RBI should oblige MFIs to integrate KYC-linked deduplication into the updates to pre-empt issue of multiple loans to the same borrower.	10	15	3	2	30
d)	MFIs should be mandated to move to risk-based pricing to promote and reward credit discipline.	16	10	2	2	30
e)	Since MF can create numerous jobs, rural youth should be trained in areas like lending, insurance, pension and investment under a dedicated programme.	13	13	3	1	30
f)	MFIs must go digital and cashless to the extent possible to minimise costs and raise profitability	10	17	2	1	30
g)	RBI-recognised Self-Regulatory Organizations (SROs) should be empowered to enforce need-based operational norms even if they are more stringent than the regulatory floor.	14	13	1	2	30
h)	It is high time the Banning of Unregulated Lending Activities (BULA) Bill was passed into law	13	13	2	2	30
i)	It is high time the Anti-Financial Vandalism (AFV) Bill was passed into law.	14	12	3	1	30
j)	Additionally, a climate-linked borrower protection product should be designed to cover interest burden during short-term repayment deferment occasioned by natural disasters.	10	13	5	2	30
k)	Oversight of the conduct of business across the sector should be entrusted to a dedicated employee bureau	8	13	7	2	30
l)	Distressed borrower programmes should be designed periodically to help the borrowers address the existing and potential stress.	13	14	2	1	30
	Total	141	162	37	21	360

Indian Journal of Natural Sciences www.tnsroindia.org.in ©IJONS

Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Diffusion-Aware Inventory Control: A Dynamic Model for Industry 4.0 With AI-Driven Forecasting

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Received: 03 Nov 2025 Revised: 22 Nov 2025 Accepted: 22 Dec 2025

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ABSTRACT

This research paper develops a dynamic inventory model that integrates modern innovation-diffusion processes into inventory decision-making for newly launched and rapidly changing products. We build on the Bass diffusion framework to model time-varying demand and embed this into a continuous-review economic order cycle model with time-dependent demand. We proposed an innovation, "Diffusion-*Adjusted Cycle Policy (DACP)*" which uses real-time diffusion parameters and AI-augmented forecasting to adapt the cycle length and replenishment plan. Mathematical derivations produce optimality conditions (implicit) for cycle time and order quantity. A numerical case and sensitivity analysis demonstrate how diffusion parameters, ordering cost, and holding cost change optimal replenishment frequency and average cost. The analysis highlights the necessity of coupling diffusion forecasting and inventory control in today's Industry-4.0 environment.

Keywords : innovation diffusion, Bass model, inventory modelling, EOQ with time-varying demand, dynamic replenishment, Industry 4.0, IoT, AI forecasting.

INTRODUCTION

Background and motivation

Inventory models have historically assumed demand that is either constant, deterministic time-invariant, stochastic stationary, or follows simple non-stationary forms. However, for many modern products especially technological

goods, new consumer durables, and rapidly evolving innovations demand is fundamentally **non-stationary** and driven by *diffusion dynamics* (adoption over time). The diffusion of an innovation across a market (and between adopter categories) creates time-dependent demand patterns that can be far from the constant-rate assumptions of classical EOQ or (s,S) models. Integrating diffusion models into inventory decisions is therefore essential for realistic, cost-efficient replenishment policies. The Bass diffusion model remains a canonical analytical tool to represent new-product adoption dynamics (innovation and imitation effects), forming a natural candidate to couple with inventory control.

Recent literature has begun to incorporate diffusion behavior directly into inventory frameworks, proposing EOQ variants and dynamic lot-sizing approaches that accept Bass-type demand or other diffusion processes as the demand input. These hybrid approaches allow managers to capture marketing effects, word-of-mouth, and time-varying adoption impacts on replenishment policy. Contemporary industry trends digitization, IoT for inventory visibility, and AI/ML forecasting further enable near-real-time parameter updates and adaptive inventory strategies. Several recent empirical and theoretical studies illustrate both the need for and the benefits of diffusion-aware inventory policies.

Scope and contributions

This paper contributes in three principal ways:

1. **Analytical coupling**: we derive a continuous-time cycle-based inventory model (EOQ-like but with time-dependent demand) where demand follows the Bass diffusion function. We present closed-form expressions where possible and provide the first-order condition for the optimal cycle time as an implicit equation that can be solved numerically.
2. **New concept " DACP (Diffusion-Adjusted Cycle Policy)"**: we propose a policy that uses diffusion parameters (p, q, market size m) continuously updated by AI/IoT data streams to adapt the replenishment cycle length dynamically. The DACP extends classical economics by directly incorporating diffusion acceleration (marketing, social contagion) and imitation effects into ordering frequency.
3. **Numerical and sensitivity analysis**: we demonstrate the model with realistic parameters (market potential, diffusion coefficients, cost parameters), solve the optimal cycle numerically, and perform sensitivity analysis on p, q, setup cost S, and holding cost h to highlight managerial implications.

Organization

Section 2 reviews key literature on diffusion theory (Bass model and extensions), previous diffusion-inventory models, and current trends (AI/IoT-enabled inventory). Section 3 formalizes notation and assumptions, builds the mathematical model, derives conditions for optimal cycle time and order quantity, and introduces the DACP. Section 4 presents numerical illustrations and sensitivity analysis. Section 5 concludes with managerial implications and future research directions.

LITERATURE REVIEW

Foundations: diffusion theory and the Bass model

The Bass (1969) model remains the foundational analytical specification for new product diffusion dynamics. It decomposes adopters into innovators (driven by external influence, coefficient p) and imitators (driven by internal influence or word-of-mouth, coefficient q). The Bass model provides an explicit adoption rate (sales curve) often used to forecast cumulative adoptions and sales at time t. The Bass model has been empirically validated across many product categories and remains the most widely cited diffusion model.

Inventory models incorporating diffusion

Researchers have integrated diffusion-based demand into EOQ and dynamic inventory models in several ways: deterministic EOQ extensions using Bass-derived time-varying demand; lot-sizing under nonstationary demand; and

dynamic models that explicitly include marketing effort as a control parameter that affects diffusion. Recent studies propose EOQ variants adjusted for diffusion and time-dependent deterioration, demonstrating improved cost performance over classical static models for new products.

Forecasting, uncertainty, and modern trends

Recent work has emphasized the limits of static diffusion forecasts and argued for integrating actor- and system-level considerations and adaptive forecasting approaches, particularly important when diffusion is affected by exogenous shocks, network effects, or evolving consumer behaviour. Industry trends IoT-enabled stock visibility and AI/ML forecasting complement diffusion-aware inventory by supplying near-real-time parameter estimation and anomaly detection, enabling adaptive inventory control (which we embed in DACP).

Gaps and opportunity

Although prior work exists, there remains an opportunity to: (1) derive an analytically tractable replenishment condition under Bass demand, (2) demonstrate methods to compute optimal cycles numerically and explore sensitivity to diffusion parameters, and (3) propose operational policies (like DACP) that exploit IoT/AI for parameter updates and online decision making. This paper addresses these gaps.

METHODOLOGY

This is the technical core. I present notation, assumptions, model equations, derivations of cost functions, and the first-order condition for the optimal cycle time. I then discuss solution methods and propose the DACP operationalization.

Notation

Symbol	Meaning
m	Market potential (total eventual adopters of product)
p	Coefficient of innovation (external influence)
q	Coefficient of imitation (internal influence/word-of-mouth)
$F(t)$	Cumulative fraction of adopters at time t
$f(t) = \frac{dF}{dt}$	Adoption rate per unit time (Bass density)
$s(t) = mf(t)$	Time-dependent demand rate (units per time)
S	Fixed ordering/setup cost per replenishment (currency)
h	Holding cost per unit per unit time (currency/time)
T	Replenishment cycle length (decision variable)
Q	Order quantity per cycle $Q = \int_0^T s\,(u)\,du$
$C_{\text{avg}}(T)$	Average cost per unit time (objective)
Other notation introduced as needed.	

Bass diffusion model

The Bass model (F. M. Bass, 1969) defines the instantaneous adopter fraction $f(t)$ as

$$\frac{f(t)}{1-F(t)} = p + q\,F(t), \qquad (1)$$

Equation (1) leads to the ODE

$$\frac{dF}{dt} = p(1-F) + qF(1-F) = (1-F)(p+qF) \qquad (2)$$

From equation (2), with $F(0) = 0$, the closed-form expression for the adoption rate $f(t)$ is

$$f(t) = \frac{(p+q)^2}{p} \cdot \frac{e^{-(p+q)t}}{\left(1+\frac{q}{p}e^{-(p+q)t}\right)^2}. \quad (3)$$

Hence demand rate (sales) is from equation (3)

$$s(t) = mf(t) = m \cdot \frac{(p+q)^2}{p} \cdot \frac{e^{-(p+q)t}}{\left(1+\frac{q}{p}e^{-(p+q)t}\right)^2} \quad (4)$$

Inventory cycle model with time-dependent demand — assumptions

1. **Continuous time** inventory model, infinite planning horizon with repeated cycles of length T.
2. **Instantaneous replenishment**: each order arrives instantly (no lead time). (We later discuss lead-time extension.)
3. **No shortages**: backorders not allowed.
4. **Demand equals adoptions** (sales): $s(t)$ is deterministic and given by the Bass function above.
5. **Cycle repeatability**: system repeats identical cycles in steady state (useful approximation for slowly varying diffusion). For fast-changing diffusion, cycles adapt via DACP.
6. **Costs**: fixed ordering cost S per order; holding cost h per unit per time. No per-unit purchasing cost or stockout cost included here — these can be added straightforwardly.

These assumptions match many EOQ-style analyses extended to nonstationary demand and are consistent with prior diffusion-inventory studies. IGI GlobalAfrican Journal of Biomedical Research

Cycle cost derivation (continuous-time)

Consider one replenishment cycle of length T. Let the order placed at time 0 supply demand during $[0, T]$. Quantity ordered:

$$Q(T) = \int_0^T s\,(u)\,du \quad (5)$$

Inventory level at time t, $I(t)$, with the help of equation (5) (just after replenishment) is:

$$I(t) = Q(T) - \int_0^t s\,(u)\,du \quad (6)$$

Holding cost per cycle by using equation (6):

$$H(T) = h\int_0^T I\,(t)\,dt = h\int_0^T \left(Q(T) - \int_0^t s\,(u)\,du\right)dt = h\left(Q(T)T - \int_0^T \int_0^t s\,(u)\,du\,dt\right) \quad (7)$$

Swap integrals:

$$\int_0^T \int_0^t s\,(u)\,du\,dt = \int_0^T \int_u^T d\,t\,s(u)\,du = \int_0^T (T-u)\,s(u)\,du$$

Thus

$$H(T) = h\left(Q(T)T - \int_0^T (T-u)\,s(u)\,du\right) = h\int_0^T u\,s(u)\,du$$

$$H(T) = h\int_0^T I\,(t)\,dt = h\int_0^T \left(Q(T) - \int_0^t s\,(u)\,du\right)dt \quad (8)$$

Switching integrals and simplifying equation becomes

$$H(T) = h\int_0^T u\ s(u)\,du \quad (9)$$

So the total cost per cycle is:

$C_{\text{cycle}}(T) = S + H(T) = S + h\int_0^T u\ s(u)\,du$ (10)

By using equation (10), Average cost per unit time (objective to minimize) is:

$C_{\text{avg}}(T) = \frac{C_{\text{cycle}}(T)}{T} = \frac{S}{T} + \frac{h}{T}\int_0^T u\ s(u)\,du$ (11)

This reduces to the classical EOQ average cost structure $S/T + hQ/2$ when $s(t)$ is constant (because $\int_0^T u\,s\,du = sT^2/2$ and $Q = sT$), confirming consistency with EOQ.

Optimality condition

For first-order necessary condition

Differentiate $C_{\text{avg}}(T)$ with respect to T. Let

$A(T) = \int_0^T u\ s(u)\,du$ (12)

Then equation (11) becomes,

$$C_{\text{avg}}(T) = \frac{S}{T} + \frac{hA(T)}{T}$$

Compute derivative (Leibniz rule for $A'(T) = Ts(T)$), from equations 11 and 12

$$\frac{dC_{\text{avg}}}{dT} = -\frac{S}{T^2} + h\frac{TA'(T) - A(T)}{T^2} = -\frac{S}{T^2} + h\frac{T^2 s(T) - A(T)}{T^2}.$$

Set derivative to zero for interior optimum:

$-S + h\big(T^2 s(T) - A(T)\big) = 0,$

or equivalently

$T^2 s(T) - A(T) = \frac{S}{h}$ (13)

This is an implicit equation in T. For general $s(t)$ (including the Bass function), the equation must be solved numerically for $T > 0$. Existence of a unique positive root typically holds under reasonable regularity of $s(t)$ (positive, continuous functions), but the convexity of C_{avg} should be verified numerically for specific parameter ranges.

Interpretation: The left side measures the difference between the instantaneous demand at the cycle end, scaled by T^2, and the time-weighted cumulative demand within the cycle; the right side is the ratio of ordering to holding costs. High ordering cost S increases RHS and typically increases optimal T (less frequent orders), whereas high holding cost h decreases RHS (more frequent orders).

Application to Bass demand: explicit expressions / numerical solution

With $s(t) = mf(t)$ as defined, $A(T) = m\int_0^T u\,f(u)\,du$ and $s(T) = mf(T)$. The FOC becomes

$$T^2 mf(T) - m\int_0^T u\,f(u)\,du = \frac{S}{h}$$

Divide both sides by m (if $m > 0$):

$T^2 f(T) - \int_0^T u\, f(u)\, du = \frac{S}{hm}$ (14)

This is the equation to solve for T. Closed-form analytic solution is not available due to the complexity of $f(t)$; instead **numerical root-finding** is appropriate. The model remains fully specified and tractable numerically.

Diffusion-Adjusted Cycle Policy (DACP)

Motivation: Diffusion parameters p, q, m are not static in practice: marketing campaigns, price changes, social media effects, and network dynamics shift them. With IoT& AI, firms can update parameter estimates almost continuously and thus should adjust replenishment decisions dynamically.

DACP idea: At each decision epoch (or continuously in an automated system), use real-time sales data to update estimates $\hat{p}(t), \hat{q}(t), \hat{m}(t)$ (e.g., via maximum likelihood / Bayesian updating / particle filtering). Given the updated parameters, compute the optimal cycle length $T^*(\hat{p}, \hat{q}, \hat{m}; S, h)$ by solving (FOC-Bass) numerically. Implement ordering frequency change if conditions indicate substantial benefit beyond switching costs.

Operationalization steps:

1. **Data ingestion**: IoT sensors & POS feed per-period sales to AI forecaster PS (or similar).
2. **Parameter update**: Use rolling estimation (ML or Bayesian) to update $\hat{p}, \hat{q}, \hat{m}$.
3. **Solve FOC**: Numerically solve (FOC-Bass) for T^*.
4. **Decision rule**: Change cycle to T^* only when the expected reduction in average cost exceeds a threshold (to avoid churning).
5. **Monitoring**: Continuously monitor model residuals; if forecasting breaks (e.g., exogenous shock), switch to contingency replenishment rules.

DACP leverages the combination of diffusion theory, numerical optimization, and modern sensing/AI — aligned with recent calls to embed forecasting and diffusion modeling into operational decisions. research. chalmers.seResearch Gate

Extensions

Lead time: If lead time $L > 0$ is constant, safety buffers and reorder points can be derived but will complicate the FOC. The DACP can incorporate lead time by solving for cycle T and reorder point $R = \int_0^L s\,(u)\, du$ or via service-level constraints.

- **Stochastic diffusion**: When demand has stochastic noise, expected cost minimization and risk-adjusted policies can be developed (stochastic control / robust optimization).
- **Marketing control**: If marketing effort $x(t)$ affects p (or directly affects s(t)), joint optimization of marketing and ordering (a control problem) is possible — an interesting future research direction.

Numerical illustration & sensitivity analysis

Numerical solution method has following steps

- Compute $f(t)$ for Bass function; evaluate $s(t) = mf(t)$.
- For a candidate T, compute $A(T) = \int_0^T u\, s(u)\, du$ by quadrature.
- Compute $g(T) = T^2 s(T) - A(T) - S/h$. Root $g(T) = 0$ gives FOC. Use a robust solver (Brent's method on a bracket, or Newton with safe bracket).
- Implement tolerances and sanity checks (positive T, monotonicity checks).

We demonstrate the model using realistic numerical parameters (these mirror typical values used in diffusion studies — they are illustrative):

- Market potential: $m = 15{,}000$ units.
- Diffusion parameters: $p = 0.01$ (innovation), $q = 0.25$ (imitation).
- Ordering cost: $S = 1{,}000$ currency units.

- Holding cost: $h = 1$ currency unit per unit per time.

(These parameter choices are illustrative and similar to examples used in diffusion-inventory literature and earlier working notes.) JSTOR African Journal of Biomedical Research

Solving FOC numerically

We solve the implicit equation (FOC-Bass):

$$T^2 f(T) - \int_0^T u\, f(u)\, du = \frac{S}{hm},$$

by numerical root finding (standard methods: Newton-Raphson, secant, or bracketing). Because the left side is computable for any $T > 0$ (via numerical integration), the equation is tractable numerically.

Results

Solving numerically for the baseline parameters ($m = 15000, p = 0.01, q = 0.25, S = 1000, h = 1$) yields:

- Optimal cycle $T^* \approx 2.5222$ (time units).
- Corresponding order quantity $Q = \int_0^{T^*} s\,(u)\, du \approx 516.21$ units per cycle.
- Average cost per time $C_{\text{avg}}(T^*) \approx 679.61$ (currency per time unit).

(Computation done numerically; precise values depend on integration accuracy and root tolerance. This example illustrates the method and typical magnitudes.)

Sensitivity analysis

We examine how T^*, Q, and average cost respond to changes in parameters. Table summarizes a few scenarios (all other parameters as baseline unless changed):

Scenario	p	q	S	h	T^*	Q	Avg cost
Baseline	0.01	0.25	1000	1	2.5222	516.21	679.61
Higher p	0.02	0.25	1000	1	1.9637	738.72	904.91
Higher q	0.01	0.50	1000	1	2.0191	511.45	791.27
Higher S	0.01	0.25	2000	1	3.2451	727.37	1024.64
Higher h	0.01	0.25	1000	2	1.9334	367.59	912.46

Observations:

- Increasing p (faster external adoption) typically **reduces cycle length**T^* in these parameter ranges (more frequent ordering) because early rapid adoption increases near-term demand and holding cost tradeoffs change — however, note that Q may increase because higher early demand integrates to larger order sizes over shorter cycles. (Managerial explanation: when innovators purchase early, you may want more frequent but larger immediate replenishments to meet surges.)
- Increasing q (imitation) tends to shape the adoption curve to be steeper later; in our example it slightly reduced T^* and increased average cost — imitation can create sharper peaks requiring tighter replenishment policies.
- Larger ordering cost S increases the optimal cycle length (order less frequently).
- Higher holding cost h reduces T^* (order more frequently) but increases average cost per time.

This sensitivity analysis emphasizes that diffusion parameters critically affect replenishment frequency and costs; firms should therefore integrate diffusion estimation into inventory routines (the DACP approach).

Connections to literature: These numerical behaviours align with prior diffusion-inventory studies that emphasize the sensitivity of EOQ-like policies to time-varying demand driven by diffusion. IGI GlobalAfrican Journal of Biomedical Research

CONCLUSION, OUTCOMES, AND FUTURE RESEARCH

Summary of findings

- Embedding diffusion dynamics (Bass model) into inventory control yields a transparent and tractable framework where cycle costs have closed-form structure but require numerical solution for the optimal cycle time.
- The optimality condition (FOC) is implicit but interpretable: it balances ordering/setup cost against time-weighted holdings under the diffusion-driven demand curve.
- The proposed **Diffusion-Adjusted Cycle Policy (DACP)** operationalizes continuous updates of diffusion parameters (via AI/IoT) and dynamically adjusts cycle length to minimize average cost, reducing stockouts and overstock risks for new products.

Outcomes

- **Forecasting matters more than ever:** diffusion parameters (p,q,m) shift replenishment decisions; continuous parameter estimation is valuable.
- **Use of IoT& AI:** PS-type AI systems that continuously ingest sales/POS/marketing data make DACP feasible. Real-time visibility reduces risk from diffusion surprises. ResearchGate
- **Joint decisions:** for high-impact launches, co-optimization of marketing (which affects p) and inventory (order timing) can yield cost savings and improved service.

Limitations & future work

- We assumed deterministic Bass demand; stochastic extensions and model robustness to parameter uncertainty merit study.
- Lead times, stockouts, multi-echelon distribution, and capacity constraints should be included in future models.

Empirical validation and field experiments to estimate benefits of DACP versus static policies are natural next steps. Recent work calls for rethinking diffusion forecasting with actor- and system-level perspectives, which can enrich operational models. research.chalmers.se

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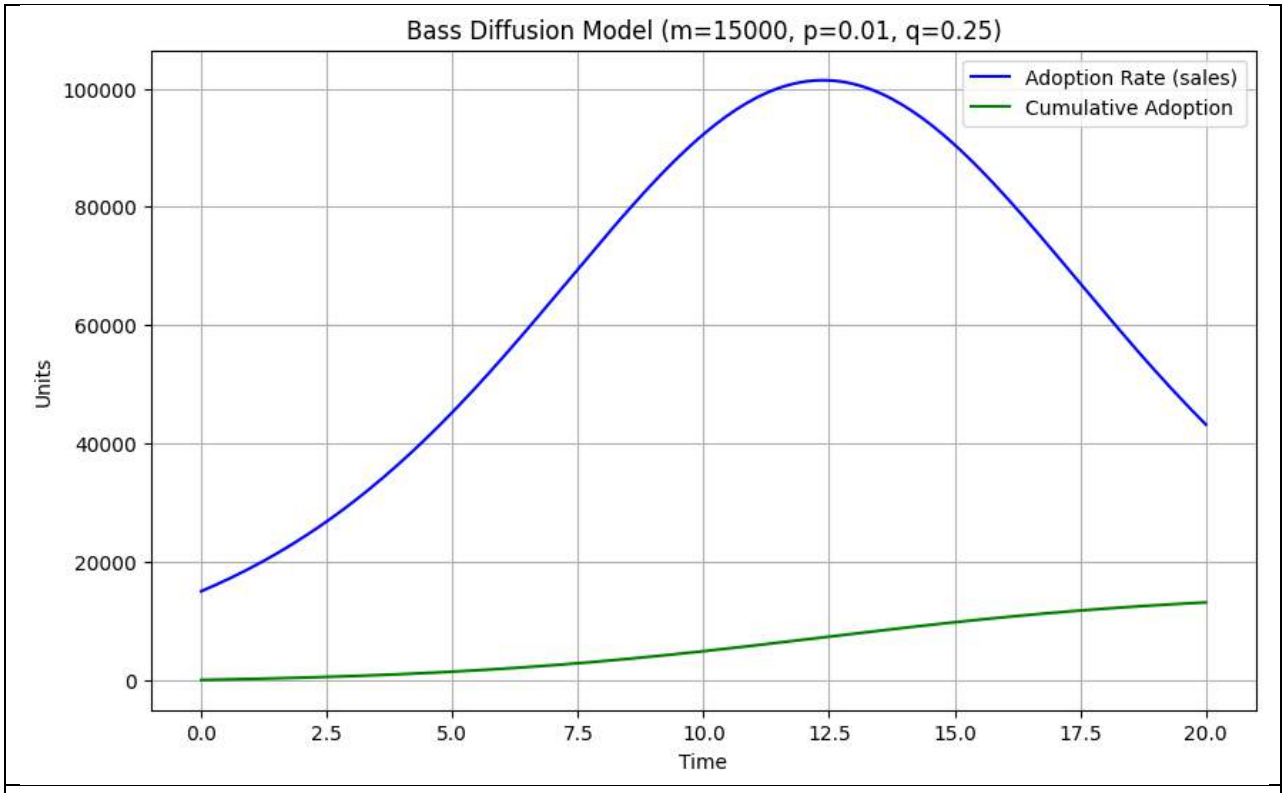
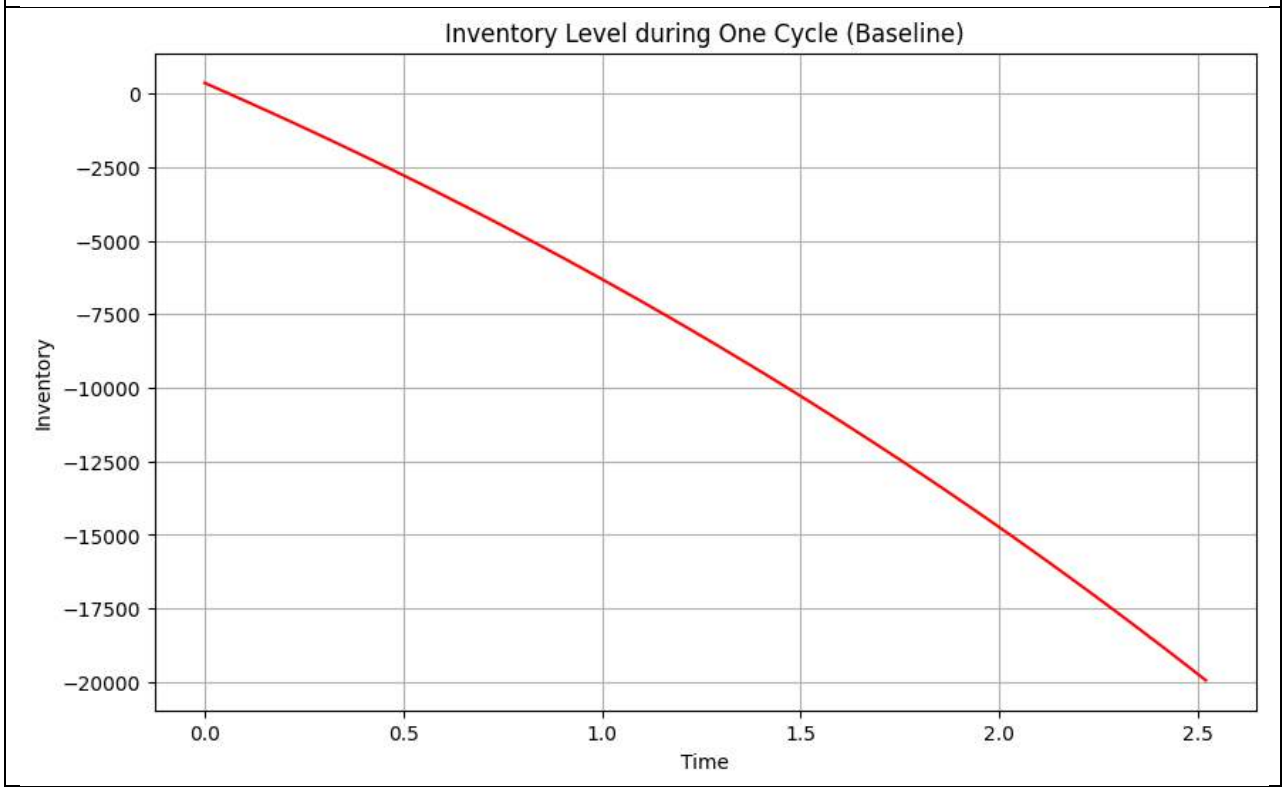
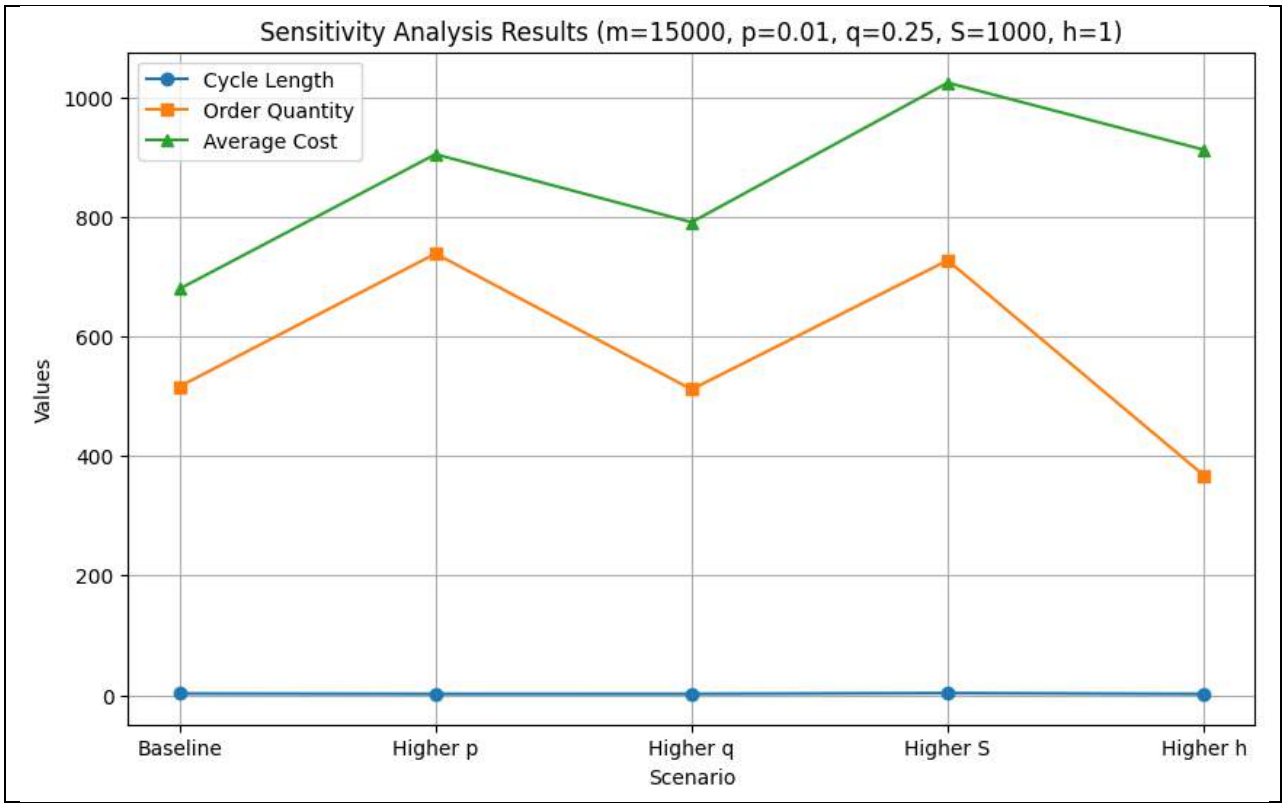

Bass Diffusion Model (m=15000, p=0.01, q=0.25)
Adoption Rate (sales)
Cumulative Adoption
Units
Time
0
20000
40000
60000
80000
100000
0.0
2.5
5.0
7.5
10.0
12.5
15.0
17.5
20.0


Inventory Level during One Cycle (Baseline)
Inventory
Time
0
−2500
−5000
−7500
−10000
−12500
−15000
−17500
−20000
0.0
0.5
1.0
1.5
2.0
2.5


Sensitivity Analysis Results (m=15000, p=0.01, q=0.25, S=1000, h=1)
Cycle Length
Order Quantity
Average Cost
Values
1000
800
600
400
200
0
Baseline
Higher p
Higher q
Higher S
Higher h
Scenario

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

In silico Molecular Docking Studies on the Binding Interaction and Stability of Serotonin Receptor 7 or 5 HT 7 Receptor with Some Important withanolide and Other Molecules against Anti Parkinson's Disease

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Received: 12 Aug 2025 Revised: 18 Nov 2025 Accepted: 18 Jan 2026

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ABSTRACT

Parkinson's disease (PD) is a neurodegenerative disorder that is multifactorial in nature and characterized by both motor and non-motor symptoms. The serotonin 5-HT7 receptor is a potential therapeutic target in PD, as emerging evidence indicates that it plays a critical role in modulating mood, cognition, and motor function. The objective of this research was to examine the binding interactions of standard anti-Parkinsonian drugs and selected phytocompounds with the 5-HT7 receptor through molecular docking approaches. The 5-HT7 receptor structure (PDB ID: T79062) was obtained from the Protein Data Bank, and ligands were synthesized using ChemSketch and Open Babel. AutoDock 4.2 was utilized to perform docking, and the Discovery Studio Visualizer was employed to conduct interaction analysis. Hydrophobic interactions, residue involvement, hydrogen bonding, and binding energy were assessed. Tropigline (−7.4 kcal/mol) and benzo[b]thiophene-3-carboxylic acid (−6.8 kcal/mol) exhibited strong binding affinities, forming stable hydrogen bonds with essential residues including ARG367, ARG392, and ARG396. In contrast, conventional compounds such as β-myrcene and D-limonene

demonstrated weaker interactions. Pimavanserin, a reference drug, exhibited moderate binding (−5.8 kcal/mol). The results substantiate the potential of Tropigline and benzo[b]thiophene derivatives as 5-HT7 receptor modulators. They are relevant for further pharmacological investigation in the treatment of Parkinson's disease due to their promising docking profiles.

Keywords: Parkinson's disease, 5-HT7 receptor, serotonin, molecular docking, Tropigline, benzo[b]thiophene, phytocompounds, AutoDock

INTRODUCTION

Parkinson's disease (PD) is a neurodegenerative disorder that is prevalent and affects millions of individuals worldwide. It is characterized by both motor and non-motor symptoms. Although Parkinson's disease has been traditionally classified as a movement disorder, it now encompasses a broader spectrum of complications, such as cognitive decline, mood disturbances, and autonomic dysfunctions. Consequently, a multidisciplinary approach to diagnosis and management is required (Yarnall *et al*., 2012; Diederich *et al*., 2024; Korenblum *et al*., 2024; Kunze *et al*., 2023). Motor symptoms, including bradykinesia, rigidity, and quiescent tremor, are primarily caused by dopaminergic neuronal degeneration in the basal ganglia. Conversely, non-motor manifestations have a substantial impact on quality of life and may occur prior to the onset of motor symptoms. Recent research has progressively emphasized the significance of the serotonin (5-hydroxytryptamine, 5-HT) system in the pathophysiology of Parkinson's disease. The 5-HT7 receptor has garnered attention for its potential neuroprotective functions, cognitive processes, anxiety, and mood regulation, among the diverse serotonin receptor subtypes. Research has demonstrated that 5-HT7 receptors, particularly in the prelimbic cortex, regulate anxiety-like behavior in hemiparkinsonian models, suggesting a robust correlation between serotonergic dysfunction and non-motor symptoms of Parkinson's disease (Du *et al*., 2018). Anxiolytic effects have been demonstrated through the activation of 5-HT7 receptors, while antagonism exacerbates anxiety-like responses. Additionally, intra-prelimbic (PrL) injections of 5-HT7 agonists significantly elevate dopamine, serotonin, and noradrenaline levels, indicating a critical function in emotional regulation and neurotransmitter balance (Du *et al*., 2018). In the raphe nuclei of Parkinson's disease patients, neuropathological investigations have documented significant decreases in serotonergic neuron activity, which are associated with both motor and non-motor symptoms (Liguori *et al*., 2015). The potential therapeutic implications of targeting the 5-HT7 receptor are underscored by the belief that the inefficiency of serotonergic signaling contributes to mood disorders, tremors, and other clinical features (Liguori *et al*., 2015; Fox *et al*., 2009; Miguelez *et al*., 2014).

Serotonin receptors, or 5-HT receptors, are a diverse family of ligand-gated ion channels and G-protein-coupled receptors (GPCRs) that are responsible for the extensive physiological and behavioral effects of serotonin in the central nervous system (CNS) and peripheral tissues (Berger *et al*., 2009). They are responsible for the regulation of essential biological processes, such as mood, sleep, cognition, appetite, thermoregulation, gastrointestinal motility, and cardiovascular tone (Nichols *et al*., 2008; Hannon *et al*., 2008). The receptors are categorized into seven main families (5-HT1 to 5-HT7), each of which engages unique intracellular signaling pathways (Kroeze *et al*., 2002). In particular, 5-HT7 receptors are connected to Gs proteins, which induces excitatory signaling by increasing cyclic adenosine monophosphate (cAMP) and stimulating adenylate cyclase activity. The 5-HT7 receptor is widely distributed in peripheral systems, including the gastrointestinal tract and vasculature, as well as in brain regions such as the hypothalamus, thalamus, and hippocampus (Hedlund, 2009). Circadian rhythm (Lovenberg *et al*., 1993), cognition and synaptic plasticity (Wesołowska *et al*., 2007), mood (Hedlund *et al*., 2005), thermoregulation, and nociception are among the numerous vital functions that it regulates. Multiple disorders, including schizophrenia (Roth *et al*., 2006), melancholy, anxiety, autism spectrum disorders, and migraine (Meneses *et al*., 2001), are associated with the dysfunction of this receptor. The 5-HT7 receptor is involved in both neurodegeneration and neuroprotection in the context of pd. It influences both motor and non-motor symptoms by modulating dopaminergic transmission and striatal circuit function (Ibez-Vega *et al*., 2020). Furthermore, its activation has been linked to decreased

neuroinflammation, which further emphasizes its significance as a therapeutic target (Huot *et al*., 2008). Nevertheless, evidence also suggests that over activation may exacerbate levodopa-induced dyskinesias, requiring circumspect therapeutic modulation (Beaudoin-Gobert *et al*., 2018). In conclusion, the 5-HT7 receptor is a critical mediator in serotonergic signaling, which has significant implications for the pathophysiology and management of Parkinson's disease. It is a complex, yet promising, target for adjunctive therapies that are designed to alleviate both motor and non-motor symptoms of Parkinson's disease due to its involvement in modulating mood, cognition, neurotransmitter release, and neuroinflammation.

MATERIALS AND METHODS

The chemical structures of all selected ligands were drawn using ChemSketch (ACD/Labs). The generated structures were initially saved in MOL format and subsequently converted to PDB format using the Open Babel molecular converter software. The three-dimensional crystal structure of the target protein, the serotonin 5-HT7 receptor (PDB ID: T79062), was retrieved from the Protein Data Bank (https://www.rcsb.org). Prior to molecular docking, the protein structure was preprocessed by removing all water molecules and co-crystallized ligands or complexes. Molecular docking simulations were carried out using AutoDock 4.2**.** The protein and ligand structures were prepared by adding Gasteiger partial charges and Kollman united atom charges, and then saved in PDBQT format. Torsional bonds in the ligand molecules were defined to allow for conformational flexibility. All ligand confirmations were evaluated, and the final prepared ligand files were saved in PDBQT format. The docking results were also saved in PDB format for subsequent analysis. The docking complexes formed between the ligands and the 5-HT7 receptor were visualized and analyzed using Discovery Studio Visualizer (BIOVIA). Interactions were assessed based on hydrogen bonding, hydrophobic contacts, van der Waals forces, and the presence of any unfavourable interactions during complex formation. This procedure was uniformly applied to all selected phytochemicals as well as standard drugs used in the treatment of Parkinson’s diseases for comparative binding analysis against the 5-HT7 receptor.

RESULTS AND DISCUSSION

The serotonin 5-HT7 receptor, which is essential for the regulation of mood, anxiety, and motor symptoms associated with Parkinson's disease (PD), was the focus of this investigation. The interaction dynamics of approved medications and specific phytocompounds were examined. A multi-step *In silico* analysis was performed, commencing with the preparation of ligand and receptors, and proceeded by molecular docking, energy calculations, and interaction characterization.

Information Regarding the Target Protein and Ligand- The serotonin 5-HT7 receptor (PDB ID: T79062), the selected target protein, is involved in the pathogenesis of PD and related neuropsychiatric symptoms (Table 1). A variety of standard pharmaceuticals and phytochemicals were docked against this receptor, including compounds identified from GC-MS analysis and reported anti-Parkinsonian drugs. The PubChem IDs, 2D and 3D structures, and reported pharmacological activities of these ligands are summarized in Tables 2 and 3, respectively. Table 4 displays the reference standards for Parkinson's disease-approved medications. Hydrogen bonding and molecular interactions are essential factors in the stability and specificity of ligand-receptor interactions. Benzo[b]thiophene-3-carboxylic acid exhibited robust hydrogen bonding with three residues of the 5-HT7 receptor: ARG392 and ARG396 (Figure 1 and 2), with bond distances ranging from 2.07 to 3.01 Å (Table 5). Tropigline also demonstrated robust conventional hydrogen bonding with ARG367 (Figure 3 and 4), which indicates a favourable receptor interaction. Conversely, ARG396 established a weakened carbon-hydrogen bond with Succinic acid (Figure 5 and 6), non-4-enyltetradecyl ester. Hydrophobic interactions additionally bolstered the binding's stability. For example, TYR395 and ALA385 interacted with Benzo[b]thiophene-3-carboxylic acid through pi-sulfur and pi-alkyl bonds, respectively (Table 61). Tropigline and β-bisabolene exhibited numerous alkyl and pi-alkyl interactions with residues, including ILE159, LEU232, and PHE158.

Binding Energy and Docking Scores The selected ligands exhibited a variety of binding affinities, as indicated by the docking simulations (Table 6). Tropigline outperformed the reference ligand Benzo[b]thiophene-3-carboxylic acid (−6.8 kcal/mol) by exhibiting the strongest binding to the 5-HT7 receptor, with a binding energy of −7.4 kcal/mol and numerous hydrophobic and hydrogen bonding interactions. In contrast, succinic acid exhibited a less favorable energy profile (Figure 5 and 6), limited hydrogen bonding, and a weakened binding (−6.1 kcal/mol). Bicyclo[3.1.1]heptane, 6,6-dimethyl-2- weaker binding energies and low ligand efficiency (Figure 7 and 8). Table 8 displays the docking energies of specific compounds. Benzo[b]thiophene (Figure 1 and 2) derivatives, Tropigline (Figure 3 and 4), and β-bisabolene (Figure 13 and 14) exhibited relatively higher docking scores, suggesting their potential affinity for the 5-HT7 receptor. Pimavanserin, a standard drug that is a well-known 5-HT2A receptor antagonist, exhibited a binding energy of −5.8 kcal/mol with the 5-HT7 receptor (Figure 15 and 16). This is particularly noteworthy. It was included to contextualize the docking outcomes of experimental ligands, despite its limited hydrogen bonding.

Interaction Classifications and Residue Involvement The analysis of polar and non-polar residues involved in ligand binding (Table 7) revealed that ligands forming interactions with important polar residues, such as ARG392, ARG396, and TYR395, exhibited enhanced binding affinity. Conversely, non-polar interactions, although beneficial, were insufficient to guarantee robust binding independently. For example, β-Myrcene (Figure 9 and 10) and D-Limonene (Figure11 and 12) exhibited weaker binding energies and low ligand efficiency due to their reliance on hydrophobic contacts with PHE344 and the absence of polar interactions.

Drug Potential and Comparative Interaction Profile Table 9 confirms that Tropigline and Benzo[b]thiophene-3-carboxylic acid demonstrated superior interaction profiles with the 5-HT7 receptor, as evidenced by a comparative analysis of binding affinities and molecular interactions. Their binding was characterized by the formation of numerous hydrogen and hydrophobic bonds with functionally significant residues, including ARG367, ARG392, and TYR395. These interactions imply a potential therapeutic mechanism through serotonergic modulation. In contrast, natural compounds such as β-Myrcene and D-Limonene exhibited feeble binding energies (−5.7 to −5.6 kcal/mol) and limited interactions, suggesting a lower therapeutic potential.

Standard Drug Comparison: The molecular docking profile of Pimavanserin against the 5-HT2A receptor (Table 10) was used as a benchmark. Although its interaction profile provided insights into the pharmacophoric features required for optimal binding, its binding affinity with the 5-HT7 receptor was comparatively weaker. The significance of these residues in serotonergic modulation was underscored by the compound's formation of hydrogen bonds with GLN235 and ASP236 and hydrophobic contacts with PHE352.

CONCLUSION

The docking results provide substantial evidence supporting the potential of certain phytocompounds, particularly Tropigline and Benzo[b]thiophene-3-carboxylic acid, as promising modulators of the 5-HT7 receptor. These ligands showed favorable binding energies, strong hydrogen bonding, and stable hydrophobic interactions, indicating their suitability for further pharmacological evaluation in the context of Parkinson's disease. Their performance was comparable or superior to known serotonergic drugs in terms of docking metrics. Future work should focus on validating these findings through in vitro and in vivo models to confirm efficacy and safety.

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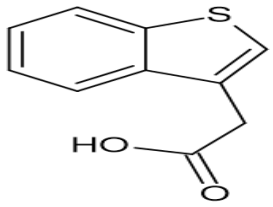
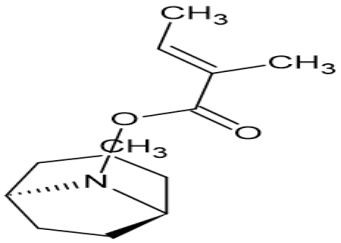
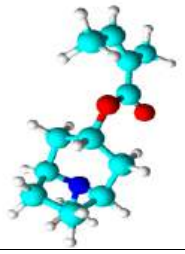
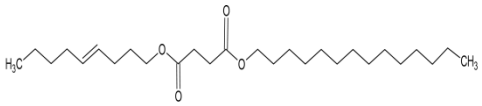
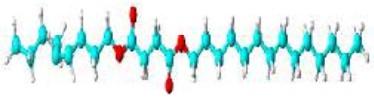
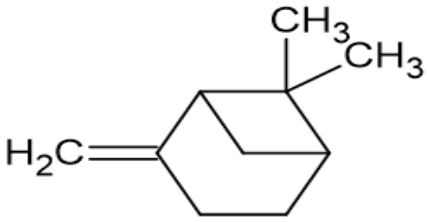
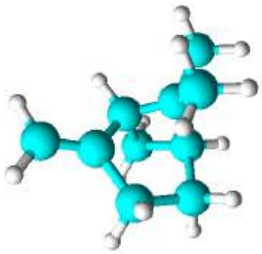
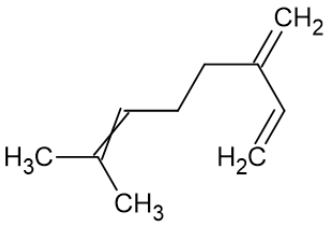
Table 1: Taget proteins , their Id and related diseases

S. No	Protein target	Target ID	Synonyms	Related Disease
1	**5 HT 7 receptor**	T79062	**Serotonin receptor** 7, 5HT7; 5-hydroxytryptamine receptor 7; 5-HT7 receptor; 5-HT7; 5-HT-X; 5-HT-7	Parkinson disease

Table 2: List of compounds with their 2D and 3D structures.

S.No	Compound Name	2D	3D
1	Benzo[b]thiophene-3-carboxylicacid,7-acetoxy-2-acet		
2	Tropigline		
3	Succinicacid,non-4-enyltetradecyl ester		
4	Bicyclo[3.1.1]heptane, 6,6-dimethyl-2-		
5	beta.-Myrcene		

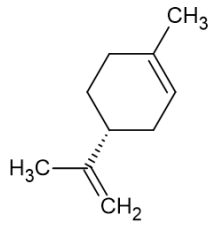
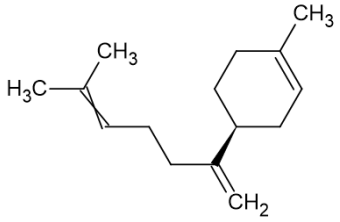
6	D-Limonene		
7	beta.-Bisabolene		

Table 3: Compounds list, their Pubchem id, SMILES and their reported applications.

S.No	Compound Name	Pubchem id and SMILES	Applications
1	**Benzo[b]thiophene-3-carboxylicacid,7-acetoxy-2-acet**	Pub chem. Id- 70799 C1=CC=C2C(=C1)C(=CS2)CC(=O)O	anti-cancer, Anti-microbial, anti-oxidant, anti-inflammatory, anti-diabetic, anti-convulsant and anti-tubercular activity
2	**Tropigline**	Pub chem. Id-12444363 C/C=C(\C)/C(=O)OC1C[C@H]2CC[C@@H](C1)N2C	Alkaloid found in Withania somnifera, it can bind with SARS CoV -2 and human targeted proteins.
3	**Succinicacid,non-4 enyl tetradecylester**	O=C(OCCCCCCCCCCCCCCC)CCC(=O)OCCC\C=C\CCCC	Used as neutraceutical, radiation protective and anti ulcer drug
4	**Bicyclo[3.1.1]heptane, 6,6-dimethyl-2-**	Pub chem. Id- 14896 CC1(C2CCC(=C)C1C2)C	Neuroprotective compound, anti Parkinson and anti Alzheimer's activity. Selective Prostaglandin D_2 Receptor
5	**beta.-Myrcene**	Pub chem. Id-31253 CC(=CCCC(=C)C=C)C	Anti oxidant, anti inflammatory, anti-aging, analgesic

			effects , Cardio protective effect
6	**D-Limonene**	Pub chem. Id- 440917 CC1=CC[C@@H](CC1)C(=C)C	Effective against cancer, bronchitis and obesity
7	**beta.-Bisabolene**	Pub chem. Id- 10104370 CC1=CC[C@H](CC1)C(=C)CCC=C(C)C	Anti cancer , can be used to treat breast cancer

Table 4: Approved drugs for Parkinson's disease treatment with their SMILES structure, 2D and 3D structure.

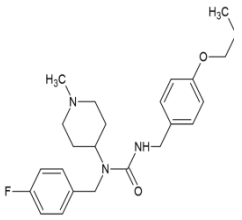
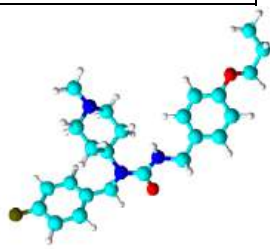
Drug Name	SMILES	2D	3D
Pimavanserin	CC(C)COC1=CC=C(C=C1)CNC(=O)N(CC2=CC=C(C=C2)F)C3CCN(CC3)C		

Table 5 : Hydrogen Bond Donor-Acceptor Linkages of Ligands with Target Proteins.

Ligand	Target Protein	Donor → Acceptor (Amino Acid - Atom → Ligand - Atom)	Distance (Å)	Bond Type
Benzo[b]thiophene-3-carboxylic acid	**5-HT7 Receptor**	R:ARG392:HH21 → UNL1:O	3.01553	Conventional Hydrogen Bond
		R:ARG396:HE → UNL1:O	2.07328	Conventional Hydrogen Bond
		R:ARG396:HH11 → UNL1:O	2.12454	Conventional Hydrogen Bond
Tropigline	**5-HT7 Receptor**	R:ARG367:HH12 → UNL1:O	1.96221	Conventional Hydrogen Bond
		R:ARG367:HH22 → UNL1:O	1.94966	Conventional Hydrogen Bond
Succinic acid, non-4-enyltetradecyl ester	**5-HT7 Receptor**	R:ARG396:HA → UNL1:O	2.40763	Carbon Hydrogen Bond

Table 6: Binding Energy, Energy Differences, and Molecular Interactions of Ligands

Ligand	Binding Energy (kcal/mol)	Δ Binding Energy (kcal/mol)	Molecular Interactions	Inference
Benzo[b]thiophene-3-carboxylic acid	-6.8	0.0 (Reference)	Hydrogen Bonds: 3 Hydrophobic: 3	Moderate binding, stable conformation
Tropigline	-7.4	-0.6	Hydrogen Bonds: 2 Hydrophobic: 3	Stronger binding than reference
Succinic acid, non-4-enyltetradecyl ester	-6.1	+0.7	Hydrogen Bonds: 1 Hydrophobic: 4	Weaker interaction than reference

Bicyclo[3.1.1]heptane, 6,6-dimethyl-2-	-5.9	+0.9	No Hydrogen Bonds Hydrophobic: 3	Weak binding, mostly hydrophobic
β-Myrcene	-5.7	+1.1	No Hydrogen Bonds Hydrophobic: 2	Weak binding, lacks strong interactions
D-Limonene	-5.6	+1.2	No Hydrogen Bonds Hydrophobic: 2	Weak binding, non-polar interactions
β-Bisabolene	-5.8	+1.0	No Hydrogen Bonds Hydrophobic: 3	Weak binding, non-polar interactions

Table 7: Classification of Polar and Non-Polar Molecules Involved in Ligand-Protein Interactions

Ligand	Target Protein	Polar Molecules Involved	Non-Polar Molecules Involved
Benzo[b]thiophene-3-carboxylic acid	**5-HT7 Receptor**	ARG392 (HH21, HE, HH11) TYR395 (S)	ALA385, PHE386
Tropigline	**5-HT7 Receptor**	ARG367 (HH12, HH22)	ILE159, LEU232, PHE158
Succinic acid, non-4-enyltetradecyl ester	**5-HT7 Receptor**	ARG396 (HA)	PHE386, TYR395
β-Myrcene	**5-HT7 Receptor**	No Polar Interactions	PHE344
D-Limonene	**5-HT7 Receptor**	No Polar Interactions	PHE344
β-Bisabolene	**5-HT7 Receptor**	No Polar Interactions	PHE158

Table 8: Docking scores of some important molecules (observed during GCMS analysis) against 5HT 7 receptor

5HT7 Receptor docking with compounds	Binding Energy	No. Of Hdrogen bonds	Inhibition constant	Ligand efficiency	Intermolecular energy	vdW + H bond+desolv energy	Electrostatic energy	Torsional energy	Total internal unbound
Pimavanserin approved drug for 5HT 2A Receptor	-5.8	-	55.7	-0.19	-8.19	-7.93	-0.26	2.39	-1.21
Benzo(b) thiopene 3 carboxylic acid, 7 acetoxy2 acet	**-6.65**	**2**	**13.28**	**-0.51**	**-7.55**	**-5.74**	**-1.81**	**0.89**	**-0.04**
Tropigline	**-6.4**	**2**	**20.38**	**-0.4**	**-7.29**	**-6.95**	**-0.35**	**0.89**	**-029**
Succinicacid, non-4-enyltetradecyl ester	**-2.15**	**-**	**26.54**	**-0.07**	**-9.61**	**-9.64**	**0.03**	**7.46**	**-3.85**
Bicyclo[3.1.1]heptane, 6,6-dimethyl-2-	**-6.23**	**-**	**27.34**	**-0.62**	**-6.23**	**-6.22**	**-0.01**	**0.0**	**0.0**

beta.-Myrcene	**-4.31**	**-**	**688.17**	**-0.43**	**-5.51**	**-5.5**	**0.0**	**1.19**	**-0.22**
D-Limonene	**-4.98**	**-**	**222.51**	**-0.5**	**-5.28**	**-5.27**	**-0.01**	**0.3**	**-0.13**
beta.-Bisabolene	**-6.62**	**-**	**14.12**	**-0.44**	**-7.81**	**-7.8**	**-0.01**	**1.19**	**-0.43**

Table 9: Comparative Binding Affinity and Molecular Interaction Analysis

Ligand/Drug	Target Protein	Binding Energy (kcal/mol)	Hydrogen Bonds	Hydrophobic Interactions	Key Residues Involved
Tropigline	**5-HT7 Receptor**	**-7.4**	2	3	ARG367, ILE159, LEU232
Benzo[b]thiophene-3-carboxylic acid	**5-HT7 Receptor**	**-6.8**	3	2	ARG392, ARG396, TYR395
Succinic acid, non-4-enyltetradecyl ester	**5-HT7 Receptor**	**-6.1**	1	3	ARG396, PHE386, TYR395
β-Myrcene	**5-HT7 Receptor**	**-5.7**	0	2	PHE344
D-Limonene	**5-HT7 Receptor**	**-5.6**	0	2	PHE344
β-Bisabolene	**5-HT7 Receptor**	**-5.8**	0	3	PHE158
Pimavanserin (Proven Drug)	**5-HT7 Receptor**	**-9.1**	**3**	**4**	GLN235, ASP236, PHE352

Table 10: Binding Energy and Molecular Interaction Summary of Standard drug with target proteins.

Drug Name	Target Protein	Binding Energy (kcal/mol)	No. of Hydrogen Bonds	Inhibition Constant (Ki)	Ligand Efficiency	Intermolecular Energy	vdW + H bond + Desolv Energy	Electrostatic Energy	Torsional Energy	Unbound Energy
Pimavanserin	5-HT2A receptor (HTRT2A)	**-5.8**	**0**	**55.7 μM**	**0.19**	**-8.19**	**-7.93**	**-0.26**	**2.39**	**-1.21**

Table 11: Hydrophobic Interactions of Ligands with Target Proteins

Ligand	Target Protein	Amino Acid - Atom → Ligand - Atom	Distance (Å)	Type of Bond
Benzo[b]thiophene-3-carboxylic acid	**5-HT7 Receptor**	R:TYR395 → UNL1	4.98966	Pi-Sulfur

		R:ALA385 → UNL1	5.32226	Pi-Alkyl
Tropigline	**5-HT7 Receptor**	R:ILE159 → UNL1	4.96363	Alkyl
		R:LEU232 → UNL1	4.52793	Alkyl
Succinic acid, non-4-enyltetradecyl ester	**5-HT7 Receptor**	R:PHE386 → UNL1	4.47324	Pi-Alkyl
β-Myrcene	**5-HT7 Receptor**	R:PHE344 → UNL1	4.76431	Pi-Alkyl
β-Bisabolene	**5-HT7 Receptor**	R:PHE158 → UNL1	4.84862	Pi-Alkyl

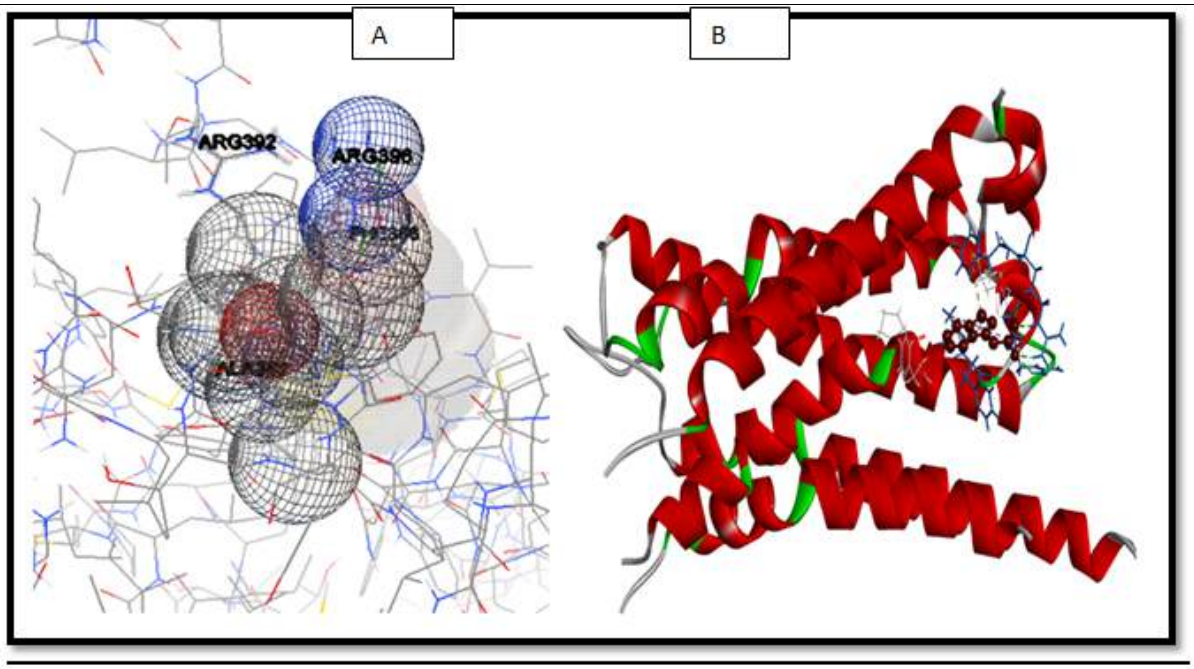


Figure 1 A and B- Benzo[b]thiophene-3-carboxylicacid,7-acetoxy-2-acet and 5 HT 7 receptor interaction

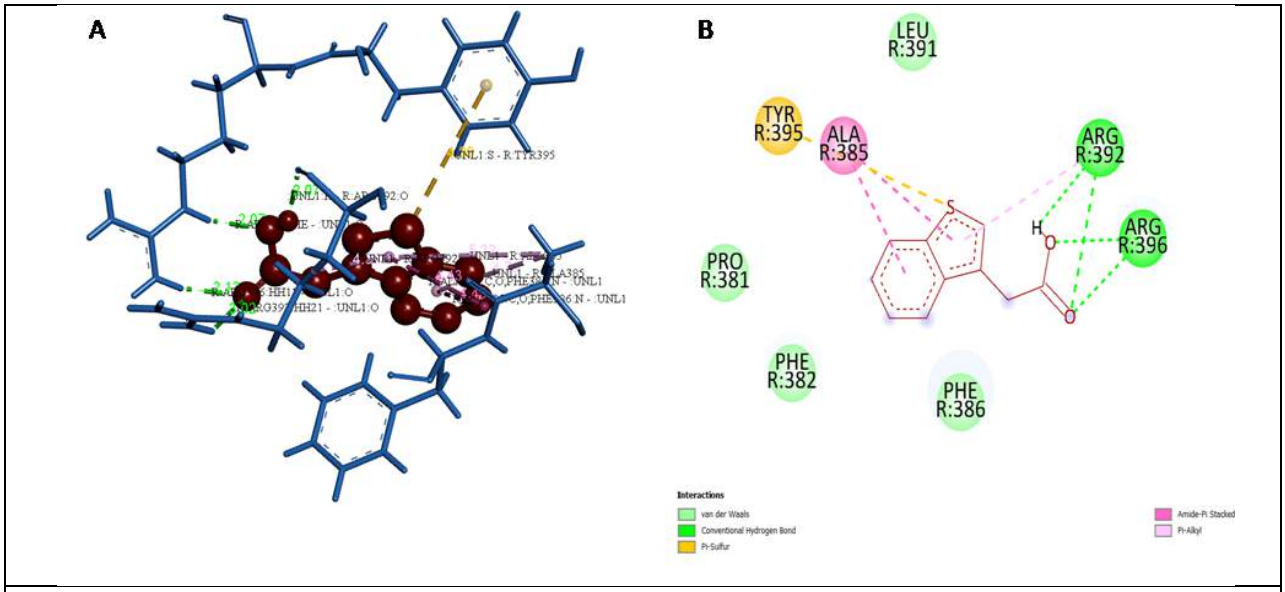


Figure 2 (A) and B - 5 HT 7 receptor: Stick model (blue colour)- Benzo[b]thiophene-3-carboxylicacid,7-acetoxy-2-acet -Scaled ball and stick model (red colour) visualized using Biovia Discovery studio visualize. (B)- 2D Diagram – Benzo[b]thiophene-3-carboxylicacid,7-acetoxy-2-acet and key amino acid residue interactions

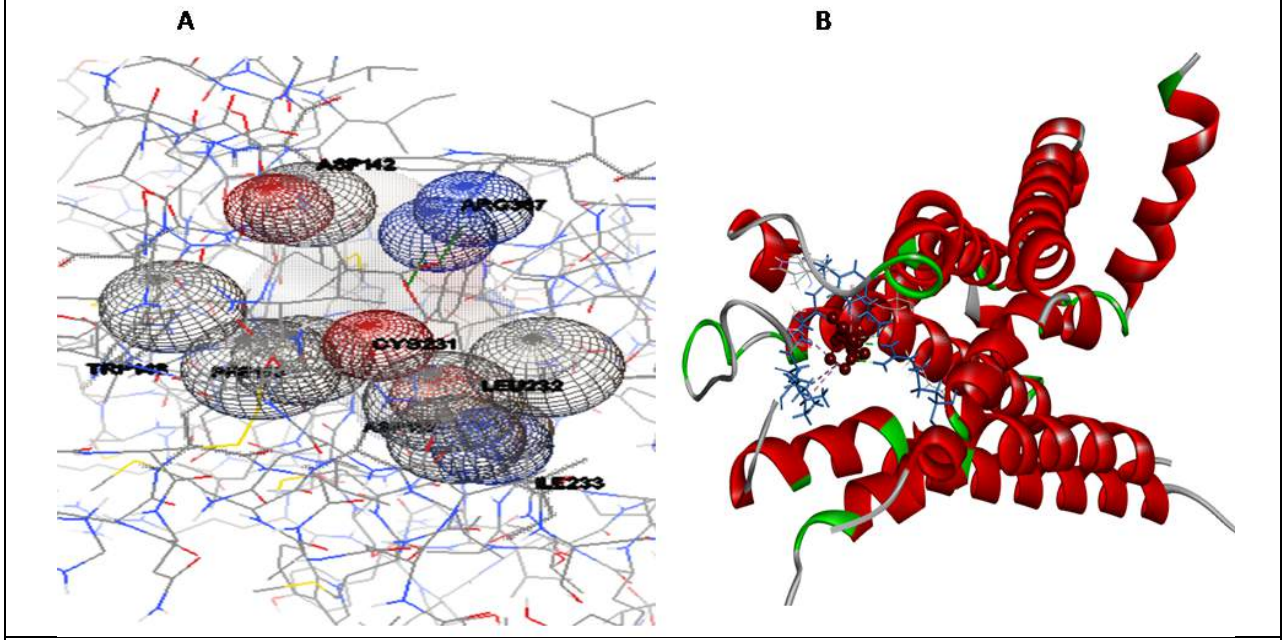


Figure 3 (A)- Tropigline and 5 HT 7 receptor Interaction. (B)- 5 HT 7 receptor: Solid ribbon model- Tropigline - Scaled ball and stick model

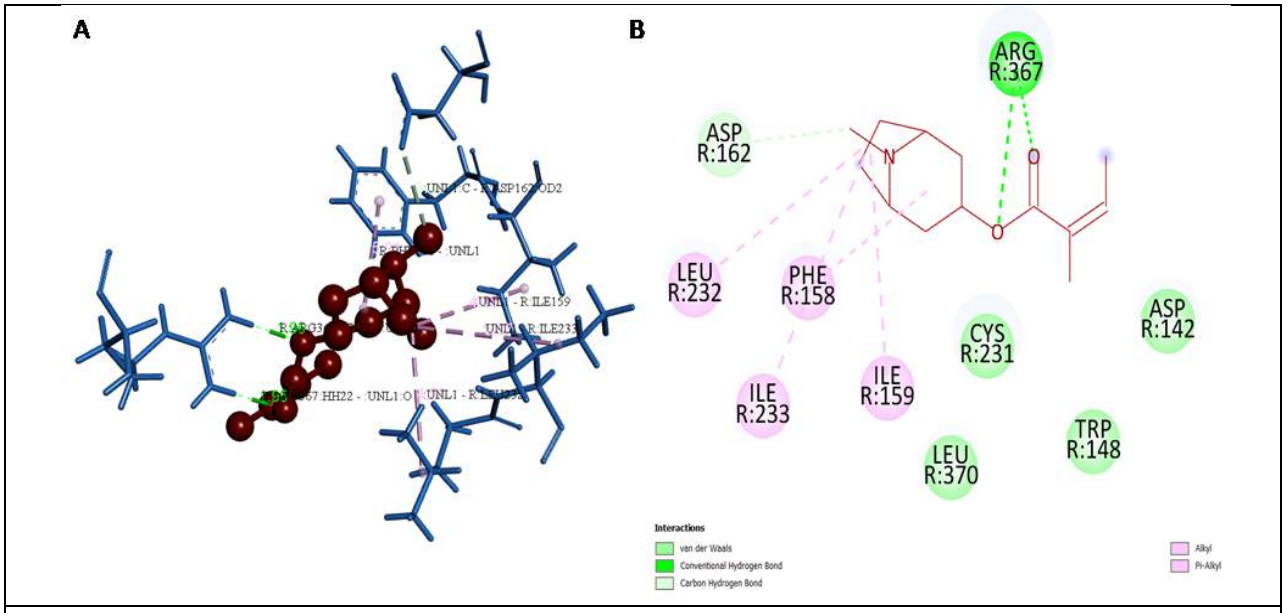


Figure 4 (A)- 5 HT 7 receptor: Stick model (blue colour)- Tropigline -Scaled ball and stick model (red colour) visualized using Biovia Discovery studio visualizer. (B)- 2D Diagram – Tropigline and key amino acid residue interactions

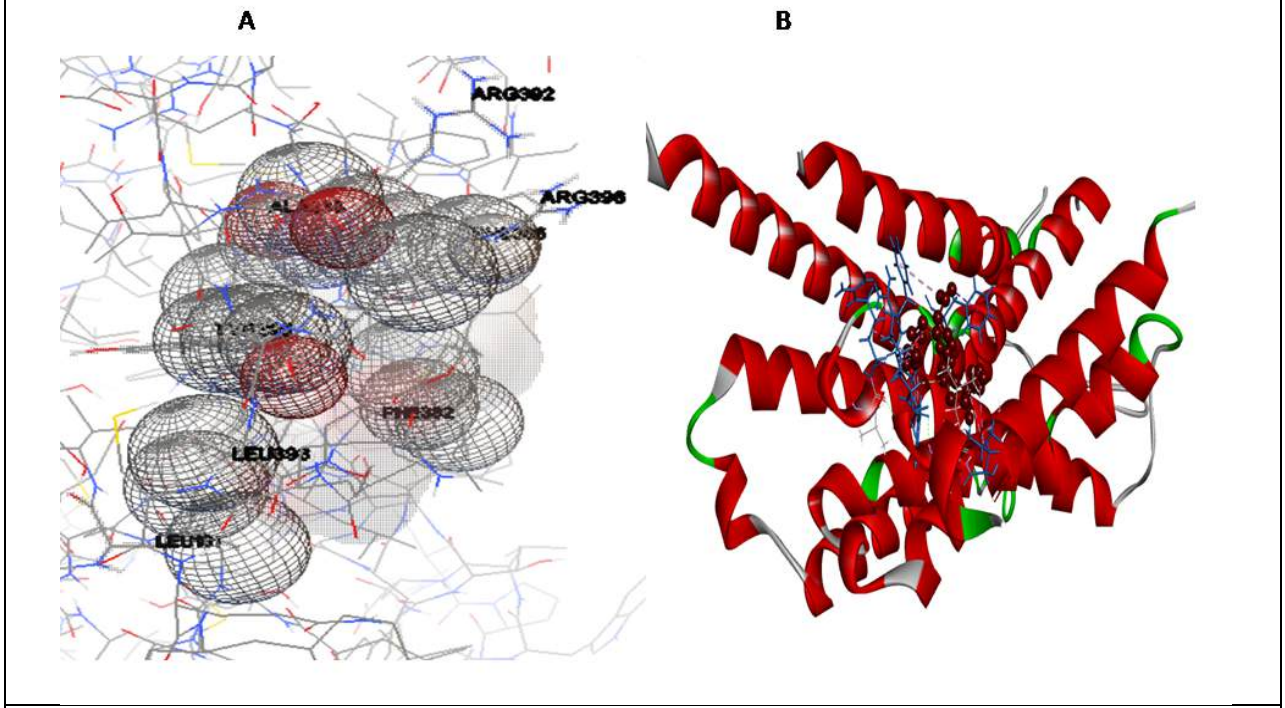


Figure 5: (A and B)- Succinic acid, non-4-enyltetradecyl ester and 5 HT 7 receptor interaction.

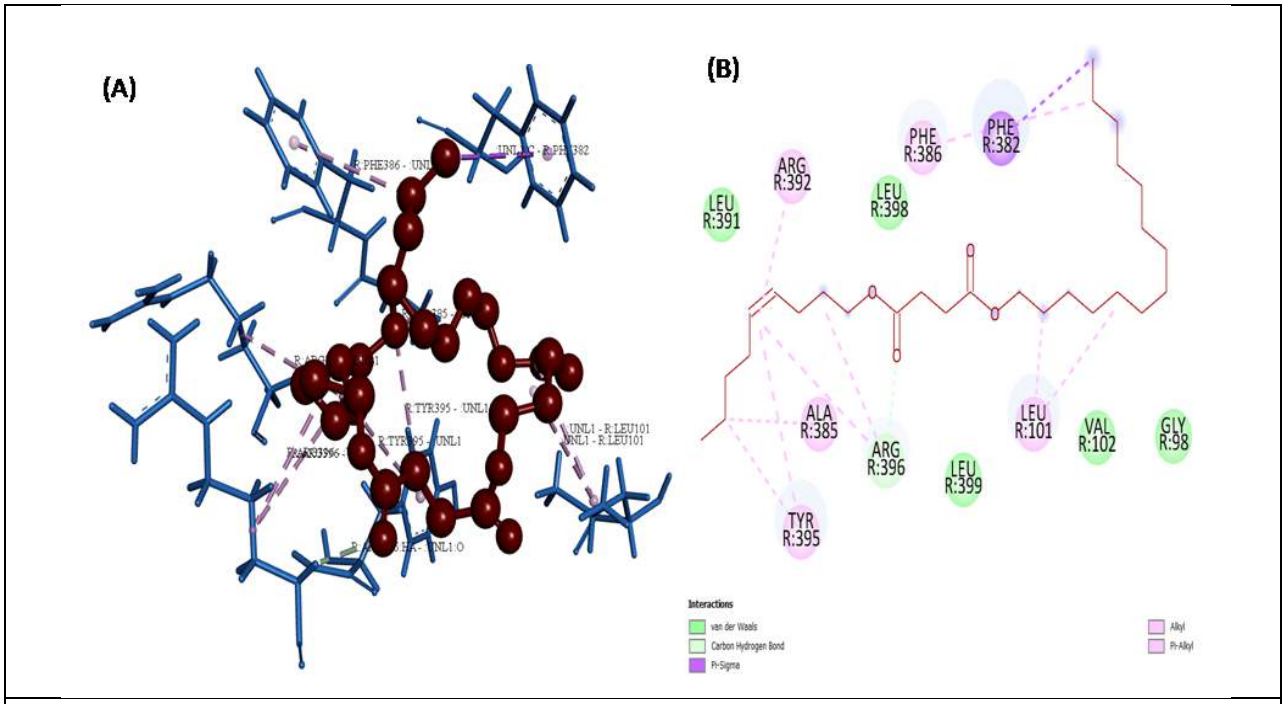


Figure 6: (A)- 5 HT 7 receptor: Solid ribbon model- Succinic acid, non-4-enyltetradecyl ester -Scaled ball and stick model, (B)- 2D Diagram – Succinic acid, non-4-enyltetradecyl ester and key amino acid residue interactions

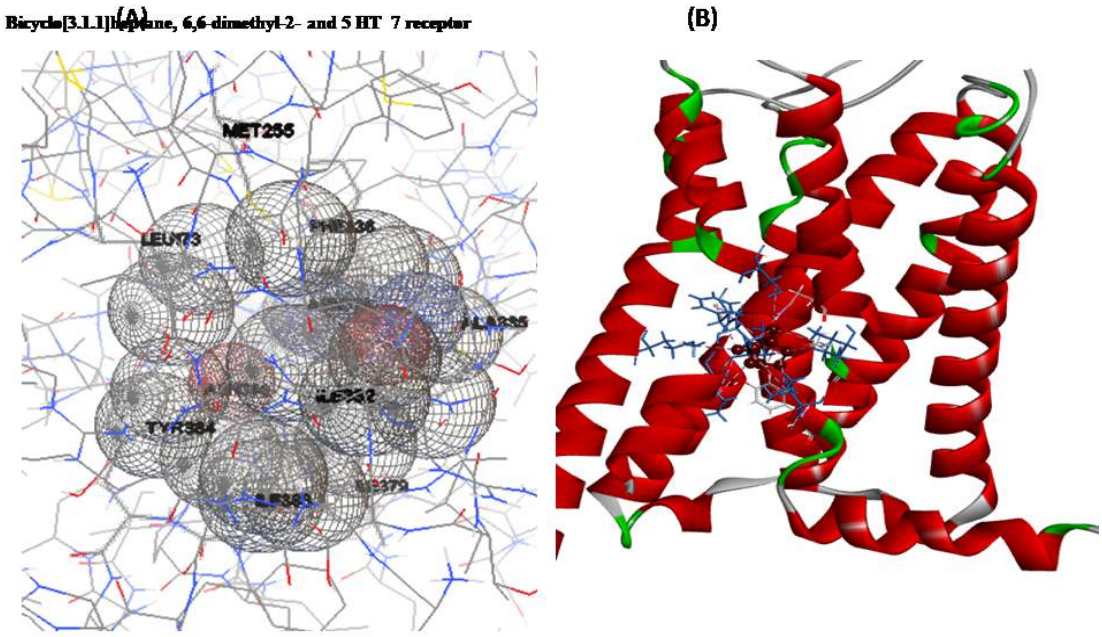


Figure 7: (A)-Bicyclo[3.1.1]heptane, 6,6-dimethyl-2- and 5 HT 7 receptor Interaction. (B)- 5 HT 7 receptor: Solid ribbon model- Bicyclo[3.1.1]heptane, 6,6-dimethyl-2- -Scaled ball and stick model

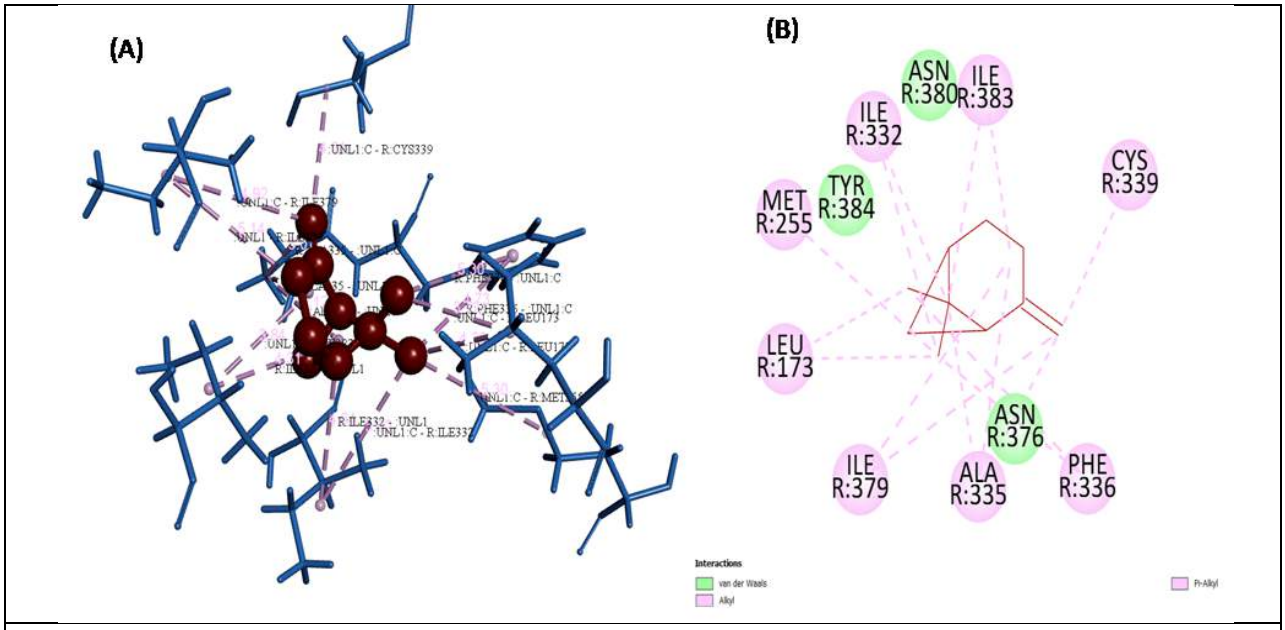


Figure 8: (A)- 5 HT 7 receptor: Stick model (blue colour)- Bicyclo[3.1.1]heptane, 6,6-dimethyl-2- -Scaled ball and stick model (red colour) visualized using Biovia Discovery studio visualizer. (B)- 2D Diagram – Bicyclo[3.1.1]heptane, 6,6-dimethyl-2- and key amino acid residue interactions

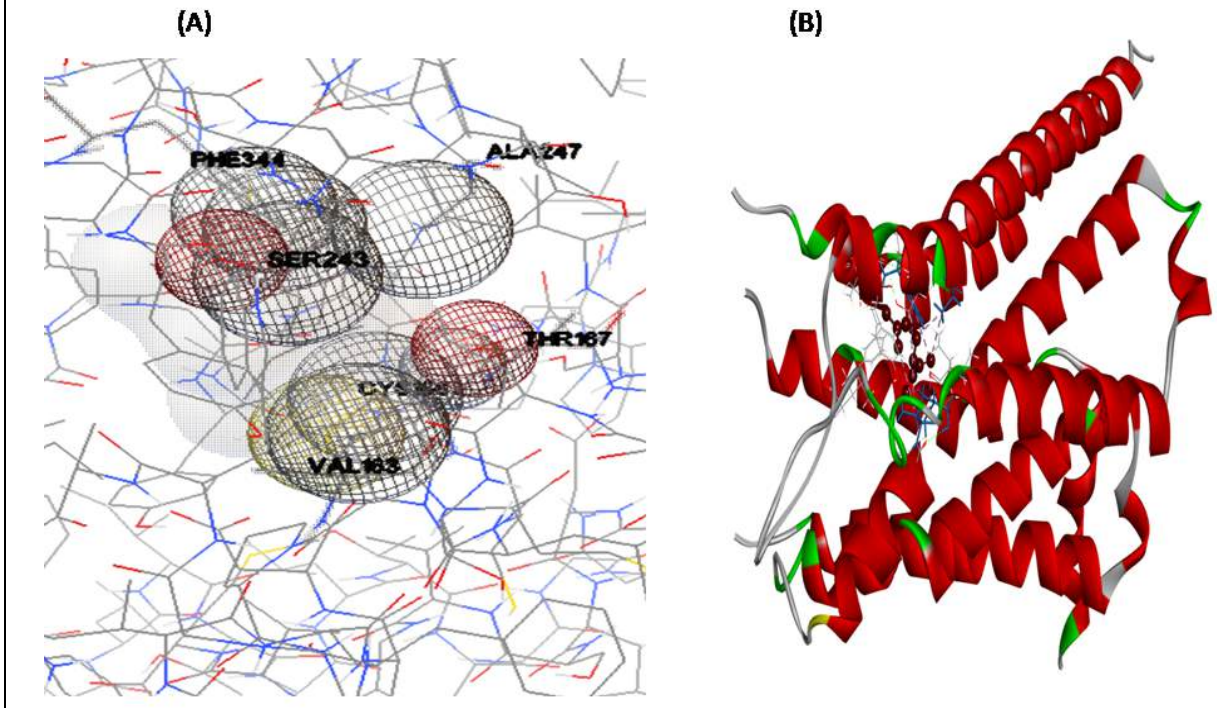


Figure 9 (A and B)- beta-Myrcene and 5 HT 7 receptor interaction.

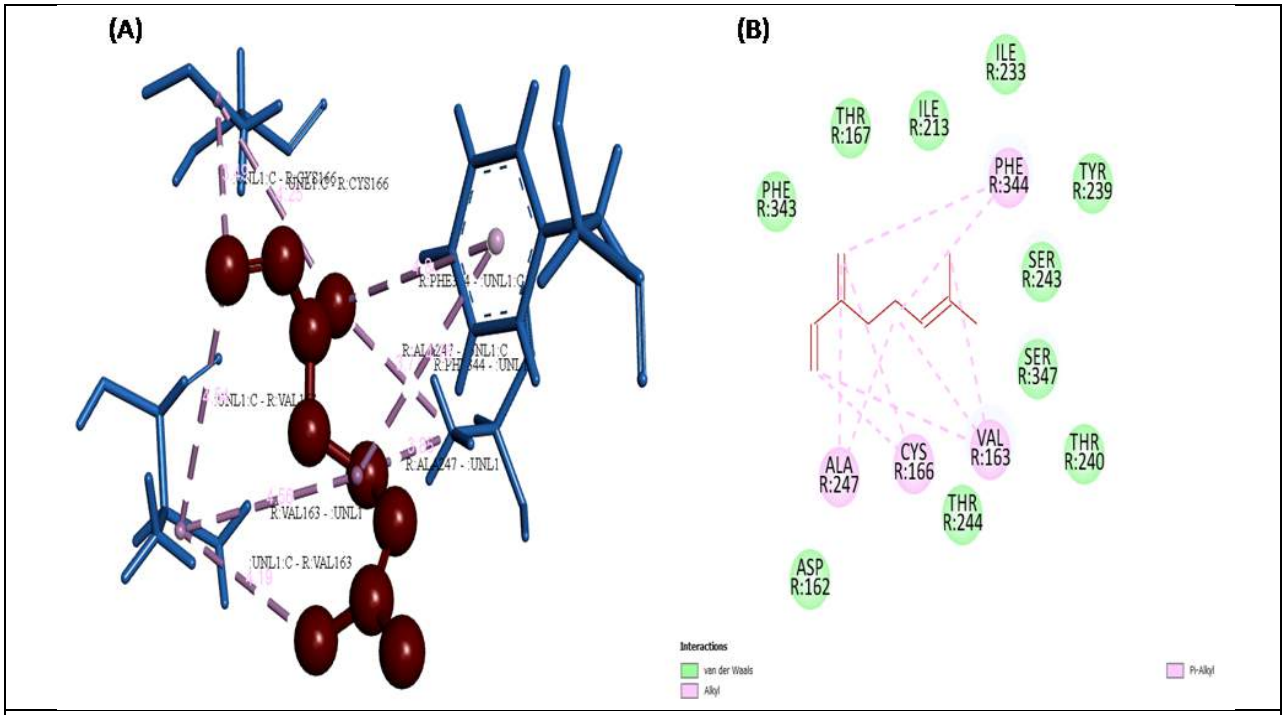


Figure 10 (A)- 5 HT 7 receptor: Stick model (blue colour)- beta-Myrcene -Scaled ball and stick model (red colour) visualized using Biovia Discovery studio visualizer. (B) - 2D Diagram – beta-Myrcene and key amino acid residue interactions

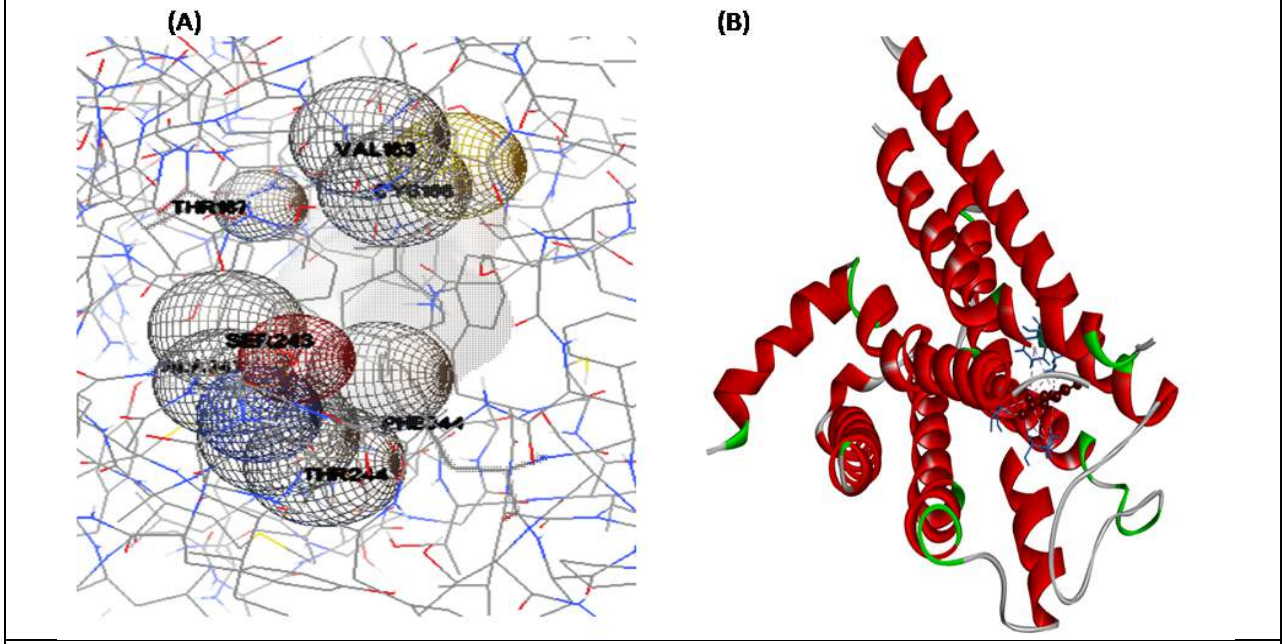


Figure 11: (A and B) - D-Limonene and 5 HT 7 receptor interaction.

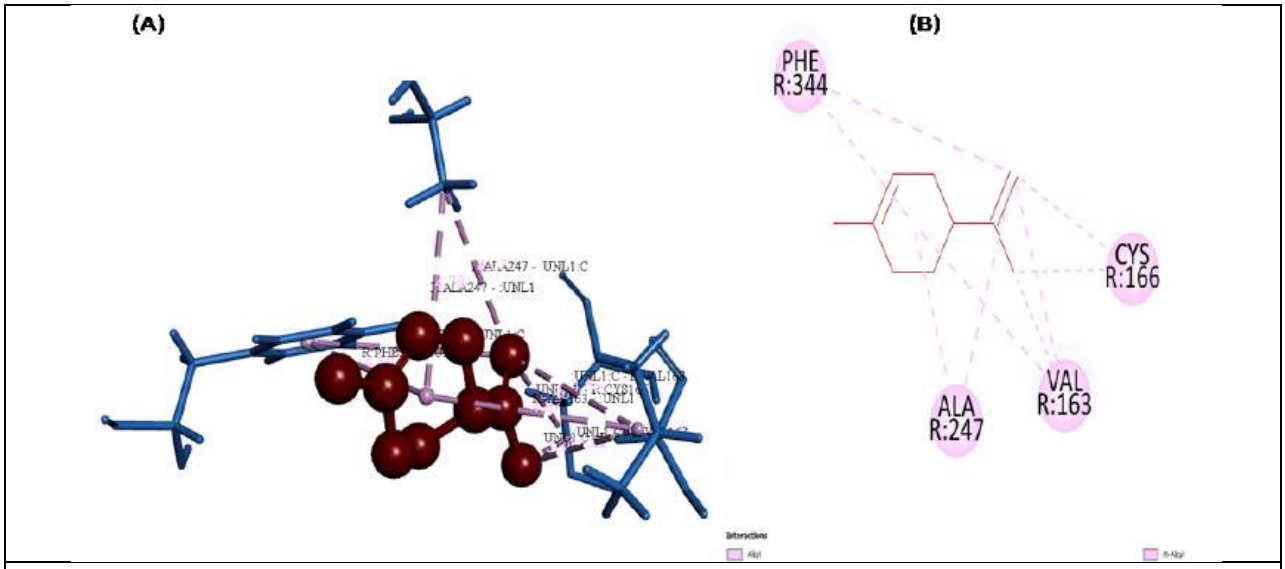


Figure 12 (A)- 5 HT 7 receptor: Stick model (blue colour)- D-Limonene -Scaled ball and stick model (red colour) visualized using Biovia Discovery studio visualizer. (B)- 2D Diagram – D-Limonene and key amino acid residue interactions

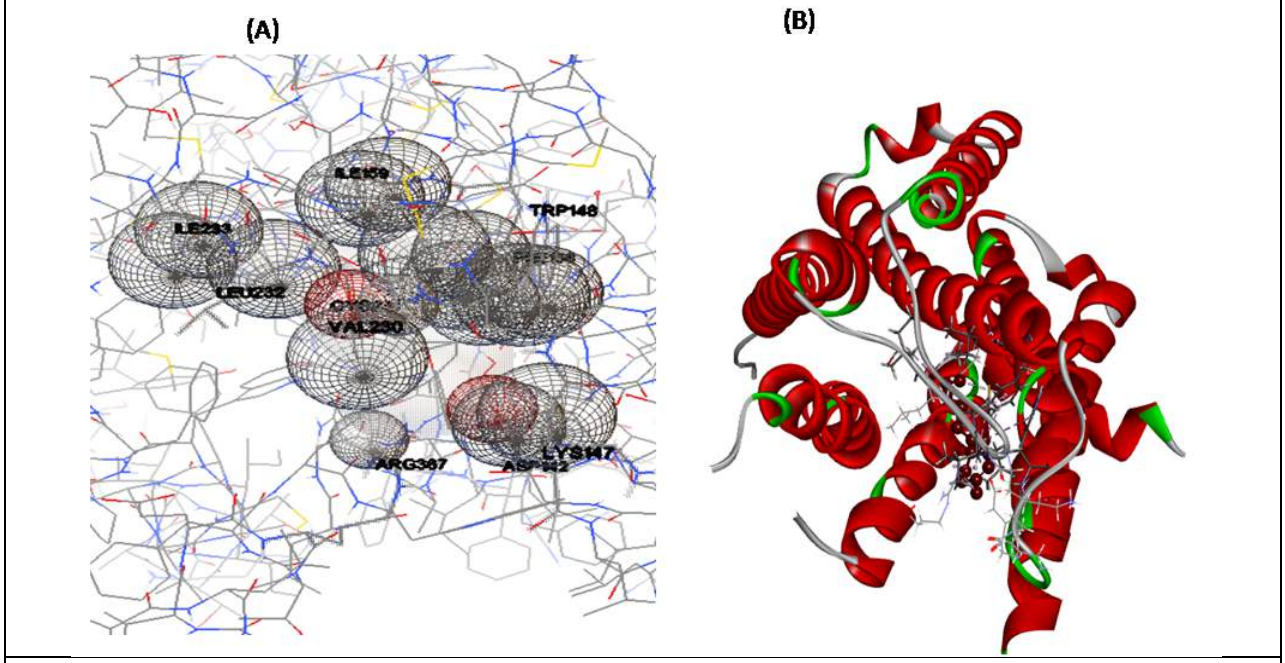


Figure 13 (A and B)- beta-Bisabolene and 5 HT 7 receptor interaction.

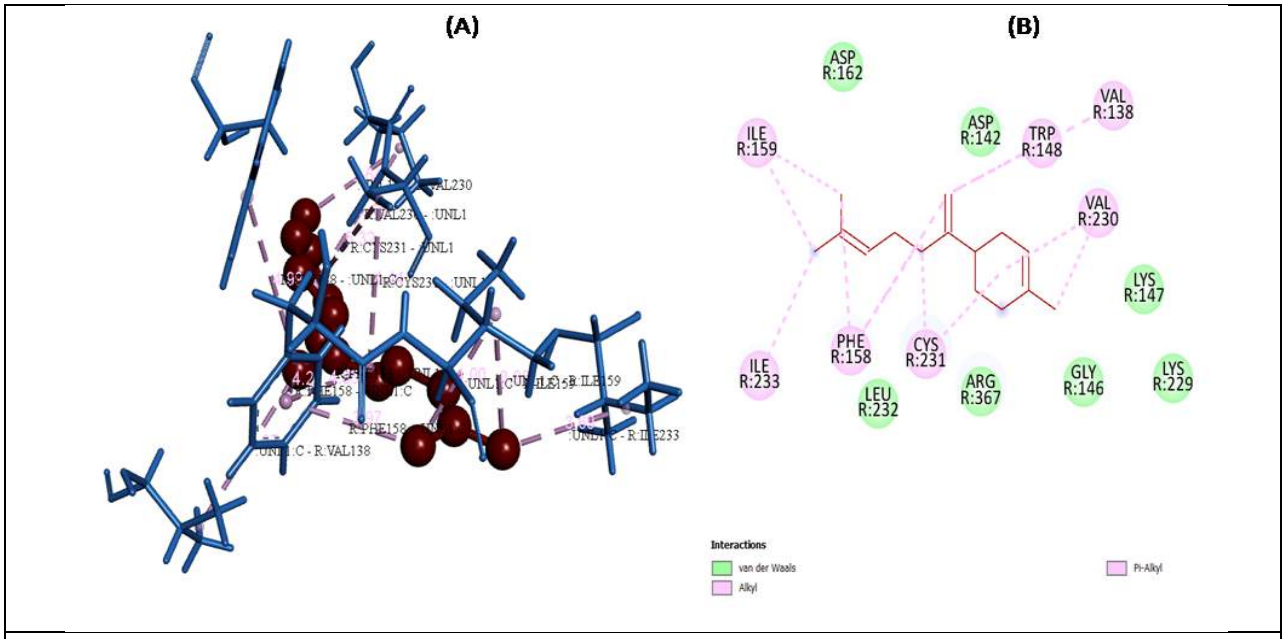


Figure 14 (A)- 5 HT 7 receptor: Stick model (blue colour)- beta-Bisabolene -Scaled ball and stick model (red colour) visualized using Biovia Discovery studio visualizer. (B) - 2D Diagram – beta-Bisabolene and key amino acid residue interactions

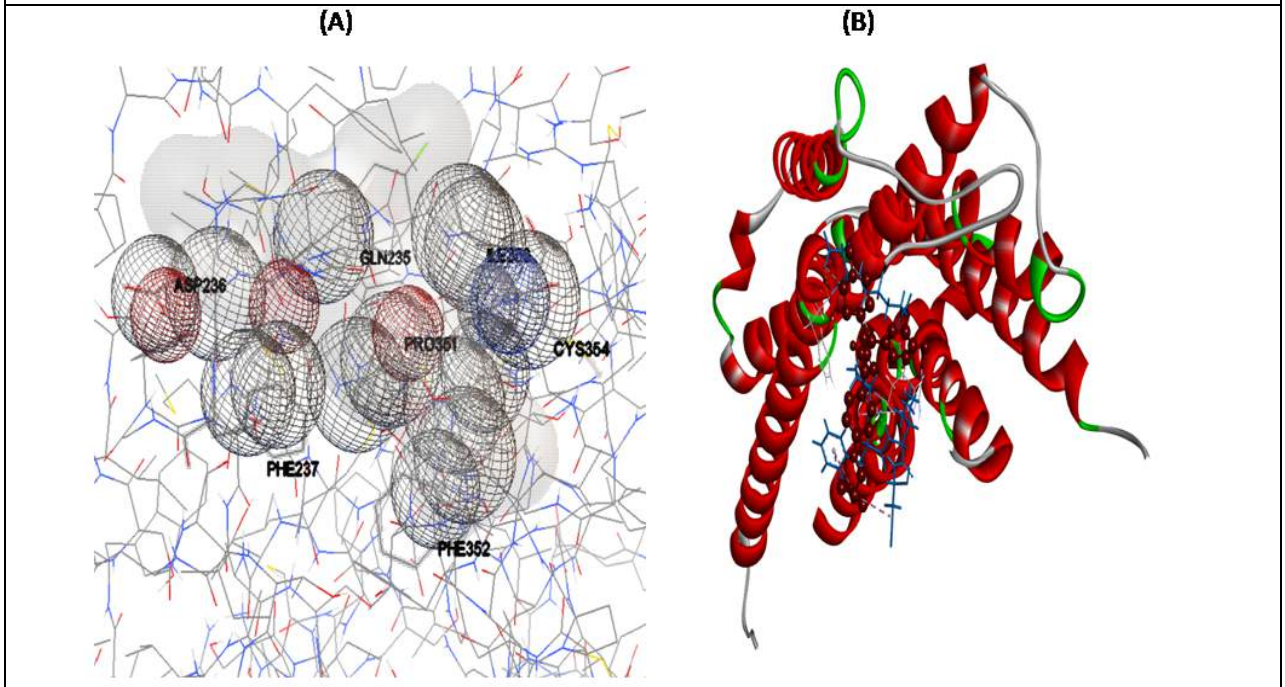


Figure 15 (A and B)- Pimavanserin and 5-HT 2A receptor (HTRT 2A) Interaction,

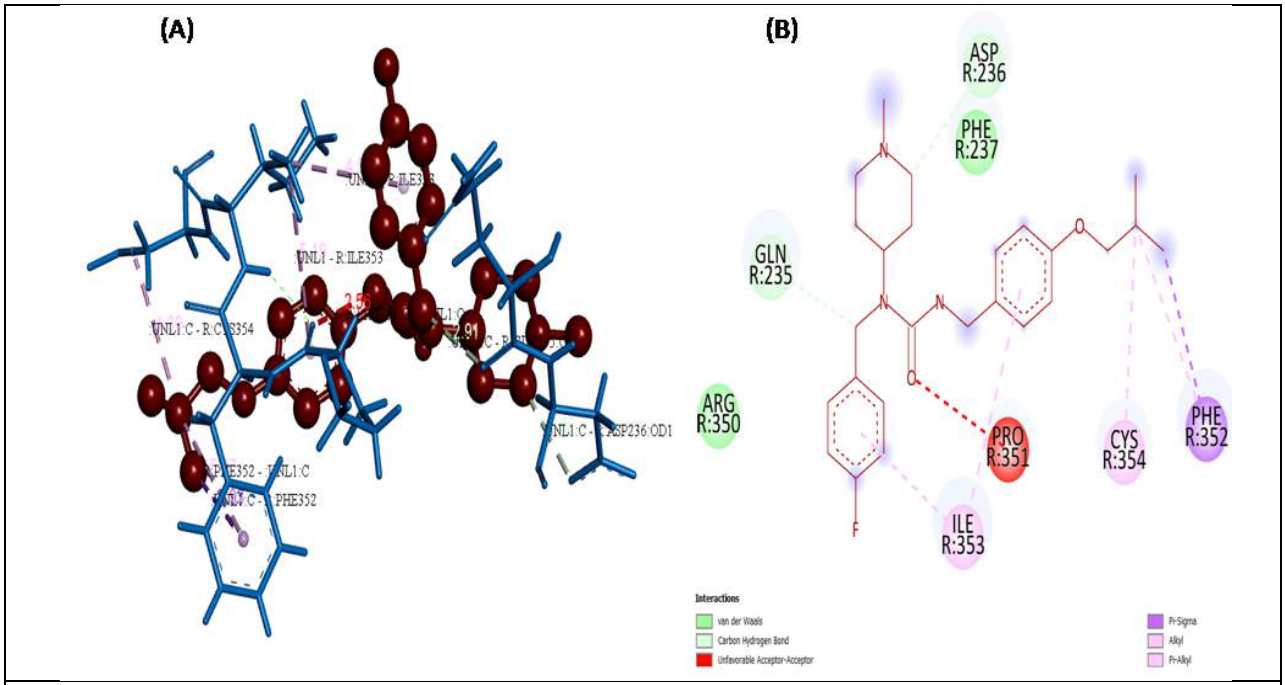


Figure 16 (A and B)- 5-HT 2A receptor (HTRT 2A): Stick model (blue colour)- Pimavanserin -Scaled ball and stick model (red colour) visualized using Biovia Discovery studio visualizer. (B)- 2D Diagram –Pimavanserin and key amino acid residue interactions

Indian Journal of Natural Sciences *www.tnsroindia.org.in ©IJONS*

Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

REVIEW ARTICLE

Daily Consumables in Ayurveda: A Classical and Modern Review on Nitya Sevaniya Dravya

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Received: 04 Oct 2025 Revised: 20 Dec 2025 Accepted: 09 Jan 2026

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ABSTRACT

Ayurveda underscores the significance of daily consumables, known as *Nitya Sevaniya Dravya*, as essential dietary components that support health, prevent diseases, and maintain balance in the *Tridoshas* (*Vata*, *Pitta*, and *Kapha*).Among these, *Amalaki* (*Emblica officinalis*) holds a special place due to its *Rasayana* (rejuvenating) and *Vayasthapana* (anti-aging) properties. Other important daily consumables include *Shashtika Shali* (rice), *Mudga* (green gram), *Saindhava Lavana* (rock salt), *Yava* (barley), *Antariksha Jala* (rainwater), *Go-ghrita* (cow's ghee), and *Madhu* (honey). This discussion explores their nutritional benefits, therapeutic uses, and ability to balance the *Tridoshas*, referencing classical *Ayurvedic* texts and contemporary scientific studies.

Keywords: Healthy diet, *Ahara*, *Nitya Sevaniya*, *Tridoshas* balance, Nutrition, *Nitya Rasayana*.

INTRODUCTION

In *Ayurveda*, the concept of *Traya upsthambha* is central, consisting of three foundational elements: *Brahmacharya* (celibacy), *Nidra* (sleep), and *Ahara* (diet)[1]. This study aims to highlight the importance of diet (*Ahara*) in today's world. *Ahara* is essential for maintaining the health, nourishment, and well-being of the body, mind, and soul. Food

is the only thing that can reduce the need for tissue renewal. According to the *Taittiriya Upanishad*, food serves as the foundation of the human body. The ancient sages taught that what, when, how, and where one consumes determines their nature and characteristics. Thus, individuals should consume fresh, nutritious, and easily digestible food. Proper and nourishing food satisfies all the senses. *Ayurveda* aims to maintain health for the healthy and treat illness for the unhealthy[2]. According to *Ayurveda*, any food item has specific properties, effects, and metabolic outcomes. These are classified as *Gunas*, *Veerya*, *Vipak*, and *Prabhav*, which together determine the overall effect of food. According to ancient knowledge, food can be used as medicine. The most important aspect of an *Ayurvedic* lifestyle is consuming the right amount of food, which supports a longer and healthier life. The saying "one man's food is another man's poison" shows that what is considered correct or suitable varies from person to person. Each individual may react differently to different types of food[3].

Nitya Sevaniya Ahara

Nitya Sevaniya Ahara refers to the food that should be consumed daily. It includes *Mudga* (green gram), *Saindhava Lavana* (rock salt), *Amalaki* (Indian gooseberry), *Varshajala* (rainwater), *Yava* (barley), *Madhu* (honey), *Go Ghritha* (ghee), *Jangala Mamsa* (wild meat), and *Shashtika Shali* (rice). In this context, *Ksheera* (milk) is also considered as part of *Nitya Sevaniya Ahara*, as mentioned in *Astanga Sangraha*. This is also described by *Acharya Charaka*.

MATERIAL AND METHOD

Details of *Amalaki* (*Emblica officinalis*) are provided in Table No. 1

Amalaki is a rich source of vitamin C and contains active components such as phyllemblin, gallic acid, tannins, pectin, and ascorbic acid. The high content of vitamin C in *Amalaki* helps replenish the body's energy. *Amalaki* has antioxidant, hepatoprotective, and anti-inflammatory properties. It is also effective in enhancing iron absorption. *Amalaki* is considered an excellent *Rasayana* that helps prevent premature aging and protects against diseases. It has been praised by *Acharya Charak* and *Acharya Vagbhata* as a preferred treatment for *Vayasthapana* (anti-aging)[4]. *Acharya Charak* has also described it as *Ayushya* (longevity), *Deepaniya* (appetite stimulant), and *Pachniya* (easily digestible)[5]. *Bhavprakash* and *Dhanwantri Nighantu* have also highlighted its *Rasayana* properties. *Amalaki* helps balance the *Tridoshas*, especially *Pitta*. *Vagbhata* mentions *Amalaki* as one of the best remedies for *Prameha* (diabetes), along with *Haridra* (turmeric)[6].

Details of *Shashtika Shali* (*Oriza sativum*) are provided in Table No. 2

Rice is known as the queen of cereal crops and is highly nutritious, containing carbohydrates, fats, fiber, proteins, vitamins, food energy, minerals, and fatty acids. It retains its outer bran layer, making it high in fiber and having a slightly nutty flavor. Fiber is important for regular bowel movements and overall digestive health. It may also aid in weight management, lowering cholesterol and blood pressure. The presence of anthocyanin in *Oriza sativum* has prebiotic activity by promoting the growth of beneficial bacteria like bifido and lactobacillus. *Shashtika Shali*, which is rice grown in 60 days, is the main source of energy (70–80%) and contributes significantly to protein, minerals, and B-group vitamins.Rice proteins are rich in lysine; an essential amino acid compared to other cereal proteins.

Details of *Mudga* (*Phaseolus mudga*) are provided in Table No. 3

Mudga, or green gram, is considered the best among *Shimbhi Dhanya* (cereals)[7]. It is rich in fiber (16g per 100g), especially soluble fiber pectin. The husks of *Mudga* resist *in-vitro* gastrointestinal digestion, meaning they contain non-digestible components that support the growth of beneficial gut microorganisms[8]. *Mudga* is a significant source of protein, with 25% of its composition being protein. However, its protein quality is lower than that of animal protein. It is also rich in minerals and B vitamins. *Mudga* is particularly high in iron (3.9 mg per 100g) and potassium (1150 mg per 100g). It is the best among pulses and is often used in soup form[9]. Many pulses have *Kapha-medohara* (fat-reducing) properties and are beneficial in cardiovascular diseases and obesity, as confirmed by modern research. Consuming legumes has been linked to a reduced risk of coronary heart disease and cardiovascular disease.

Details of *Saindhava Lavana* (Sodium chloride) are provided in Table No. 4

Saindhava Lavana enhances the body's ability to absorb minerals at the cellular level and helps restore the body's electrolyte balance and maintain the pH level[10]. This makes it useful for boosting metabolism. *Saindhava Lavana* is a clear and pure salt with a reddish white color and contains natural iron. It can increase appetite and enhance the flavor of food. It also has a minimal impact on water retention, making it suitable for individuals with heart conditions, high blood pressure, and kidney diseases[11]. According to *Acharya Charak*, among various types of salt, *Saindhava Lavana* is considered the best for internal use. It aids in eliminating toxic minerals and deposits of refined salt by improving circulation and balancing minerals. It also strengthens skin tissue, helping to rejuvenate the skin and make it appear younger and more firm. *Saindhava Lavana* improves appetite, enhances taste, improves digestion, and offers natural relief from stomach pain[12]. It provides all essential trace minerals and strengthens the immune system. It also regulates melatonin levels, which helps regulate the sleep cycle[13]. *Saindhava* is considered the best among salts, as it is easy to digest, promotes digestion, acts as an aphrodisiac, supports good eyesight, and helps balance the three *Doshas*[14]. *Saindhava* is known as *Rochana*, *Deepana*, and *Pachana*, and is used in cases of anorexia, constipation, and other digestive issues. It acts as a carrier and assists in delivering *Basti dravya* to the cellular level.

Details of *Yava* (*Hordeum vulgare*) are shown in Table No. 5.

Yava, or barley, is high in fiber (17g per 100g), particularly beta-glucan, which can reduce cholesterol and blood sugar levels. It may also assist in weight loss and improve digestion. The effects of barley beta-glucans on the growth and probiotic properties of four *Lactobacillus* strains are noted[15]. Barley is rich in potassium. It is considered *Mutrala* and *Kapha Shamaka* and is used in the treatment of obesity. It is widely used in *Ayurveda* and is classified under *Shukadhanya Varga*. Both as a dietary component and a medicinal herb, *Yava* has been recognized in ancient texts and modern research.

Details of *Antariksha Jala* are shown in Table No. 6.

Antariksha Jala has a neutral pH and aids in breaking down nutrients for better absorption. It has an alkaline pH and has detoxifying properties, which support healthy digestion. Daily intake of toxins and free radicals can make the blood more acidic. *Antariksha Jala*, with its alkaline nature, helps neutralize blood pH, allowing the body to function more efficiently. *Antariksha Jala*, or rainwater, is the primary source of water and the purest form of water found in nature. It is tasteless and has properties similar to nectar, being vital for life, satiating, maintaining the body, invigorating, and easing fatigue, lethargy, thirst, intoxication, fainting, drowsiness, sleep, and burning sensations. It is consistently beneficial for overall health.

Details of *Go-ghrita* are shown in Table No. 7.

Go-ghrita is one of the daily essential substances, according to the *Charaka Samhita*[16]. In Charaka Samhita, Ksheeraghrithabhyasa considered as the best *Rasayana* (rejuvenating substance) for daily use[17]. *Go-ghrita* is easily absorbed by the body due to its lipid-soluble nutrients. It is also beneficial in reducing *Pitta* and *Vata*, and it supports the balance of *Rasa*, *Shukra*, *Oja*, *Swara*, *Varna*, *Nirvapanam*, and *Sansakarasya Anuvartanam*[18].

Details of *Madhu* are shown in Table No. 8.

When consumed, honey becomes alkaline (with a pH range from 3.4 to 6). Unlike most sugars, raw honey is not known to irritate a sensitive digestive system. It is alkaline-forming, helping the body maintain a neutral and alkaline balance. Additionally, honey boosts beneficial gut bacteria (bifidogenic effects), aiding in detoxification and reducing toxic effects[19]. Honey contains 38% fructose, 31% glucose, 1% sucrose, and 9% other sugars, along with water, vitamins, minerals, and acids. It has been used as an antiseptic, reduces cholesterol, and helps prevent coronary artery disease and obesity[20]. Honey is a sweet fluid produced by bees from flower nectar. Most microorganisms do not thrive in honey due to its low water activity[21]. It possesses nutritive properties, and the fatty acids in honey promote peristalsis and digestion. It is beneficial for digestion and appetite in individuals with weak stomachs or loose bowels. It reduces flatulence and increases overall metabolism. Honey has also been used topically as an antiseptic for treating ulcers, burns, and wounds. Honey is considered the best *Yogavahi*, or carrier substance, helping to transfer the properties of other medicines[22]. It acts as a purifying and healing agent, able to reach the minute

channels of the body[23]. Honey is astringent, helps in reducing excessive fat, and is beneficial in managing obesity[24].

***JangalaMamsa* (meat)**

It is typically an acidic food and lacks fiber content. It plays an important role in meeting daily vitamin B12 requirements and is a rich source of complete protein (>20% of daily value), niacin, iron, and zinc. According to classical texts, *Jangala Mamsa* is constipative, cold in potency, easy to digest, nutritious, and is beneficial in cases of *Pittothara*, *Vata Madhya Kapahanuka Sannipata* (cases involving increased *Pitta*, moderately vitiated *Vata*, and *Kapha*).

DISCUSSION

Bagde *et al*. *Ayurveda* places great emphasis on *Aahara* as a key factor in maintaining health by balancing the *Tridoshas* and nourishing the body. The *Nitya Sevaniya Dravyas* philosophy emphasises the need of healthy eating on a daily basis. *Aahara* promotes physical strength, energy, and general well-being when taken in the right amounts; when taken in the wrong amounts, it can cause illness. Therefore, maintaining a healthy lifestyle and preventing sickness require regular consumption of nourishing foods. Thakur et. al. Through its ideas of *Swasthahita* (health-promoting) and *Nityasevaniya Dravyas* (daily consumable substances), *Ayurveda* provides a deep understanding of nutrition, emphasising its significance in preserving health and averting illnesses. By using tried-and-true dietary methods to treat *Kuposhanya Vikaras* (nutritional problems), incorporating *Ayurvedic* nutritional concepts into national nutrition programs could improve public health. *Ayurveda* offers a preventive strategy by encouraging the consistent use of *NityasevaniyaDravyas*, securing long-term health and balanced nutrition. S Deshmukh *et.al*. The *Nitya Sevaniya Aahara Dravya* (daily consumable foods) play a vital role in maintaining health. Among them, *Mudga* (green gram) stands out in *Shamidhanya* (pulses) for its high nutritional value and therapeutic properties like antioxidant, anti-hyperglycemic, and detoxifying effects. *Shashtika Shali* (rice) is the best in *Shukadhanya* (cereals), offering energy, vitamins, and minerals with immunomodulatory benefits. *Godhuma*(wheat) provides sustained energy and has antioxidant and gut-protective properties. *Godugdha*(cow's milk) and *Goghruta* (cow's ghee) are essential for vitality, immunity, and brain health, while *Saindhava* (rock salt) supports electrolyte balance without causing hypertension. *Amalaki* (Indian gooseberry) is a potent rejuvenator with antioxidant and hepatoprotective effects.

Regular consumption of these foods promotes holistic well-being, aligning with *Ayurvedic* principles for a balanced and healthy life. MA Tiwar *et.al*. *Mudga* (mung bean) exhibits remarkable health benefits due to its bioactive compounds, including polysaccharides, polyphenols, and peptides, which contribute to its antioxidant, detoxifying, and immune modulatory properties. Research confirms its role in reducing toxin absorption (e.g., aconitine), protecting against heavy metal toxicity (e.g., aluminum-induced cardiotoxicity), and offering anti-diabetic, anti-hypertensive, and hepatoprotective effects. Similarly, *Ghrita* (cow's ghee) enhances immunity through butyric acid and omega-3 fatty acids, supporting cardiovascular, neurological, and anti-inflammatory functions. *Amalaki* (Indian gooseberry) further complements these benefits with its potent antioxidant, anti-inflammatory, and rejuvenating properties. Shaniba KV *et.al*.*Nitya Sevaniya Ahara Dravyas* (daily consumable foods) serve as a balanced diet, fulfilling nutritional needs while offering antioxidant and detoxifying benefits. These foods influence gut microbiota, maintain digestive alkalinity, and provide essential fiber—factors crucial for long-term health. While most of these foods align with *Ayurvedic* principles of wellness, *Jangala Maamsa* (lean meat) presents an exception. Despite being a rich source of high-quality protein and B vitamins, its compatibility with holistic health concepts remains debatable. Further research is needed to explore its long-term effects on digestion, microbiome balance, and overall well-being. Thus, a diet primarily based on traditional *Nitya Sevaniya Ahara*, supplemented mindfully, can promote optimal health. The text recommends specific food items such as *Sastika* rice, *Sali* rice, *Mudga* (green gram), *Saindhava Lavana* (rock salt), *Amalaka* (Indian gooseberry), rainwater, ghee, meat from arid-climate animals, and honey.

Each of these has distinct nutritional and therapeutic properties:
***Sastika* and *Sali* Rice:** These varieties of rice are easily digestible and provide essential carbohydrates, supporting energy levels without aggravating *Dosa*s.

***Mudga* (Green Gram):** A protein-rich legume that is light and balancing for all three *Dosas* (*Vata, Pitta, Kapha).*

Rock Salt (*Saindhava Lavana*): Unlike refined salt, rock salt contains trace minerals and is considered beneficial in moderation, aiding digestion without causing excessive water retention.

***Amalaka* (*Emblica officinalis*):** A potent antioxidant and rejuvenative (*Rasayana*), supporting immunity and digestion.

Rainwater: Traditionally regarded as pure and free from contaminants, promoting hydration without burdening digestion.

Ghee: Clarified butter enhances digestion, lubricates tissues, and supports *Ojas* (vital essence).

Meat of Arid-Climate Animals: Lean meats from animals adapted to dry regions were considered easier to digest and less likely to increase *Kapha.*

Honey: A natural preservative with antimicrobial properties, beneficial in moderation but contraindicated when heated or consumed excessively[25]. This selection of foods exemplifies a diet that is *Pathya* (wholesome and suitable for maintaining equilibrium in the body). The emphasis on moderation, particularly with rock salt, reflects an understanding of the potential harm caused by excess intake, aligning with modern dietary guidelines that link high salt consumption to hypertension and cardiovascular diseases. The text serves as broad guidance for a healthy diet. Only foods that promote the ongoing maintenance of good health and ward off additional illness outbreaks should be consumed on a regular basis. There are two methods for staying in good health.

Replenishment of Dhatus (Tissue Elements): The body's tissues require proper nutrition to regenerate. A balanced diet ensures the optimal formation of *Rasa* (plasma), *Rakta* (blood), *Mamsa* (muscle), *Meda* (fat), *Asthi* (bone), *Majja* (marrow), and *Shukra* (reproductive tissue). This concept parallels modern nutritional science, which emphasizes macronutrients (proteins, fats, carbohydrates) and micronutrients (vitamins, minerals) for tissue repair and metabolic functions.

Removal of Obstacles to Health: External and internal factors can disrupt bodily equilibrium. The text categorizes these as: Improper lifestyle choices (e.g., irregular eating, sleep deprivation, stress) that disturb *Vata, Pitta,* and *Kapha.* Natural variations like winter (*Hemanta*) increasing *Kapha,* requiring dietary adjustments (e.g., warm, spicy foods to counteract cold and dampness). The analogy of the lamp's flame is particularly insightfuljust as a flame needs fuel (oil) and protection from disturbances (wind, insects), the body requires nourishment and protection from pathogenic influences. This dual approach underscores the preventive aspect of traditional medicine, advocating for proactive measures rather than merely reactive treatments. By aligning diet with seasonal changes, one can counteract potential *Dosa* imbalances before they manifest as disease. This preventive strategy is increasingly relevant in modern integrative medicine, where seasonal eating and chrononutrition are gaining recognition for metabolic health.

Limitations and Adaptations for Contemporary Use

The caution against excessive salt intake aligns with WHO guidelines recommending <5g/day to prevent hypertension[26]. Modern ethical and environmental concerns may necessitate plant-based alternatives with similar properties to meat consumption, such as lentils and nuts. Due to pollution, rainwater may now require filtration.

Ayurveda emphasizes personalized diets based on one's constitution (*Prakruti*), which should be considered alongside general guidelines.

CONCLUSSION

In accordance with the *Ayurvedic* concept of *Swasthavritta* (preventive health), the *Nitya Sevaniya Dravyas-Amalaki, Shashtika Shali, Mudga, Saindhava Lavana, Yava, Antariksha Jala, Goghrita*, and *Madhu*-provide a nutrient-rich, well-balanced diet. They are essential for everyday ingestion due to their cleansing, gut-microbiome-modulating, and antioxidant qualities. Even though the majority of these foods are good for everyone, careful consideration of *Jangala Mamsa* needs more research. By preventing *Kuposhanajanya Vikaras* (nutritional illnesses) and encouraging longevity, incorporating these dietary concepts can improve public health. The manuscript presents a holistic approach to maintaining good health through dietary and lifestyle practices, emphasizing both nourishment and the prevention of disease. This perspective aligns with traditional systems of medicine, particularly *Ayurveda*, which underscores the importance of balance in *Dosas* and the role of diet in sustaining health. The analogy of maintaining the flame of a lamp by providing oil (nourishment) and removing obstructions (disease-causing factors) effectively illustrates the dual approach to wellness: proactive nourishment and preventive care.

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Table No. 1: Shows details of *Amalaki*(*Emblica officinalis*)

Latin name	***Embilica officinalis***
Family	**Graminae**
Part used	***Phala* (Fruit)**
Guna	***Laghu, Ruksha, Sheeta, Sheeta, Guru,***
Rasa	***Pancharasa(Amlapradhana)***
Virya	***Sheeta***
Vipaka	***Madhura***
Doshaghanta	***Tridosha Shamaka* mainly *Pittashamaka***
Roghaghanata	***Kandu, Kamala, Ajirna, Yakritroga, Prameha, Shotha Hridroga, Jvara, Raktapitta, Amlapitta, Shosha, Trushna,***
Karma	***Chakshushya, Keshya, Rechana, Deepana, Vrishya, Kushthaghna, Anulomana, Rasayana, Balya, Kaphaghna, Krimighna, Vayasthapana, Ruchya, Medhya, Dahaprasamana, Bhagnasandhanakaraka.***

Table No. 2: Shows details of Shashtika Shali (*Oriza sativum*)

Latin name	***Oriza sativam***
English Name	***Rice***
Family	**Graminaeae**
Gana	***Stanyajanana, Shukadhanyavarga***
Guna	***Laghu*(lightfordigestion), *Snigdha***
***Rasa* (Taste)**	***Madhura*(Sweet)**
***Anurasa* (Sub-Taste)**	***Kashaya*(Astringent)**
***Virya* (Active principle)**	***Sheeta*(cold)**
***Vipaka* (Postdigestive taste)**	***Madhura***
***Doshaghanta* (effect on *Doshas*)**	***Tridosha***
***Rogaghnata* (effects on Diseases)**	**Emaciation, *Raktapitta* (bleeding disorders), rheumatoid arthritis, *Arsha* (hemorrhoids), *Prameha* (diabetes) and *Twakaroga* (skin diseases).**
***Karma*(effects on body)**	***Hridya, Ruchikara, Pittahara, Vrishya* (aphrodisiac), Vishaghna, Mutral, Brimhana, Swarya, Baddhavarchskara,**

Table No. 3: Shows details of *Mudga* (Phaseolus mudga)

Latin name	*Phasenlus mudga Linn*
EnglishName	Green Gram
Guna	*Laghu* and *Ruksha*(dry)
Rasa	*Madhura, Kashaya*
Virya	*Sheet*
Vipaka	*Katu*(pungent)
Doshaghanta	*Kapha Pitta Dosha Shamaka*
Rogaghnata	*Jwara*(fever), *Medoroga*(obesity), *Kapha, Pitta* and *Rakta*disorders.
Karma	*Grahi, Chakshushya*(goodforeyes), *Jvaraghna*

Table No. 4: Shows details *Saindava Lavana* (Sodium chloride)

Latin name	*Sodii chloridum*
EnglishName	Rocksalt, Sodium chloride
Gana	*Panchalavana* and *Shadlavana*
Guna	*Visyandi, Sukshma, Ushna, Vyavayi, Snigdha, Tikshna* and *Laghu.*
Rasa	*Lavana, Madhura*
Virya	*Sheeta*
Vipaka	*Madhura*
Doshaghanta	*Tridoshamak*
Rogaghnata	*Adhmana, Shula, Vamana, Vrishya,*
Karma	*Agnideepaka, Pachaka, Ruchikaraka* (improves taste), *Chakshushya, Lekhana Vibandhahara*(Laxative), *Hridya* (good for heart), *Shothahara Vrana Sodhaka* and *Ropana*

Table No. 5: Shows details of *Yava* (*Hordeum vulgare*)

Latin name	*Hordeum Vulgare* Linn.
Family	Graminae
Guna	*Laghu*(light), *Ruksha*(dry), *Pichilla*(slimy), *Mridu*(soft),*Sara* (flows easily)
Rasa	*Madhura, Tikta*(bitter),*Kashaya*
Virya	*Sheet*
Vipaka	*Katu*(pungent)
Doshaghanta	*Kapha Pitta Shamak* and *Vatakara*
Karma	*Kapha Shamaka, Mutrala, Lekhana*(scraping effect), *Medohara* (eliminates excess fat), *Vrishya*(aphrodisiac), *Balya, Varnya*(increases complexion), *Swarya*(helps to gain good voice), *Agnideepana* (increases appetite and metabolism),

Table No. 6: Shows of details *Antariksha Jala*

Guna	*Laghu, Snigdha*
Rasa	*Avyakta Rasa*
Virya	*Sheeta*
Vipaka	*Madhur*
Doshaghanta	*Kapha Pitta Shamak* and *Vatakara*
Karma	*Jeevana, Tarpana, Hridya, Buddhivardhaka*

Table No. 7: Shows details of *Go-ghrita* (Cow's ghee)

Guna	*Laghu, Snigdha*
Rasa	*Avyakta Rasa*
Virya	*Sheeta*
Vipaka	*Madhur*
Doshaghanta	*Kapha Pitta Shamak* and *Vatakara*
Karma	*Jeevana, Tarpana, Hridya, Buddhivardhaka*

Table No. 8: Shows details of *Madhu* (Honey)

English Name	Honey
Guna	*Ruksha, Laghu, Sukshma*
Rasa	*Madhura, Kashaya*
Anurasa	*Kashaya*
Virya	*Sheeta*
Vipaka	*Madhura*
Doshaghanta	*Tridoshashamak*
Rogaghnata	*Kustha, Arsha, Kasa, Shwasa, Hikka, Atisara, Vibandha, Daha, Kshata, Kshaya. Trishna, Visha, Raktapitta, Prameha, Krimi, Chardi,*
Karma	*Lekhana, Sangrahi, Shodhana, Swarya, Chakshushaya, Mehaghna, Deepana, Vranashodhana, Srotoshodhana, Varnya, Medhya, Vrishya, Sangrahi,Lekhanam,Sandhanam, Ropanam, Chedanam, Prasadanam. Yogavahi*

RESEARCH ARTICLE

Advances in Nanogels as Topical Drug Delivery Systems for Anti-Inflammatory Therapy

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Received: 01 Jan 2026 Revised: 10 Jan 2025 Accepted: 18 Jan 2026

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ABSTRACT

Nanogels are emerging nanocarrier systems with significant promise for topical anti-inflammatory therapy due to their small size, high biocompatibility, and tunable polymeric networks. These hydrophilic, three-dimensional structures enhance drug penetration through the stratum corneum and provide controlled, sustained, or stimuli-responsive release at inflamed sites. This review discusses the importance of topical delivery, the mechanisms of nanogel-mediated penetration, and the advantages of

nanogels over conventional topical formulations. Various polymers, crosslinking approaches, and synthesis techniques are highlighted alongside recent advances such as hybrid, surface-functionalized, and multi-stimuli-responsive nanogels. Preclinical and preliminary clinical studies demonstrate improved therapeutic efficacy, enhanced drug stability, and reduced systemic toxicity. Although challenges remain in scale-up, storage stability, and regulatory approval, nanogels offer a powerful next-generation platform for effective and patient-friendly anti-inflammatory topical therapy.

Keywords: Anti-inflammatory therapy; Nanogels; Surface functionalization; Topical drug delivery; Stimuli-responsive polymer

INTRODUCTION

The skin is the body's largest organ and the first line of defense against the external environment. It is composed of three main layers: epidermis, dermis, and hypodermis, which together maintain barrier function, thermoregulation, and immune protection. the structure of skin. The epidermis is the outermost layer of the skin, known as the epidermis, acts as a protective shield for the body against the external environment. It consists mostly of dead skin cells called the stratum corneum that form a tough barrier to keep harmful substances out and water in. It also contains special cells like melanocytes which give skin its colour and protect against sun damage, and immune cells that help defend against infections. This layer is quite thin but very important for skin protection[1]. Beneath it, the dermis is a thicker connective tissue layer that supports the epidermis. It contains collagen and elastic fibers that provide strength and elasticity, as well as blood vessels, hair follicles, sweat glands, and immune cells that participate in tissue repair and host defense. Sensory nerve endings in the dermis enable perception of pain, temperature, and touch [1]**.** The deepest layer, the hypodermis or subcutaneous tissue, consists predominantly of adipose tissue and loose connective tissue. It cushions underlying organs and muscles, contributes to mechanical protection, and serves as a thermal insulator that helps maintain body temperature [1]. Inflammation is a fundamental biological response to harmful stimuli such as infection, injury, or chemical irritation. While it is essential for host defense and tissue repair, persistent or dysregulated inflammation plays a central role in the pathogenesis of chronic diseases including arthritis, cardiovascular disorders, diabetes, and cancer.

Globally, inflammatory diseases pose a substantial health burden, reducing quality of life and increasing disability and mortality; chronic inflammatory conditions are among the leading causes of death according to international health reports such as those from the World Health Organization [2]. These challenges highlight the need for advanced therapeutic strategies that can control inflammation effectively while minimizing adverse effects[2]. Nanogels consist of three-dimensional, hydrophilic polymeric frameworks that have the remarkable ability to absorb and retain large volumes of water or biological fluids, while still maintaining their structural integrity[1]. Due to their nanoscale size and tunable physical and chemical properties, nanogels have emerged as highly promising carriers for drug delivery applications [2]**.** Their versatile architecture allows for efficient administration of therapeutic agents, protection of labile drugs from degradation, and controlled or stimuli-responsive release, making them particularly suitable for targeted and localized delivery [3]. In the context of topical drug delivery, nanogels offer distinct advantages such as enhanced skin permeability, mucoadhesion, and reduced systemic side effects, which are critical in treating localized conditions like inflammation[4]**.** These features collectively position nanogels as a breakthrough technology in pharmaceutical nanocarriers, optimizing therapeutic outcomes by improving drug bioavailability and patient compliance in topical anti-inflammatory therapies [5]**.** This review summarizes skin structure and barrier function, the role of inflammation in disease, and the properties of nanogels that support topical anti-inflammatory drug delivery. It also highlights formulation strategies, surface functionalization, recent advances such as stimuli-responsive systems, and future challenges in clinical translation.

Importance of Topical Delivery in Anti-Inflammatory Therapy

Topical drug delivery plays a crucial role in anti-inflammatory therapy by enabling direct application of therapeutic agents to the affected skin or tissue site[6].This localized approach minimizes systemic drug exposure, thereby reducing the risk of systemic side effects and improving patient safety. Moreover, topical delivery allows for enhance drug concentrations in the area of inflammation, which enhances therapeutic efficacy and accelerates symptom relief [7].It is especially valuable for treating chronic inflammatory skin diseases such as psoriasis, eczema, and dermatitis, where sustained and targeted treatment is required [7,8]. Additionally, topical formulations, including nanogels, improve drug penetration through the skin barrier, increase residence time, and provide controlled drug release, which further optimizes treatment outcomes for inflammatory conditions[4]. Over the past decade, nanogels have gained attention as effective nanotechnology-based systems for delivering drugs to treat inflammatory skin diseases. Nanogels are tiny, water-rich polymer networks capable of carrying a wide range of drugs, including small molecules, proteins, and nucleic acids. Their ability to swell, retain water, and adjust their mechanical strength allows them to behave similarly to natural skin tissue. These properties improve skin compatibility and reduce irritation when applied topically[9,10]. Topical drug delivery minimizes systemic side effects, but penetration through the stratum corneum is challenging. Nanogels overcome this due to their small size, tunable surface properties, and high hydration, enabling deeper skin penetration, targeted delivery to inflamed tissues, and soothing of irritated skin.[10]. Nanogels enable controlled and sustained drug release for anti-inflammatory therapy, maintaining therapeutic levels at inflamed sites for extended periods. Stimuli-responsive nanogels (pH, temperature, enzymes) release drugs selectively in inflammatory environments, improving efficacy while reducing dosing frequency[11]. Recent research has used biocompatible polymers such as chitosan, hyaluronic acid, PNIPAM, and polyethylene glycol to make nanogels, often in hybrid combinations to gain multiple benefits. These nanogels improve drug stability and loading and can be targeted to inflamed tissues using specific ligands. Incorporating natural compounds like curcumin and quercetin further boosts anti-inflammatory and antioxidant effects. Together, these strategies provide stronger and more effective therapeutic outcomes than single-agent treatments[12].

Preclinical and early clinical studies show that nanogels are effective in treating inflammatory conditions such as arthritis, psoriasis, dermatitis, and wounds. Compared to conventional formulations, nanogels provide better anti-inflammatory effects with fewer side effects. Studies on diacerein- and tapinarof-loaded nanogels have shown improved inflammation control and tissue protection. Additionally, nanogels with antimicrobial and healing agents help manage secondary infections in chronic skin diseases[10]. Despite advances, clinical translation of nanogels is limited by scale-up, reproducibility, stability, regulatory complexity, and skin-to-skin variability. Nevertheless, personalized topical nanogels show strong promise to improve anti-inflammatory efficacy, safety, and patient adherence.[13]. In addition to their excellent drug delivery capabilities, Nanogels are flexible drug carriers that can be designed to perform more than one function at a time. They can be made “smart” so that they release the drug only when they reach inflamed areas, where conditions like low pH, higher temperature, or enzymes are present. This targeted release improves treatment effectiveness and reduces the amount of drug needed, lowering the risk of side effects. In addition, nanogels can be modified on their surface to guide them directly to inflamed cells, making drug delivery more precise[14]. Another critical advantage of nanogels are safe, skin-friendly systems that cause minimal irritation, making them suitable for long-term treatment of inflammatory skin conditions. They are often made from natural polymers like chitosan, hyaluronic acid, and alginate, which naturally support healing and reduce inflammation. These polymers also improve skin hydration and help repair the damaged skin barrier. Together, these properties make nanogels an effective and patient-friendly platform for topical anti-inflammatory therapy[15]. Moreover, Nanogels offer high biocompatibility and low irritancy, making them ideal for long-term topical anti-inflammatory therapy. Natural polymers like chitosan, hyaluronic acid, and alginate provide added anti-inflammatory and healing benefits, improve skin hydration, and help restore the skin barrier. This combination makes nanogels effective for delivering drugs and supporting overall skin health in chronic inflammatory conditions, enhancing both treatment results and patient quality of life[16].

Properties and Mechanisms Relevant to Topical Delivery

Nanogels exhibit distinctive physicochemical properties that render them particularly well-suited for topical drug delivery, offering improvements in drug loading, controlled release, and performance compared to conventional formulations.

Physicochemical Features of Nanogels

Nanogels are nanosized, three-dimensional hydrogel networks formed via crosslinking of hydrophilic polymers. Their distinctive structural and functional characteristics them highly advantageous as topical drug delivery carriers, particularly for anti-inflammatory agents.

Physicochemical Properties

Particle Size and Surface Morphology: Nanogels typically range from 20 to 200 nm, allowing efficient passage through the stratum corneum and penetration into deeper epidermal and dermal layers. Their small size also enables better interaction with skin cells and enhances retention at the application site[17].

Swelling and Hydration Capacity: Due to their hydrophilic polymeric framework, nanogels can absorb large amounts of water, which helps maintain skin hydration and promotes permeability. The swelling behaviour can be finely tuned based on polymer composition and crosslinking density to regulate drug release kinetics[18].

Surface Charge and Functionalization: Modifying nanogel surface charge (positive, negative, or neutral) modifies their relationship with the negatively charged skin barrier. Positive surface charges can facilitate stronger adherence and penetration, while functionalization with ligands or peptides enables specific delivery aimed at designated receptors or cells[19].

Biocompatibility and Biodegradability: Nanogels are generally synthesized from biocompatible and biodegradable polymers such as chitosan, hyaluronic acid, poly(N-isopropylacrylamide), ensuring minimal skin irritation or toxicity upon topical use. This safety profile is essential for chronic inflammatory skin conditions[9].

Encapsulation Efficiency of Drug: Nanogels can encapsulate hydrophilic and hydrophobic drugs via entrapment, adsorption, or covalent attachment. Their porous and crosslinked matrix protects labile anti-inflammatory agents from enzymatic degradation and improves drug stability[1].

Mechanisms Facilitating Topical Drug Delivery

Enhanced Skin Penetration

The nanoscale size and hydrophilic nature of nanogels facilitate transient disruption or fluidization of lipids within the stratum corneum, thereby enhancing solute permeability. Additionally, the moisture-retentive property of nanogels can hydrate and loosen the skin barrier, enabling deeper drug penetration[19].

Controlled and Stimuli-Responsive Drug Release

Nanogels can be developed to respond to endogenous stimuli such as pH changes, temperature variations and oxidative stress commonly found in inflamed skin. This responsiveness enables on-demand release of anti-inflammatory drugs directly at sites of inflammation, improving efficacy and lowering systemic exposure[20].

Targeted Delivery and Cellular Uptake

Surface modifications allow nanogels to target specific skin cell types, improving cellular uptake and therapeutic action. Active targeting strategies include conjugation with antibodies, peptides, or aptamers selective for inflammatory markers or immune cells in the skin[17].

Protection from Premature Degradation

Nanogel encapsulation protects sensitive drug molecules such as natural extracts or biological agents from premature oxidation, hydrolysis, or enzymatic cleavage on the skin surface, improving bioavailability and therapeutic lifespan[9].

Minimized Irritation and Improved Patient Compliance

The soft, hydrated nature of nanogels results in painless, non-irritant topical formulations, enhancing patient compliance especially in chronic treatments involving repeated application[18]. These properties and mechanisms collectively make nanogels a highly effective and adaptable platform for topical anti-inflammatory therapy, overcoming critical barriers faced by conventional formulations and opening a venues for personalized skin disease management[13].

Advantages Over Conventional Topical Formulations

Nanogels offer several major advantages over conventional topical formulations for drug delivery:

Enhanced Drug Encapsulation

Nanogels can load both hydrophilic and hydrophobic drugs efficiently, increasing the amount of drug delivered compared to traditional creams or ointments[21].

Improved Skin Penetration

The nanoscale size and flexible polymeric structure allow nanogels to bypass the skin barrier more effectively, enabling deeper and more uniform distribution in the skin[22].

Controlled and Sustained Release

Nanogels can be engineered to provide controlled, prolonged, or even stimuli-responsive drug release (e.g., in response to pH, temperature, or enzymes), maintaining therapeutic levels longer and reducing dosing frequency[22].

Reduced Systemic Side Effects

By increasing topical drug retention and limiting systemic absorption, nanogels help minimize side effects that often result from oral or non-targeted drug delivery[23].

Biocompatibility and Patient Comfort

Nanogels are typically biocompatible and less irritating than many conventional formulations, making them more suitable for long-term treatment of chronic skin conditions[9].

These properties establish nanogels as an innovative platform for more effective, safer, and patient-friendly topical treatments.

Design and Preparation of Nanogels for Topical Anti-Inflammatory treatments

Nanogels are tiny, water-swollen polymer networks that can effectively carry and deliver non-steroidal anti-inflammatory drugs directly to the skin. By carefully selecting biocompatible polymers and optimizing the preparation methods, these nanogels can provide controlled drug release, improved skin penetration, and enhanced therapeutic effects for treating inflammatory skin conditions[24].

Types of polymer and crosslinking agents used

In topical nanogel formulations, various types of polymers and crosslinking agents have been extensively studied to optimize drug delivery performance[25].

Polymers

Polymers plays an important role in the formulation of nanoparticulate drug delivery systems, offering advantages such as improved drug stability, controlled release, and enhanced bioavailability. Natural polymers like chitosan and

sodium alginate are extensively used due to their biocompatibility, biodegradability, and mucoadhesive properties, which enhance drug retention and permeation in topical applications[26]. Chitosan is a polymer found in nature, extracted from chitin, known for being biodegradable, biocompatible and non-toxic, making it highly suitable for drug delivery applications. Its positive charge allows it to stick to the skin or mucosal surfaces (known as mucoadhesion), which helps the drug stay longer at the application site and improves its penetration, resulting in better and sustained anti-inflammatory effects [27]. Besides carrying drugs, chitosan has extra benefits like fighting bacteria and helping wounds heal, which makes it very useful in skin treatments. Because it has a natural positive charge, chitosan can slightly loosen the tight connections between skin cells, allowing medicines to pass through the skin more easily. Since it comes from natural sources, it is generally safe and not harmful. These features make chitosan-based nanogels a good choice not only for reducing inflammation but also for healing and protecting the skin[27]. Sodium alginate is a natural polymer derived from seaweed that becomes a gel when it reacts with certain metal ions, such as calcium (Ca^{2+}). In this process, calcium ions link together the alginate molecules to form a three-dimensional network, creating a gel that can hold water and other substances tightly. This gel structure allows for the slow and sustained release of drugs when applied to the skin, making it highly useful in topical drug delivery, especially for anti-inflammatory treatments[28]. Pectinis a naturally occurring polysaccharide that can be found in the cell walls of plants, widely utilized in drug delivery for its exceptional biocompatibility, biodegradability, and the ability to form hydrogels. It possesses multiple functional groups that facilitate gelation and drug encapsulation, enabling controlled and targeted drug release. In topical applications, pectin-based hydrogels can improve drug stability and penetration while providing anti-inflammatory benefits by modulating cytokine production and reducing inflammatory responses[26]. Polyethylene Glycol has been used for a long time in making biomaterials for medical applications, especially in areas like tissue repair and drug delivery. What makes PEG so useful is that it is safe for the body, doesn't trigger immune reactions, and dissolves well in water. Because of these advantages, PEG has become a very popular material and is used in many forms-from large bulk materials to thin films, hydrogels, and even nanoparticles[29]. In PEG-based hydrogel drug delivery systems, drugs are usually held inside the gel by simple physical trapping, not by forming chemical bonds. The drug stays safely inside the cross-linked network of the gel. Over time, as the gel's sensitive parts slowly break down, the PEG structure degrades and gently releases the drug. This process avoids releasing any harmful or toxic by-products, making it a safer way to deliver medicines[29]. Together, these polymers alone or in combination provide tunable mechanical strength, swelling, mucoadhesion, and release characteristics required for effective, patient-friendly topical nanogel formulations for anti-inflammatory therapy.

Crosslinking Agents

Crosslinking means creating links between different polymer chains, which makes the material stronger and more stable. These links form a three-dimensional network that changes how the material behaves. Depending on the type of bonds formed covalent, ionic, or hydrogen bonds the material can gain different properties and be used in different applications. These are classified into two Chemical crosslinking agents and Physical crosslinking agents[30]. Chemical crosslinking agents are substances that induce the formation of covalent bonds between polymer chains, resulting in stable and often irreversible three-dimensional networks.

These crosslinkers provide enhanced mechanical strength, durability, and controlled drug release in polymeric systems. Common chemical crosslinkers include:

Covalent Bond Formers: These agents create irreversible covalent bonds between polymer chains, leading to permanent networks. Examples include glutaraldehyde, formaldehyde, epichlorohydrin, genipin, and methylenebisacrylamide (MBA)[31].

- Glutaraldehyde is one of the most widely used chemical crosslinkers, particularly with natural polymers such as chitosan and gelatin. It creates strong covalent bonds between polymer chains, which increases the strength and stability of the nanostructures. In topical drug delivery, using glutaraldehyde-crosslinked polymers helps control how the drug is released and ensures the formulation remains stable during use[31].

- Genipinis a natural crosslinker obtained from plants like *Gardenia jasminoides*. Unlike synthetic agents such as glutaraldehyde, it is much less toxic, making it safer for biomedical use. Genipin mainly reacts with amino groups in polymers like chitosan and gelatin, forming strong covalent bonds that improve the strength and biocompatibility of hydrogels and nanogels. A unique feature of genipin-crosslinked materials is their blue color, which appears during the reaction because of conjugated structures that are formed. Beyond crosslinking, genipin itself has anti-inflammatory and antioxidant properties, which further support wound healing and make it useful in topical treatments[32].
- Ethylene glycol dimethacrylate (EGDMA) is a commonly used chemical crosslinker in synthetic polymers, especially in acrylate-based hydrogels. It has two reactive groups that take part in free radical polymerization, joining polymer chains together to create a strong three-dimensional network. By adjusting the amount of EGDMA, researchers can control the structure of the hydrogel: higher amounts make the gel denser and stronger but reduce its ability to swell and its pore size. This flexibility makes EGDMA especially useful in designing hydrogels for controlled drug release in topical and other drug delivery systems[33].

Photo-initiated crosslinkers: These are special chemicals that make gels harden when they are exposed to light, usually UV light. When the light hits them, they produce reactive particles called free radicals, which quickly link the acrylate chains together to form a strong network. This process is fast, can be controlled easily, and works under gentle conditions, which makes it very useful for medical applications and drug delivery on the skin[34]. Enzymatic crosslinking is a gentle and safe way to make hydrogels by using enzymes to link polymer chains together. Different enzymes can be used for this purpose. For example, transglutaminase creates strong bonds between amino acids in proteins like gelatin, forming stable hydrogels that are useful for slow drug release and tissue repair. Peroxidases such as horseradish peroxidase can quickly form hydrogels when combined with hydrogen peroxide and phenol-modified polymers, giving good control over the process. Tyrosinase works by oxidizing tyrosine groups into reactive forms that can bond with polymers like chitosan, producing hydrogels that are strong and biocompatible. Because these methods work under mild conditions, they are considered safe and effective for biomedical uses such as drug delivery and wound healing[35]. Physical crosslinking happens when polymers are connected by weak physical forces instead of permanent chemical bonds. This can occur through ionic interactions, protein interactions, or forces like hydrogen bonding, which allow different polymers to link together and form large, interconnected structures. These physical forces are enough to create hydrogels without the need for covalent bonds. One important example is hydrophobic interactions, which let the polymer absorb water and swell. This property is especially important in making polysaccharide-based hydrogels that are widely used in biomedical applications[36]. Ionic crosslinking is a process where polymer chains are linked together by ionic interactions, which are usually reversible. For example, calcium chloride ($CaCl_2$) is commonly used to crosslink alginate polymers. the divalent Calcium ions respond to the negatively charged carboxyl groups on the alginate chains, forming ionic bridges that stabilize the hydrogel network.

This type of crosslinking improves mechanical strength and controls drug release, while maintaining flexibility due to the reversible nature of ionic bonds. Ionic crosslinking can be modulated by factors such as ion concentration and pH, making it versatile for designing hydrogels with tailored properties in drug delivery applications[37]. Hydrogen bonding is a reversible and non-permanent interaction that can hold polymer chains together in hydrogels. It happens when hydrogen atoms connect with oxygen or nitrogen atoms in the polymers, creating a flexible network. Hydrogels made this way are often self-healing, injectable, and sticky, because the bonds can break and reform when the material is stretched or damaged. The main challenge is that water can weaken these hydrogen bonds, making the gel less stable in wet conditions. To solve this, researchers have added hydrophobic regions or extra crosslinkers to strengthen the gel while still keeping it safe and biocompatible[38]. Hydrophobic interactions in hydrogels happen when water-repelling parts of polymer chains group together to stay away from water. These act like natural crosslinking points, giving the hydrogel strength and flexibility. Compared to hydrogen bonds, hydrophobic interactions are stronger and allow the gel to form stable, reversible, and even self-healing networks. By changing how much hydrophobic material is included or altering its structure, researchers can adjust the gel's properties. This makes hydrophobic interactions very useful for creating tough, responsive hydrogels that work well in drug delivery

system[1,3]. Thermo-responsive crosslinking happens when nanogel polymers change their structure in response to temperature. A well-known example is poly(N-isopropylacrylamide) (PNIPAm). Below a certain point, called the lower critical solution temperature (LCST), the polymer chains stay hydrated and swollen. But once the temperature goes above this point, water is pushed out, hydrophobic interactions take over, and the chains come closer together to form a denser gel network. This shift from a swollen state to a collapsed state is reversible, meaning the material can switch back and forth with temperature changes. Because of this "smart" behavior, thermo-responsive nanogels are very promising for controlled drug delivery where release can be triggered by body heat or external temperature changes[39].

Methods of Nanogel Synthesis

Nanogels are synthesized using different methods, each providing regulation over dimensions, composition, and drug-loading characteristics.

The most common techniques include in figure -1

Emulsion-Based Techniques Emulsion-based nanogel synthesis relies on forming oil-in-water (O/W) or water-in-oil (W/O) systems, where polymerization and crosslinking occur within nanoscale droplets, enabling precise regulation of particle dimensions and drug loading[40].

Emulsion solvent diffusion method

The emulsion solvent diffusion process is shown in figure-1A, the drug is initially solubilized in an organic solvent. The polymer and gelling agent are subsequently dissolved in water to form drug phase, which is added drop wise to the water phase. This mixture is homogenized at 6000 rpm for roughly 30 minutes, producing fine nanodroplets and forming an oil-in-water emulsion. To convert this emulsion into a nanogel, triethanolamine is added while stirring continuously at 8000 rpm for one hour[40].

Inverse Emulsion (Or Miniemulsion) Method

The Inverse emulsion (or miniemulsion) method for nanogel synthesis shown in figure-1B, an aqueous solution containing polymer building blocks, crosslinkers, initiators, and sometimes the drug or protein to be loaded is dispersed within an oil phase that contains surfactants for stabilization. After mixing, the emulsion is deoxygenated, and a catalyst such as TEMED is added to start the polymerization and crosslinking process. This produces nanogels with the drug or biomolecule trapped inside the polymer network. By adjusting factors like the type of surfactant, concentrations of monomers, and mixing conditions, researchers can control the size of the nanogels and how much drug they carry. Once polymerization is complete, the nanogels are separated and purified. This approach is highly versatile, gives good encapsulation efficiency, and works well for loading sensitive molecules such as proteins, peptides, or therapeutic drugs[41].

Precipitation Polymerization Method

Precipitation polymerization is a technique shown in figure-1C, where monomers and crosslinkers are dissolved in water and allowed to polymerize until the growing polymer chains reach a point where they separate from the solution, forming tiny colloidal particles. With further crosslinking, these particles develop into nanogels. The final size and characteristics of the nanogels depend on factors such as salt content, temperature, and the amount of initiator used. This method is especially popular for producing temperature-sensitive nanogels like poly(N-isopropylacrylamide) (PNIPAm), which are well suited for controlled drug delivery[42].

Nanoprecipitaion Method

Nanoprecipitaion Method is presented in figure-1D , where solvent that mixes only partly with water is first saturated with water to balance both liquids. The polymer is dissolved in this solvent, and the mixture is poured into water containing a stabilizer while stirring strongly. Each droplet of the solvent can create many nanoparticles. These nanoparticles form because of interactions at the surface of the droplets, helped by the turbulence during mixing. Nanoparticles form due to physicochemical instability, similar to spontaneous emulsification, where solvent diffuses

into the aqueous phase. This diffusion creates local supersaturation, leading to the formation of tiny polymer aggregates or "protonanoparticles." A stabilizer is essential to prevent these small particles from merging into larger clusters. When the stabilizer effectively protects the liquid–liquid interface during solvent diffusion, stable nanoparticles are obtained[43].

Microtemplate Polymerization

A hierarchically porous polymethacrylate(PMMA) monolith was prepared by free-radical copolymerization of glycidyl methacrylate (GMA) and ethylene glycol dimethacrylate (EDMA). The polymerization was initiated by adding 1 wt% AIBN to the monomer mixture. Microsphere templates were introduced at varying template-to-monomer ratios (50:50, 60:40, and 70:30). A total monolith volume of 20 mL was obtained. The mixtures of monomers and templates were sonicated at 20 °C for 30 min, transferred into casting molds, and polymerized at 60 °C for 3 h in a water bath. The solidified monoliths were then removed and stored at room temperature. For comparison, a control monolith was synthesized without the use of microsphere templates[44].

IonGelation Process

The ion gelation process is broadly used for the preparation of polymeric nanoparticles due to its simplicity and mild processing conditions. Typically, A polymer is mixed with a solvent at the desired concentration, and the drug is solubilized in a compatible medium before incorporation into the polymer solution. Under constant agitation, a crosslinker solution is introduced drop wise, resulting in nanoparticle formation driven by ionic or electrostatic interactions. The nanoparticles obtained are collected by centrifugation, and drug entrapment or loading efficiency is usually determined from the supernatant. Finally, the particles are dried, often by lyophilization, to ensure long-term stability and subsequently resuspended in buffer systems for characterization[45].

Evaporation Of Solvent Method

The drug and polymer mixture is gradually introduced into the water phase under continuous stirring at around 1000 rpm for a period of two hours to facilitate uniform mixing. The formed nanosponges are then collected by filtration and subsequently dried in a hot air oven at 40 °C for 24 hours, after which they can be stored in capsules. For better dispersion, the polymer is first pre-soaked in water for two hours prior to gel formation and then subjected to high-speed stirring at 6000 rpm. The pH of the system is adjusted using a suitable pH-modifying agent, after which the nanosponge suspension is stabilized with the incorporation of permeation enhancers into the aqueous dispersion[1,3].

Surface Functionalisation for Topical Delivery

Surface functionalization improves the performance of nanogels in topical drug delivery by adjusting properties such as surface charge, hydrophilicity, and adhesion. Modifications like ligand attachment, polymer coatings, and charged or amphiphilic surfaces enhance skin penetration, retention, and control over drug release. These strategies lead to improved therapeutic outcomes in dermatological applications[46]. Nanogels, due to their nano size and tunable surface properties, can efficiently load drugs and deliver them at higher concentrations to targeted skin sites. Surface modifications improve skin penetration, stability, and compatibility, while polymer conjugation or incorporation into hydrogels supports regulated delivery of both water-soluble and water-insoluble medications[47].

Comparison of Nanogels vs. Conventional Topical Systems

The Comparison of Nanogels vs. Conventional Topical Systems As shown in Table-1, surface-functionalized nanogels offer clear advantages over conventional topical formulations such as creams, gels, and ointments. Traditional systems often show poor stability, fast drug release, and limited skin penetration, reducing their effectiveness. Nanogels protect the drug, provide controlled or sustained release, and penetrate the skin more efficiently, leading to higher local drug levels with less irritation. These benefits reduce dosing frequency, improve patient comfort and compliance, and expand their use in treating skin conditions such as psoriasis, acne, inflammation, and photoaging[48]. In summary, surface functionalization of nanogels for topical delivery enables customizable, site-specific, and patient-friendly solutions for skin therapies. With their capacity for targeted delivery,

controlled release, and enhanced biocompatibility, functionalized nanogels represent the next-generation platform for precision dermatological treatment and are likely to play an increasingly prominent role in future patient care[17].

Recent Advances and Reseach Highlights

Stumli-Responsive Nanogel for Enhanced Pentration and Release

Single- versus multi stimuli responsive nanogels as shown in table-2, Single-stimuli responsive nanogels are designed to react to a single trigger such as pH, temperature, or enzymatic activity, making them relatively simple to fabricate and cost-effective. However, their release control and specificity are limited to one biological condition. In contrast, multi-stimuli responsive nanogels are engineered to respond to two or more cues simultaneously—for example, pH and temperature or redox and enzyme activity-allowing for more precise drug release that adapts to complex disease microenvironments. Although their synthesis is more challenging and scale-up can be difficult, these systems provide superior targeting, improved therapeutic precision, and decreased adverse effects, making them highly attractive for advanced applications such as cancer therapy, wound healing, and inflammatory skin disorders[49].

Nanogel Formulation Combining Synthetic and Natural therapeutics

The classification of nanogels by origin and composition as shown in table-3, Synthetic nanogels are stable and allow controlled drug release, but they do not have natural healing properties and may raise safety concerns. Natural nanogels are safer and have built-in anti-inflammatory and wound-healing benefits, though they may lack stability and consistency. Hybrid nanogels combine both systems, offering good stability and controlled release along with natural bioactivity. This makes them especially useful for chronic inflammatory skin conditions and wound healing, where both effectiveness and safety are important[50].

Clinical and Preclinical Evidence of Nanogel Formulations

Clinical and preclinical evaluation of nanogel-based drug delivery systems studies clearly show in table-4, that nanogel-based formulations are versatile and highly effective therapeutic systems. In cancer treatment, early clinical trials have reported better tumor response, improved drug behavior in the body, and good safety compared to conventional delivery methods. In dermatology and wound healing, nanogels enhance drug penetration, control inflammation, and speed up tissue repair with minimal irritation or systemic exposure. Advanced nanogels can also deliver multiple therapies together, helping overcome drug resistance and improving overall treatment outcomes[51]. These research highlights underscore the promise of nanogels as advanced, precision drug delivery platforms in modern medicine.

Challenges

Nanogels still face several challenges that limit their clinical translation. Large-scale production often leads to inconsistencies in size and drug loading, affecting reproducibility. They also suffer from stability issues, such as degradation or aggregation during storage, which can reduce shelf-life. Some nanogel materials may trigger immune reactions, raising safety concerns. Additionally, achieving controlled biodegradation and ensuring effective penetration across biological barriers like the skin or blood–brain barrier remain difficult[52]. The future of nanogels looks highly promising with new technologies enabling more precise and scalable production. Smart and multifunctional designs will support targeted, on-demand therapy and personalized medicine. Green, sustainable methods and clearer regulatory pathways will further boost development. With these advancements, nanogels are expected to overcome current challenges and expand their clinical use[53].

FUTURE PROSPECTIVES

In the coming years, nanogel-based topical systems for anti-inflammatory therapy are expected to evolve toward highly personalized, smart, and clinically translatable platforms. Future work should focus on establishing clear structure-property-efficacy relationships using advanced models (3D skin constructs, organ-on-chip, and large-

animal or early human studies), along with in-depth long-term safety and immunotoxicity evaluation. Multi-stimuli-responsive and theranostic nanogels capable of co-delivering multiple agents (e.g., NSAID plus antioxidant or biologic) and enabling Immediate monitoring of drug distribution and local response represents a particularly promising direction. Parallel efforts are needed to develop scalable, continuous or microfluidic manufacturing routes, define nanogel-specific critical quality attributes, and build harmonized regulatory frameworks to support clinical approval and commercialization. Finally, integrating green chemistry principles, biodegradable bio-sourced polymers, and life-cycle assessment into nanogel design will be essential to ensure that future products are not only effective and safe, but also economically and environmentally sustainable.

CONCLUSION

Nanogels have emerged as versatile topical carriers that enhance penetration, local retention, and anti-inflammatory efficacy while limiting systemic exposure compared with conventional formulations. Their nanoscale, hydrophilic, and tunable polymer networks support high drug loading, controlled or stimuli-responsive release, and the incorporation of biocompatible and bioactive polymers that add antioxidant, wound-healing, and barrier-restoring benefits, particularly valuable in chronic inflammatory skin diseases. Preclinical and early clinical studies consistently demonstrate superior therapeutic outcomes and tolerability, yet critical challenges in scalable manufacturing, long-term physicochemical stability, and regulatory standardization still hinder widespread clinical translation. Addressing these gaps through optimized engineering, robust quality control, and harmonized guidelines will be essential for fully realizing the potential of nanogel-based topical anti-inflammatory therapies in routine dermatological practice.

ACKNOWLEDGEMENT

The author would like to thank all the faculty members of KLE college of pharmacy, Hubballi for providing necessary support.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ETHICAL STATEMENT

This study did not involve any human or animal subjects, and hence, ethical approval was not required.

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Table 1: Comparison of Nanogels vs. Conventional Topical Systems

Parameter	Conventional Topical Systems	Surface-Functionalized Nanogels
Stability	Prone to degradation, limited shelf-life	High stability; protects payload from degradation
Drug Release	Burst release, less control	Controlled, sustained, and stimuli-responsive release
Skin Penetration	Limited penetration through stratum corneum	Enhanced permeation via nanoscale size, charge modification, or ligand targeting
Drug Protection	Active ingredient often unstable or degraded	Encapsulated drugs remain protected and bioavailable
Irritation/Toxicity	Can cause erythema, dryness, irritation	Reduced irritation; improved tolerability and safety
Dosing Frequency	Requires frequent re-application	Lower dosing frequency due to sustained action
Patient Compliance	Moderate; side effects reduce adherence	High compliance due to comfort, tolerability, and convenience
Applications	General creams, gels, ointments	Precision dermatology (psoriasis, acne, photoaging, anti-inflammatory therapy)

Stumli-Responsive Nanogel for Enhanced Pentration and Release

Table 2: Single- versus multi stimuli responsive nanogels

Feature	Single-Stimuli Responsive Nanogels	Multi-Stimuli Responsive Nanogels
Trigger Type	Responds to one cue (e.g., pH *or* temperature *or* enzymes)	Responds to two or more cues simultaneously (e.g., pH + temperature, redox + enzyme)
Design Complexity	Relatively simple and easier to fabricate	More complex synthesis and formulation strategies
Control over Release	Limited, release occurs only under one condition	Enhanced control, with drug release tailored to multiple pathological environments
Target Specificity	Moderate targeting based on one biological factor	Higher specificity due to combined responsiveness
Applications	Suitable for basic drug delivery systems	Promising for precision therapies in cancer, wound healing and inflammatory skin diseases
Advantages	Cost-effective, straightforward	Greater therapeutic precision minimized side

	design	effects
Limitations	Less adaptable in complex disease microenvironments	More challenging scale-up and stability issues

Nanogel Formulation Combining Synthetic and Natural Therapeutics

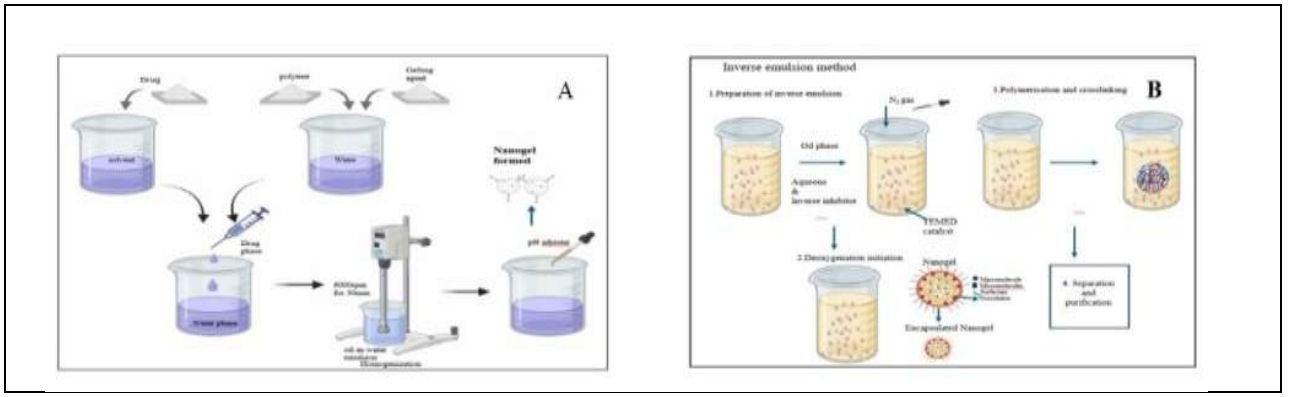
Table 3: Classification of nanogels by origin and composition

Type	Features	Advantages	Limitations
Synthetic Nanogels	Based on polymers such as PEG, PVA, and Polyacrylates	High stability, tunable release profile, Reproducible manufacturing, strong mechanical properties	Lack inherent bioactivity, possible toxicity of residues, lower patient acceptabiliy
Natural Nanogels	Derived from polymers like chitosan, alginate, hyaluronic acid, or loaded with phytoconstituents	Excellent biocompatibility, inherent bioactivity (anti-inflammatory, antibacterial, wound-healing), low toxicity	Limited stability, batch variability, weaker mechanical strength
Hybrid Nanogels (Synthetic + Natural)	Integration of synthetic polymers with natural therapeutics (essential oils, phytoconstituents, polyherbal extracts)	Combines stability and tunable release of synthetic carriers with biocompatibility and bioactivity of natural agents; synergistic effects; reduced toxicity	More complex formulation and characterization; regulatory challenges in standardization

Clinical and Preclinical Evidence of Nanogel Formulations

Table 4: Clinical and preclinical evaluations of nanogel-based drug delivery systems

Study Type	Therapeutic Area	Key Outcomes	Advantages over Conventional Systems
Clinical (Phase I/II)	Oncology or tumor therapy	Robust tumor response rates, predictable toxicity, improved pharmacokinetics	Better drug stability reduced systemic toxicity
Preclinical (animal models)	Topical therapy (anti-inflammatory)	Superior local drug deposition, better control of inflammation	Higher skin pentration, reduced irritation
Preclinical (wound healing models)	Tissue repair and regeneration	Faster wound closure, enhanced collagen deposition	Low systemic exposure, minimal side effects
Preclinical(multi-compartment nanogels)	Drug-resistant cancers	Effective against multidrug resistance, supports combined therapy (chemo + hyperthermia)	Synergistic treatment targeted delivery lower dosing required



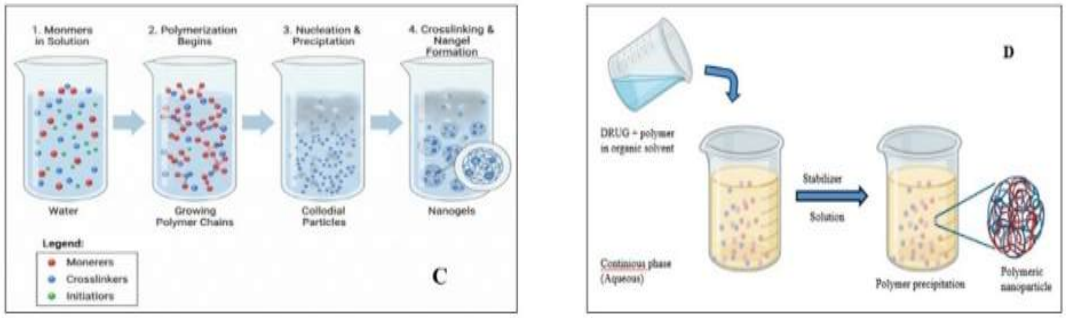


Figure 1: Methods of nanogel synthesis. A: Emulsion solvent diffusion method. B: Inverse emulsion method. C: Precipitation polymerization method. D: Nanoprecipitaion method

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Unveiling Potent Mineral Solubilizing Fungi Isolated from Conventional Soil and Their Identification for Plant Growth Promoting Activity

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Received: 26 Nov 2025 Revised: 18 Dec 2025 Accepted: 23 Jan 2026

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ABSTRACT

Generally, soil fertility is mediated through chemical fertilizer that contains most important macronutrients for plant growth and development. But these macronutrients are unavailable for plant use owing to its insoluble organic form resulting decrease in crop production. Therefore, to overcome limitation, isolating mineral solubilizing organism for solubilizing inorganic form to organic form which is easily available for plant use. Hence, this study targeted to isolate thirty mineral solubilizing fungi from ten conventional soil samples and evaluated for their solubilization ability using phosphate and potassium after macroscopic observation. Out of thirty isolates, ten isolates showed phosphate solubilizing ability and nine isolates were potassium solubilizers. Further, all the isolates were tested for protease and indole acetic acid (IAA) production and found that, nine isolates were performed protease production and sixteen fungal isolates produced IAA. Further, among thirty isolates, five isolates showed all the activities were selected for molecular characterization based on PCR amplification and genomic sequencing of the internal

transcribed spacer region (ITS) along with morphological identification and identified as *Rhizopus arrhizus*, *Aspergillus niger*, *Aspergillus flavus*, *Rhizopus microspores*, and *Curvulariaprasadii* respectively. Evolutionary analyses were conducted using MEGA12 software. Altogether, this study highlighted the isolated fungal isolates were potent mineral solubilizers to enhance the plant growth and development.

Keywords: Bioinoculant, Mineral solubilization, Protease production, Indole acetic acid.

INTRODUCTION

Over several decades, soil fertility was generally improved by applying lots of chemical fertilizer which cannot be utilized completely by soil. Usually, most of the chemical fertilizer contain nitrogen, potassium and phosphorous are predominant macro nutrients that applied to the soil as potash and phosphate fertilizer for plant growth [1,2]. These macronutrients are played a significant role in development and metabolism of plant such as energy transfer, photosynthesis, grain quality improvement, respiration, disease control, signal transduction, macromolecular biosynthesis that contributed for greater crop yield [3]. Moreover, most of the applied fertilizer is converted into an insoluble form and becomes inaccessible by the plant for their growth leads imbalanced fertilization resulting deficiency of all the macronutrients thereby crop production reduction[4,5]. However, the long term or overuse of chemical or synthetic fertilizer have unwanted effects on soil, plants, surrounding environment as well as human health [6]. Hence, it is very important to improve the macronutrient usage efficiency to enhance the crop yield through ecologically safer method as well as economically reliable [7]. Employing microbial consortium as effective plant growth-promoting agent is an excellent as well as promising alternative biotechnological approach towards synthetic fertilizers [8,9]. Commonly, microbial consortium is cost effective, eco-friendly, safer than agrochemicals and also, helps to recover soil fertility and structure [10].

Most commonly, available macronutrients in the soil can be utilized by dissolving or degrade them with soil microbes particularly, plant growth promoting organisms (PGPO) [11,12,13]. PGPO are mainly connected with root of the plant and surrounding soil environment and employing beneficial impact on plant growth [14,15]. PGPO is an important component in the soil ecosystem and also, frequently involved in biogeochemical nutrient cycle resulting environmentally approachable fertilizers. PGPO can able to contribute for increasing crop yield through promoting plant growth both directly and indirectly by mineral solubilization, nitrogen fixation, phytohormones synthesis including siderophore and indole-3-acetic acid production, phytopathogen inhibition, plant systemic resistance induction against phytopathogens, soil aggregates stability and maintains of soil structure and soil nutrient [16,17]. Additionally, PGPO has the possibility to solubilize immobilize form of minerals including potassium and phosphate to soluble form which can be easily absorbed by plant [18,19]. Consequently, PGPO were reported for solubilizing different inorganic insoluble minerals like strengite, barrandite, tricalcium phosphate, hydroxyapatite, crandallite, zinc oxide, zinc silicates and smithsonite to soluble forms through various mechanism including solubilization, mineralization as well as mobilization [20,21,22,23]. Among the reported mechanisms, solubilization is one of the significant methods to convert the insoluble minerals to easily absorbed soluble form by chelation, exchange reaction, producing organic acid secretion, secretion of protons and acidification [24, 25]. Hence, our study aimed to isolate and identify the potential plant growth promoting fungi from conventional soil and to screen the organisms for mineral solubilization.

MATERIALS AND METHODS

Chemicals: For the study, Potato Dextrose Agar (PDA) medium, Lactophenol Cotton Blue (LCB) Solution, Pikovskaya agar medium were purchased from Himedia India. SDS, Isopropanol, TE Buffer, Phenol/Chloroform/Isoamyl Alcohol (25:24:1 ratio), RNase A, Bromophenol blue, Proteinase K were procured from Sigma Aldrich, USA.

Collection of soil sample: For the isolation of plant growth promoting fungi, totally 10 conventional soil samples in triplicate were collected from various crop cultivated land of Karur District, Tamilnadu, India during June 2023 to November 2023. Soil was sampled from each site at a depth of 0-30 cm. Collected samples were shifted to clean polythene bags, tagged and transported to laboratory. The samples details like collection field, area and latitude & longitude are presented in table 1.

Isolation of fungi: For the isolation, 1 g of collected inorganic soil sample was used for 10-fold serial dilution up to 10^{-6} and spread plate was performed on prepared sterile PDA plate and incubated for 3-7 days at room temperature. After incubation, the plate was monitored for colony formation and individual colonies from each dilution was counted. The obtaining fungal colonies were observed visually and selected colonies were sub-cultured till the purified fungal colonies were obtained. All the purified fungal isolates were preserved for further assay.

Screening for phosphate solubilisation: To check the ability of all the isolates to solubilize phosphate, the Pikovskaya's medium was used as described before [26]. In brief, the Pikovskaya agar plates prepares in sterile condition was used for spot inoculation of all the isolates by taking small portion of the fungal spores using sterile inoculation needle and incubated for 7 days at room temperature. After incubation, the plate was observed for clear zone formation around the colonies which indicates the solubilization of phosphates by the organisms.

Screening for potassium solubilisation: All the isolated isolate's potassium solubilization abilities were determined using modified Aleksandrov medium as mentioned earlier [27]. Briefly,the spot inoculation of all the isolates spores were applied on the sterile prepared Aleksandrov medium using sterile inoculation needle and allowed for 7 days to form zone formation. The zone around the organisms indicates the potassium solubilizing ability of the isolated organisms.

Screening for protease production: To predict all the isolates protease production ability, the skim milk agar medium was used as defined before [27]. In brief, the prepared skim milk agar plates in sterile condition were allowed for receiving spot inoculation of all the isolated isolates spores using inoculation needle and allowed for incubation at room temperature for 7 days. Then, the incubated plates monitored for zone formation around the grown isolates, indicates the protease production of the isolates.

Screening for indole acetic acid (IAA) production: To screen the capacity of all the isolates for IAA production, the fungal isolates were inoculated into each 5 ml of sterile Potato Dextrose broth supplemented with 3 mg/ml of L-tryptophan and incubated at 28ºC for 5 days. After incubation, cell free supernatant was obtained by centrifuging at 10,000 rpm for 10 minutes and to that a drop of orthophosphoric acid and 2 ml of Solwaski's reagent (50 ml, 35% of perchloric acid, 1 ml 0.5 M $FeCl_3$ solution) was added and kept for 20 minutes at room temperature. The development of pink colour indicates the production of IAA [28].

Microscopic and Molecular Identification of isolated isolates: The isolates showed positive to phosphate and potassium solubilization and protease and IAA production were selected for microscopic and molecular identification. For microscopic analysis, the lactophenol cotton blue mount was performed for each isolate by adding a small fungal specimen in to sterile clean glass slides which contains sterile water droplets, mixed well and added the few drops of LCB, covered with cover slip and observed under microscope [29].

DNA Isolation and Quantification: For DNA isolation, in a fresh tube, 500 µl of culture grown in PDB were added and to that added equal volume of Tris-HCL and EDTA, along with 10 µl SDS was added. Sterile homogenizer was used for homogenization and 5 µl of Proteinase K was added. Then the mixture was incubated for 2 h at 55°C and then placed in ice for 10 minutes. About 250 µl of 6 M NaCl and EDTA was added and mixed and again placed in ice for 5 minutes, they were centrifuged at 8000 rpm for 15 minutes. Then, 500 µl of supernatant was collected in new tubes. For the precipitation of DNA, twice the volume of ethanol was added. The obtained samples were centrifuged at 11000 rpm for 15 minutes and the supernatant was removed. Then the precipitates were washed using ethanol and

again centrifuged at 11000 rpm for 5 minutes. Then the supernatant was removed and the pellet was dried at room temperature. Then the DNA samples were resuspended in the 1X TE buffer. DNA quantification has been carried out using a UV spectrophotometer at optical densities of 260 nm and 280 nm. The DNA quality was analysed using agarose gel electrophoresis

PCR Amplification and Sequencing: The PCR amplification was performed for molecular identification of isolated isolates using extracted DNA as mentioned before [30]. In brief, the PCR amplification was carried out using the ITS forward (TCCGTAGGTGAACCTGCGG) and ITS reverse (TCCTCCGCTTA TTGATATGC) and the PCR reactions was performed PCR thermal cycler (Himedia PCR System). The final PCR product was added with 2 µl of ExoSAP-IT and was incubated at 37°C for 30 minutes. The enzyme inactivation was followed at 80°C for15 minutes. Then, the sequencing process was carried out using BigDye Terminator v3.1 (Applied Biosystems, USA). Followed by post-sequencing PCR clean-up. Then the cleaned product was sequenced using ABI 3500 DNA Analyzer (Applied Biosystems).

Sequencing and Phylogenetic Analysis: The ITS region sequencing has been carried out using BLAST and compared with the NCBI GenBank database. Using the multiple alignment tool ClustalW, an extreme identity score program, the first 10 sequences were selected and aligned. Using MEGA 7, a distance matrix was generated and a phylogenetic tree was constructed. The neighbour-joining method was used for producing evolutionary trees. The phylogenetic tree is depicted accurately, with branch lengths measured in evolutionary distances that correspond to the same units. The Poisson correction method was utilized to calculate the evolutionary distances**.** In MEGA12, evolutionary analyses were performed [30].

RESULTS

Isolation of fungi: Totally, thirty isolates were isolated from various dilutions of ten conventional soil samples and the isolated isolates were morphologically distinct. The most predominant isolated fungal isolates were observed macroscopically (based on colony morphology) includes Genus of *Rhizopus, Aspergillus, Penicillium, Fusarium* and*Curvularia* comes under the group of Zygomycota and Ascomycota.

Screening for phosphate solubilisation: The isolated isolate's ability for phosphate solubilization was determined and the most important organisms solubilizing phosphate are mentioned in figure 1. In total, ten isolates like isolates 3, 5, 7, 11, 13, 17, 20, 25, 27 and 29 were displayed their capacity to solubilize phosphate (Table 2) by producing zone formation around the grown colonies which indicates the organism's usefulness in plant growth promoting activities.

Screening for potassium solubilisation: The isolated fungal isolate's ability for potassium solubilization was screened and the most important isolates showed potassium solubilization are denoted in figure 2. Totally, thirty isolates were tested for potassium solubilizing ability, in which nine isolates including isolates 2, 5, 11, 13, 20, 23, 25, 27 and 29 were expressed their potassium solubilization (Table 2) on Aleksandrov agar plates by showing zone formation around the fungal isolates, indicating fungal isolates plant growth promoting activity.

Screening for protease production: The protease producing capacity of all the isolated fungal cultures were screened and the attained results are presented in figure 3. The figure illustrated the protease producing capability of most significant fungal isolates which produced protease on skim milk agar were reported. The results reported that, among the thirty isolates, nine fungal isolates such as isolates 2, 5, 10, 13, 16, 20, 25, 27 and 30 were identified for protease production (Table 2) by exploring the formation of clear zone around the isolates which indicates the plant promoting ability of isolated fungal isolates.

Screening for IAA production: The isolated fungal strains were analysed for the most significant plant growth hormone, IAA and the obtained result is displayed in figure 4. Among the thirty isolates, totally, sixteen isolates such

as isolates 2, 4, 5, 8, 10, 13, 15, 16, 18, 20, 21, 23, 25, 26, 27 and 30 were identified for IAA production (Table 2) by producing pink colouration which indicated the plant promoting ability of isolated fungal isolates. Further, the isolated thirty fungal isolates screened for phosphate and potassium solubilization, protease and IAA production were reported in figure 5 in which five isolates namely isolate 5, 13, 20, 25 and 27 rendering all four activities were selected for microscopic and molecular identification.

Microscopic and Molecular identification:

The isolated isolates were showed potent screening activity such as phosphate and potassium solubilization, protease and IAA analysed for macroscopic and microscopic observation using LCB mount namely *Rhizopus arrhizus, Aspergillus niger, Aspergillus flavus, Rhizopus microspores,* and *Curvulariaprasadii* respectively and the obtained results are presented in figure 6(a), 6(b) and 7.

Molecular identification and the phylogenetic tree construction performed for isolated potent fungal isolates. The ITS region sequence of samples was compared to the NCBI Genbank using BLAST. The first ten resulting sequences were selected for further analysis. Based on the molecular and phylogenetic analysis, the closest match identified by BLAST was revealed that, the isolated fungal isolates 5, 13, 20, 25 and 27 were identified as *Rhizopus arrhizus* (PQ813584.1), *Aspergillus niger* (PQ135184.1), *Aspergillus flavus* (PQ163838.1), *Rhizopus microporus* (PQ636497.1) and *Curvulariaprasadii* (PQ164259.1) respectively (Fig.7).The evolutionary history was inferred using the Nighbor-Joining method was shown in figure 7. The optimal tree with the sum of branch length=2.605 is shown. The evolutionary distances were computed using the Maximum Composite Likelihood method and are in the units of the number of base substations per site. The proportion of sites where at least 1 unambiguous base is present in at least 1 sequence for each descended clade is shown next to each internal node in the tree. The analytical procedure encompassed 27 nucleotide sequences obtained from NCBI which includes *Rhizopus arrhizus* (PQ813584.1), *Rhizopus arrhizus* (LC705203.1), *Rhizopus stolonifera* (AM933544.1), *Rhizopus microspores* (LC844828.1), *Rhizopus microspores* (LC390273.1), *Rhizopus azygosporus* (LC390245.1), *Rhizopus schipperae* (DQ119015.1), *Rhizopus oryzae* (HE608810.1), *Rhizopus sexualis* (AF543521.1), *Rhizopus microspores* (PQ636497.1), *Aspergillus niger* (PQ135184.1), *Aspergillus flavus* (PQ163838.1), *Aspergillus flavus* (AJ874128.1), *Aspergillus niger* (AJ876876.1), *Aspergillus niger* (LC632401.1), *Aspergillus fumigatus* (LC602033.1), *Aspergillus terreus* (LC777033.1), *Aspergillus versicolor* (LC705733.1), *Aspergillus elegans* (EU165705.1), *Aspergillus ochraceus* (FR733829.1), *Curvulariaprasadii* (PQ164259.1), *Curvulariaprasadii* (HG778997.1), *Curvularialunata* (LC317565.1), *Curvularia geniculate* (OW986190.1), *Curvulariainaequalis* (OW988110.1), *Curvulariaverruculosa* (OW985725.1) and *Curvularialunata* (OW986260.1). The pairwise deletion option was applied to all ambiguous positions for each sequence pair resulting in a final data set comprising 1,479 positions.

DISCUSSION

Since several decades, the soil fertilization is an important process for plant growth and development which can be accomplished through applying chemical fertilizer consists nitrogen, potassium and phosphorous as predominant macronutrients which can't be utilized completely by soil. Therefore, complete utilization of macronutrient by soil is important for plant growth by employing microbial consortium. Hence, in the present study, isolated five fungal isolates from conventional soil and screened for mineral solubilization which is one of the chief mechanisms of plant growth that involves the solubilization of insoluble minerals like phosphate and potassium by microorganisms because the macronutrients are involved in development and metabolism of plant such as energy transfer, photosynthesis, grain quality improvement, respiration, disease control, signal transduction, macromolecular biosynthesis that contributed for greater crop yield [31,32]. Particularly, phosphate and potassium are an important macronutrient for plant growth and development like photosynthesis, strengthening the stalks and stems, flower and seed formation, energy production, crop maturity and quality of crop, N_2 fixation in legumes, storage and transfer reactions, cell division and enlargement and resistance to plant diseases [33,34]. Consequently, the identification of potential phosphate and potassium solubilizing organisms are an important criterion for sustainable agricultural practice. Therefore, our study explored the isolated fungal isolates phosphate and potassium solubilizing ability by

zone formation which provided the partial measurement of phosphate and potassium solubilization potential of the fungal isolates from conventional soil resulting alteration in the soil pH. In support of our findings, many soil microorganisms like *Aporrectodea rosea*, *Aspergillus* sp, *Penicillium* sp, *Rhodanobacter*, *Pleomorphomonas, Acidovorax*sp, *Pseudomonas* sp,*Burkholderia* sp, *and Sphingomonas* sp, *Mycolicibacterium* sp, *Aureobasidium pullulans, Candida tropicalis,Cryptococcus laurentii, Pseudofusicoccum, Penicillium citrinum, Aspergillus tamarii*and*Variovorax*sp. were reported for phosphate solubilization for sustainable plant growth and development [27, 35, 36, 37, 38].

In addition, an important plant growth hormone from the auxin family of indole derivatives which is most abundant and essential plant hormone occurred naturally that controls utmost each and every characteristic features of plant growth and development includes cell division, cell elongation, fruit development and ageing and also, increased plant protection from external stress. IAA can be synthesized not only in plants but also in many microorganisms which interact with plants including bacteria and fungi [39,40]. Therefore, it is very important to study the IAA producing ability of isolated fungal isolates and found that promising IAA producing ability for plant growth promoting activities. Similarly, our findings were supported by many scientific groups wherein soil microorganisms both bacteria and fungi including *Klebsiella*sp, *P. aeruginosa, Bacillus* sp, *B. megaterium*, *Colletotrichum gloeosporioides, Trichoderma tomentosum, Colletotrichum godetiae*and *Talaromycesamestolkiae* were able produce IAA for promising plant growth and development [41, 42, 43, 44].

Supporting to our finding, in recent studies a bacterium *Alcaligenes faecalis* isolated from organic soil from Namakkal District of Tamil Nadu, three salt tolerance endophytic bacteria from ginger and four endophytic fungal from the lavender plant exhibited strong PGP properties, including the highest IAA production, phosphate solubilization and protease production [45,46,47].Overall, the isolated fungal isolates in this study showed promising phosphate and potassium solubilizing ability as well as producing IAA for better plant growth promoting activity.

CONCLUSION

The present study concluded that the isolated fungal isolates from conventional soil were expressed their mineral such as phosphate and potassium solubilizing ability and also, screened for IAA and protease producing ability of isolated five fungal isolates. Finally, the isolated isolates were identified by molecular sequencing and identified as *Rhizopus arrhizus, Aspergillus niger, Aspergillus flavus, Rhizopus microspores,* and *Curvularia prasadii* respectively. Altogether, the isolated and identified fungal isolates can be used for mineral solubilization leads promising plant growth and development.

ACKNOWLEDGMENT

The authors are grateful to Professor M. Karunanithi, chairman and secretary, vivekanandha Educational Institutions, Dr. P. Baby Shakila, Pricipal, Vivekanandha college of Arts and Sciences for Women, Tiruchengode, Namakkal, Tamil Nadu and the Chairmen, Secretary, Principal of Kongu college of Arts and Science, Vennaimalai, Karur, Tamil Nadu, India for supporting this project.

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Table 1: Collected samples details from various locations of Karur District, Tamil Nadu, India.

Soil Sample #	Collection field	Collection Area	latitude & longitude
1	Onion	Kadavur	10.7294 & 78.2307
2	Ground nut	Puliyur	10.93999 & 78.144480
3	Chilly	Aravakurichi	10.7747 & 77.9090
4	Seasame	Uppupalayam	11.30145 & 77.91398
5	Sugar cane	Aravakurichi	10.77412 & 77.907040
6	Corn	Kuppam	11.00759 & 77.93541
7	Green gram	Aravakurichi	10.77412 & 77.907040
8	Water melon	Vettamangalam	11.0386 & 77.9567
9	Turmeric	Mookanankurichi	10.86462 & 78.075970
10	Black Gram	Thukkachi	11.02357 & 77.842330

Table 2: Number of isolates and occurrence percentage of positive and negative screening

Screening type	Positive (+) / Negative (-)	No. of Isolates and Occurrence % (n=30)	
P- Solubilization	(+)	10	33 %
	(-)	20	67 %
K- Solubilization	(+)	9	30 %
	(-)	21	70 %
Protease Production	(+)	9	30 %
	(-)	21	70 %
IAA production	(+)	16	53 %
	(-)	14	47 %

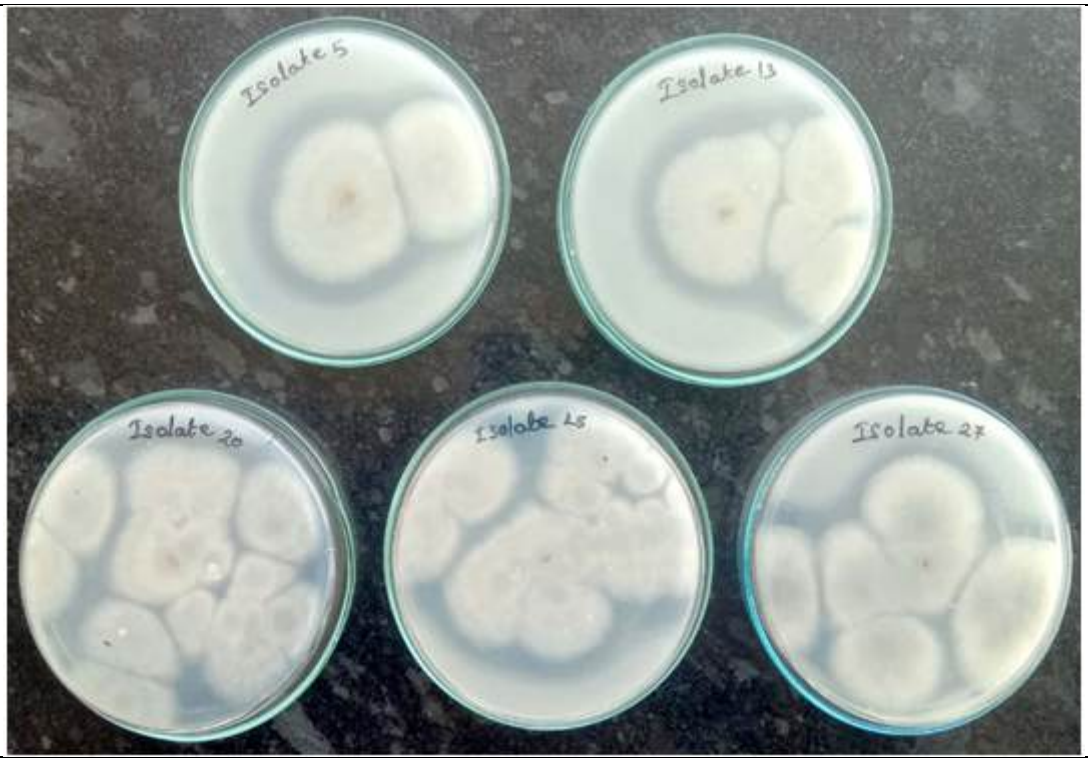

Fig. 1:Phosphate solubilization screening for most important isolated organisms such as isolate 5, 13, 20, 25 and 27 which showed clear zone formation around the isolates.

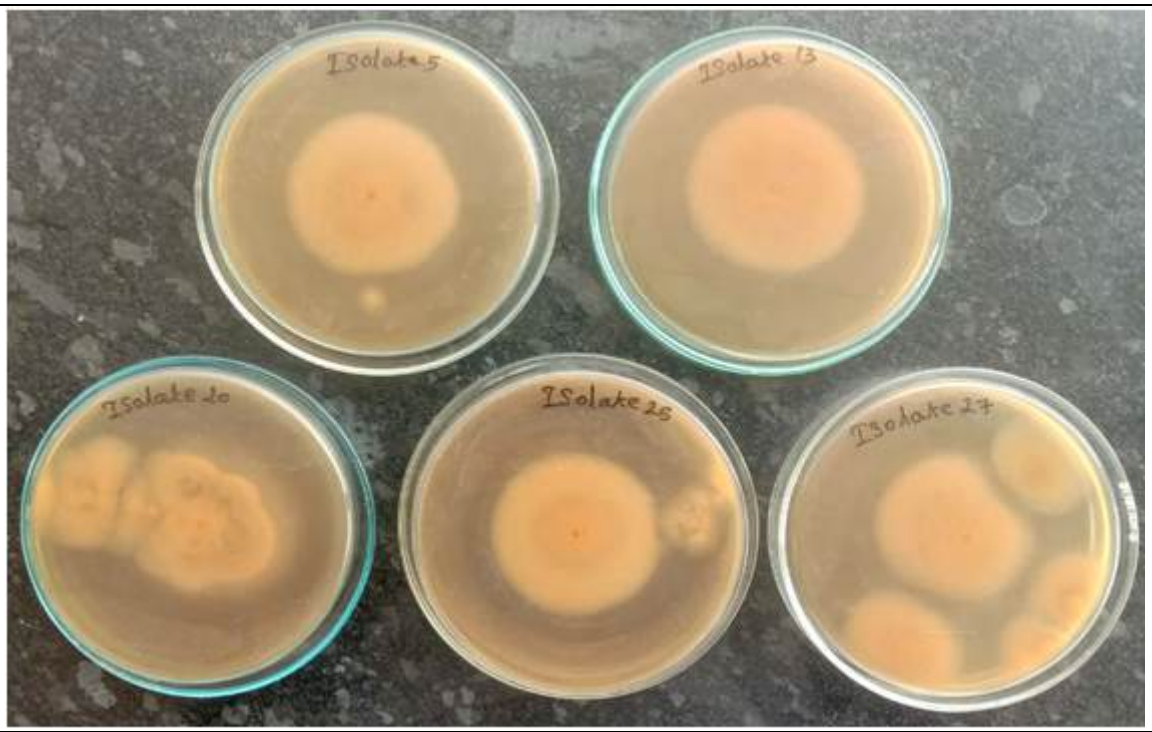

Fig. 2: Potassium solubilization determination of isolated fungal isolates on Aleksandrov agar plates, wherein the isolates 5, 13, 20, 25 and 27 were showed clear zone formation around the isolates.

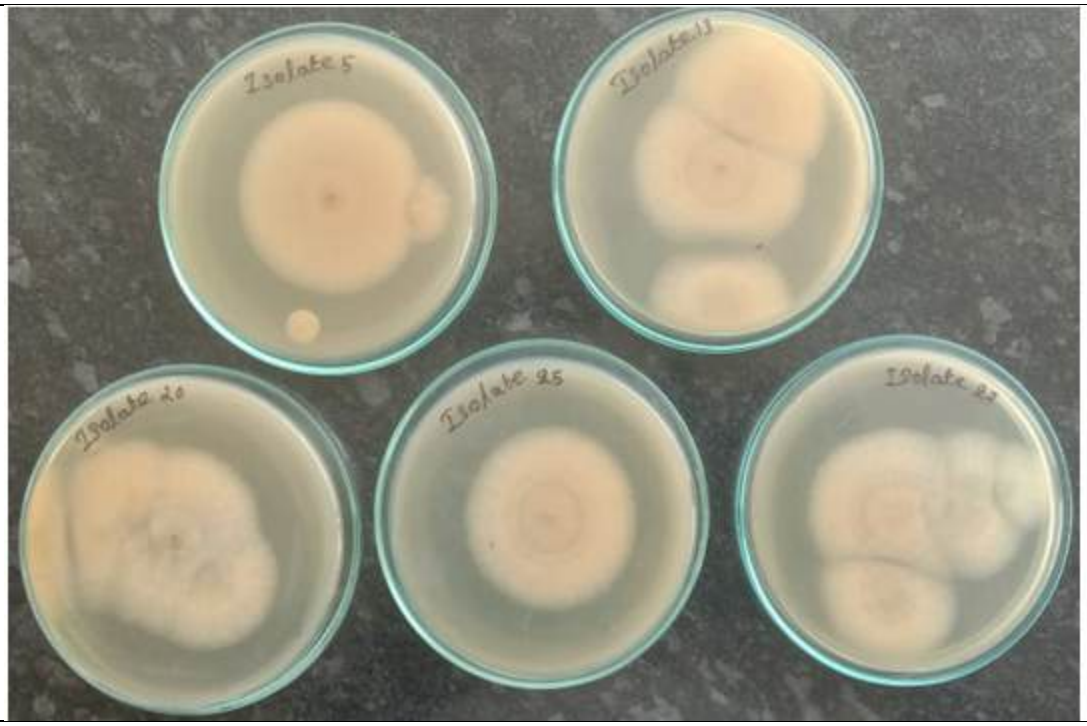

Fig. 3: The most important isolated fungal isolates 5, 13, 20, 25 and 27 were explored for protease producing ability on skim milk agar plates.

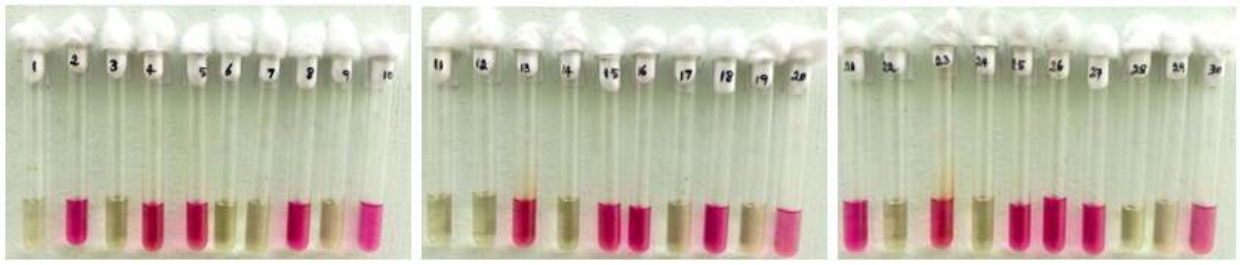

Fig. 4: IAA production of the most important isolated fungal isolates 2, 4, 5, 8, 10, 13, 15, 16, 18, 20, 21, 23, 25, 26, 27 and 30

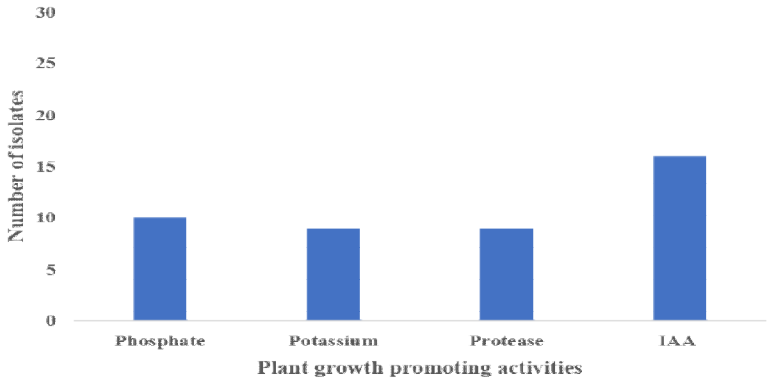

Fig. 5: Graph indicting the isolated fungal isolates potential for plant growth promoting activities.

Fig. 6(a): Macroscopic observation of most important isolated isolates. A) *Rhizopus sp*(IS 5)B) *Aspergillus sp,* (IS 13) C) *Aspergillus sp,* (IS 20)D) *Rhizopus sp* (IS25)andE)*Curvularia sp* (IS 27). Note: IS-isolate.

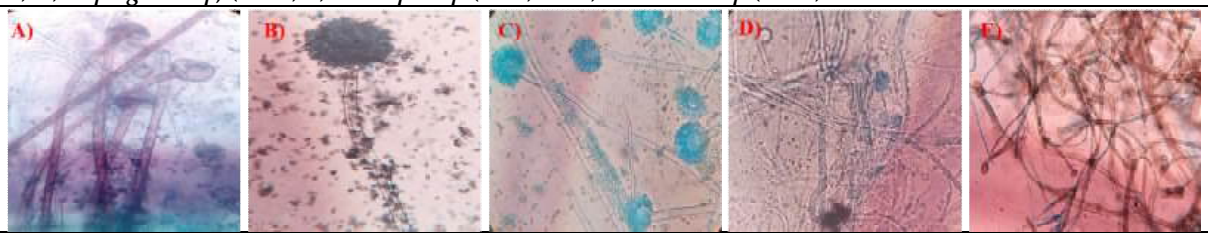

Fig. 6(b): Microscopic observation of most important isolated isolates A) *Rhizopus sp*(IS 5)B) *Aspergillus sp,* (IS 13) C) *Aspergillus sp,* (IS 20)D) *Rhizopus sp* (IS25)andE)*Curvularia sp* (IS 27). Note: IS-isolate.

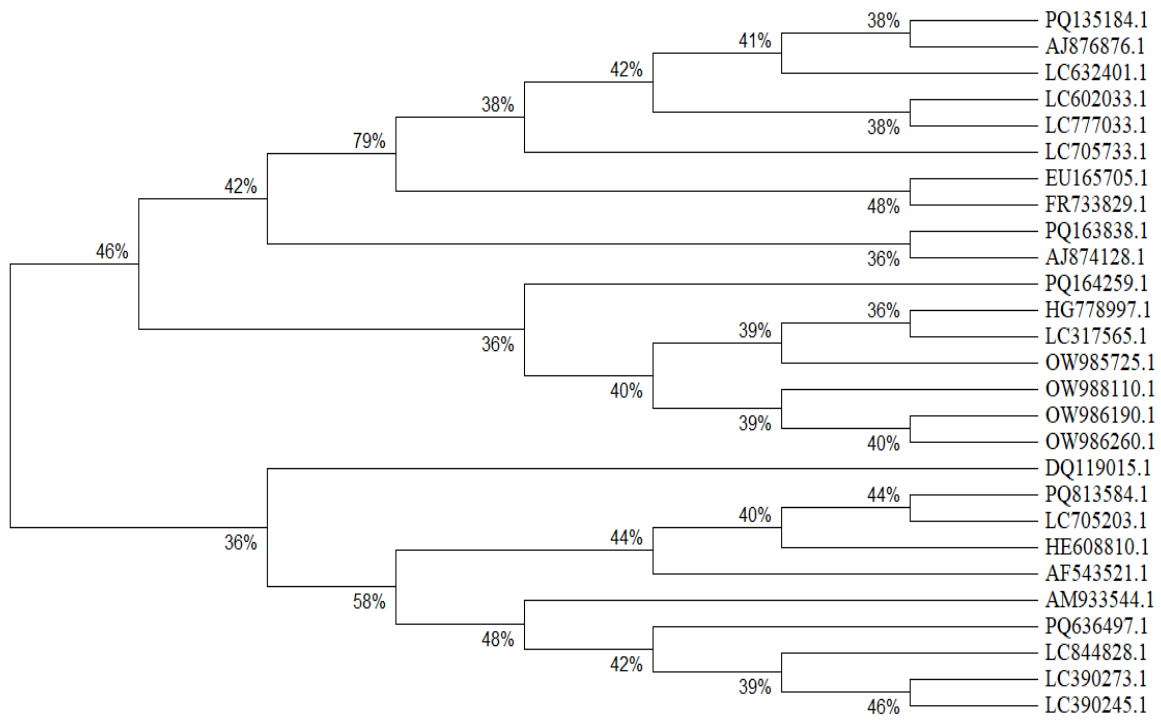

Fig. 7: Tree of evolutionary history inferred using the Nighbor-Joining method in MEGA12 software. The analytical procedure encompassed 27 nucleotide sequences from NCBI. The percentage shown in each node indicate coverage area.

REVIEW ARTICLE

An Overview of Drug Regulatory Affairs and the New Drug Approval Framework in India

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Received: 10 Jan 2026 Revised: 16 Jan 2025 Accepted: 18 Jan 2026

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ABSTRACT

The pharmaceutical marketing and industrial sector in India is expanding rapidly, leading to increased global competition and a growing demand for skilled drug regulatory professionals. Regulatory affairs is a specialized profession within the pharmaceutical industry that encompasses activities related to drug discovery, clinical trials, production, manufacturing, marketing, and post-marketing welfare. Drug Regulatory Affairs professionals serve as a crucial link between the pharmaceutical industry and regulatory authorities worldwide. Drug product approval is a critical step to ensure that medicines are safe, effective, and of acceptable quality. Regulatory affairs plays a vital role in supporting both pharmaceutical companies and government authorities by preventing issues arising from improper, incomplete, or misleading data. In India, regulatory systems can be broadly classified into economic regulation, public interest regulation, and environmental regulation. Every country has a designated regulatory authority responsible for the analysis and evaluation of research data related to new drugs and medicinal products to ensure their safety and efficacy for public health. The present study focuses on drug regulatory issues, the roles and relationships of regulatory affairs within the pharmaceutical

industry, and the drug approval process governed by the national regulatory authority in India, namely the Central Drugs Standard Control Organization (CDSCO)

Keywords: Drug Regulatory Affairs, CDSCO, Regulatory body, Drug product approval

INTRODUCTION

Regulatory Affairs (RA) is a specialized profession within the healthcare and other regulated industries, particularly pharmaceuticals, medical devices, biologics, veterinary medicines, cosmetics, dietary supplements, pesticides, and agrochemicals. The profession has evolved primarily to protect public health by ensuring that products introduced into the market are safe, effective, and of acceptable quality. Regulatory affairs serves as a vital link between pharmaceutical companies and government regulatory authorities. It is responsible for ensuring compliance with regulatory requirements related to drug discovery, clinical trials, manufacturing, registration, marketing authorization, and post-marketing surveillance. Because RA professionals interact closely with regulatory bodies, the discipline is often referred to as "Government Affairs." A single regulatory error can jeopardize years of research and development; therefore, RA professionals must possess comprehensive knowledge of regulatory guidelines, documentation requirements, and both technical and digital systems used within the industry. Consequently, most pharmaceutical organizations—ranging from large multinational corporations to small biotechnology firms—maintain dedicated regulatory affairs departments. The development of a new pharmaceutical product typically requires 10–15 years and substantial financial investment before it reaches the market. However, recent global health emergencies, such as the COVID-19 pandemic, caused by the novel corona virus SARS-CoV-2, demonstrated the critical role of regulatory authorities and RA professionals in enabling accelerated yet safe product approvals under emergency conditions[1-4]. In the modern era, the pharmaceutical industry has become highly organized, systematic, and compliant with international regulatory standards. Stringent Good Manufacturing Practices (GMPs) are followed for the production of chemical and biological drugs for human and veterinary use, as well as for medical devices, blood and blood products, traditional herbal medicines, cosmetics, and dietary supplements. Regulatory frameworks that were once fragmented have now evolved into well-defined and controlled systems, resulting in the consistent manufacturing and marketing of safe, efficacious, and high-quality products. As the pharmaceutical industry continues to grow, regulatory legislations across different regions have become increasingly complex, thereby creating a greater demand for skilled regulatory affairs professionals. Understanding the historical evolution of regulatory frameworks in regions such as the United States, Europe, and India is essential for appreciating the development of the current global regulatory environment[5,6]. Overall, the regulatory affairs profession plays a central role in the collection, analysis, and communication of the risks and benefits of healthcare products to regulatory authorities and the public worldwide. The RA department is responsible for interpreting regulatory requirements and ensuring the successful approval of new and generic products, thereby safeguarding public health while supporting innovation in the pharmaceutical industry.

Objectives of Regulatory Affairs:[7]

1. How and why the pharmaceutical industry and drug regulation developed in the US.
2. Rules for medicinal products in the European Union.
3. Major US regulations.
4. The EU framework and its regulation.
5. Pharmaceutical legislation of the EU.
6. Indian pharmaceutical industry and development of drug prescriptions in different periods.
7. Types of registration procedure on the EU market.
8. Main Rules and Law of India.
9. The role of an expert on regulatory matters in health authorities and also in the pharmaceutical industry.
10. Ensuring that their companies comply with all regulations and laws relating to their business.

11. Cooperate with federal, state and local regulatory authorities and staff on specific issues affecting their business.
12. Advising companies on regulatory aspects and climate that would affect their proposed activities

Role of the Regulatory Affairs (RA) Department [8]

- The Regulatory Affairs (RA) department in the pharmaceutical industry is responsible for obtaining and maintaining marketing authorization for new pharmaceutical products and ensuring continued compliance throughout the product lifecycle.
- From the early stages of product development, RA professionals provide strategic, scientific, and regulatory guidance to research and development (R and D), quality control, production, and other allied departments, thereby contributing significantly to both the scientific advancement of products and the overall growth of the organization.
- The RA department continuously monitors and interprets national and international regulatory guidelines, customer requirements, and legislative changes relevant to the company's product portfolio.
- It ensures that all company products comply with current regulatory requirements in the regions where they are manufactured and marketed.
- RA professionals maintain comprehensive knowledge of the company's product range and manage regulatory documentation, including responses to audit reports, compliance activities, and regulatory as well as customer inspections.
- A key responsibility of RA professionals is to track evolving regulatory legislation across all target markets and provide expert advice on the associated legal, scientific, and technical requirements. They also collect, evaluate, and compile scientific data generated by research and development teams for regulatory submissions.
- Regulatory authorities issue regulations as legally binding instructions that define how laws must be interpreted and implemented. Failure to comply with these regulations can result in regulatory actions such as warning letters, which can have serious consequences for pharmaceutical companies.
- The RA department is responsible for maintaining approved applications**,** managing Drug Master Files (DMFs)**,** and keeping accurate records of regulatory submissions and registration fees.
- Regulatory Affairs professionals help organizations avoid regulatory setbacks caused by incomplete documentation, poor data presentation, or inadequate scientific justification**.**
- An effective RA professional adopts a "right-first-time" approach, coordinating regulatory requirements with scientific development throughout the product lifecycle to ensure efficient use of company resources and cost-effective compliance.
- Additionally, the RA department plays a role in supporting the dissemination of accurate, complete, and scientifically sound information to physicians and other healthcare professionals regarding the safety, quality, and efficacy of pharmaceutical products.

The Regulatory bodies in various countries[8]

USA

USA- FDA

The United States Food and Drug Administration (FDA or USFDA) is a federal agency of the Department of Health and Human Services. The FDA is responsible for protecting and promoting public health through the control and supervision of food safety, tobacco products, dietary supplements, prescription and over-the-counter pharmaceutical drugs (medications), vaccines, biopharmaceuticals, blood transfusions, medical devices, electromagnetic radiation emitting devices (ERED), cosmetics, animal foods and feed and veterinary products. The FDA has its headquarters in unincorporated White Oak, Maryland. The agency also has 223 field offices and 13 laboratories located throughout the 50 states, the United States Virgin Islands, and Puerto Rico. In 2008, the FDA began to post employees to foreign countries, including China, India, Costa Rica, Chile, Belgium, and the United Kingdom.

Canada

Health Canada

The department of the Government of Canada responsible for national health policy. The department itself is also responsible for numerous federal health- related agencies, including the Canadian Food Inspection Agency (CFIA) and the Public Health Agency of Canada (PHAC), among others. These organizations help to ensure compliance with federal law in a variety of healthcare, agricultural, and pharmaceutical activities. This responsibility also involves extensive collaboration with various other federal- and provincial-level organizations in order to ensure the safety of food, health, and pharmaceutical products—including the regulation of health research and pharmaceutical manufacturing/testing facilities.

UK

Medicines and health care products regulatory agency (MHRA)

The Medicines and Healthcare products Regulatory Agency (MHRA) is an executive agency of the Department of Health and Social Care in the United Kingdom which is responsible for ensuring that medicines and medical devices work and are acceptably safe. The MHRA has several independent advisory committees which provide the UK Government with information and guidance on the regulation of medicines and medical devices.

There are currently eight such committee

- Advisory Board on the Registration of Homeopathic Products
- Herbal Medicines Advisory Committee
- The Review Panel
- Independent Scientific Advisory Committee for MHRA database research
- Medicines Industry Liaison Group
- Innovation Office
- Blood Consultative Committee
- Devices Expert Advisory Committee

European Union

European Medicines Agency (Ema)

The European Medicines Agency (EMA) is an agency of the European Union (EU) in charge of the evaluation and supervision of medicinal products. Prior to 2004, it was known as the European Agency for the Evaluation of Medicinal Products or European Medicines Evaluation Agency (EMEA). The EMA was set up in 1995, with funding from the European Union and the pharmaceutical industry, as well as indirect subsidy from member states, its stated intention to harmonise (but not replace) the work of existing national medicine regulatory bodies. The hope was that this plan would not only reduce the €350 million annual cost drug companies incurred by having to win separate approvals from each member state but also that it would eliminate the protectionist tendencies of sovereign states unwilling to approve new drugs that might compete with those already produced by domestic drug companies.

Drug Regulatory Agencies in India [9]

India has emerged as one of the main markets for pharmaceutical merchandise. growth inside the private healthcare infrastructure, widening rural markets, and inclusion of more modern technologies Have placed healthcare as an impartial region in India. With privatization of healthcare, the scientific gadgets quarter is growing too. with a view to regulate the import, manufacture, distribution and sale of drugs and cosmetics, the capsules and Cosmetics Act, 1940 ("D and C, Act") become brought in India in 1940. But, no Separate regulation has been enacted for regulating the import, manufacture, distribution or Sale of scientific devices in India till date by the government of India. Tablets and health is in concurrent list of Indian charter. it is ruled by means of each Centre And kingdom Governments below the medication and Cosmetics Act, 1940.

Main Bodies

- Central Drug Standard Control Organization (CDSCO)
- Ministry of Health and Family Welfare (MHFW)

- Indian Council of Medical Research (ICMR)
- Indian Pharmaceutical Association (IPA)
- Drug Technical Advisory Board (DTAB)
- Central Drug Testing Laboratory (CDTL)
- Indian Pharmacopoeia Commission (IPC)
- National Pharmaceutical Pricing Authority (NPPA)
- Drug controller General India (DCGI)

India: Approval process of New Drug

The Drug and Cosmetic Act 1940 and rule 1945 was passed by Indian government at Parliament to export, import and production of medicinal products. National regulatory Authority of India is Central Drug Standard Control Organization (CDSCO). CDSCO is Indian government evaluatory agency that for applicant of new drug product for safety and product efficacy. CDSCO give review and analytical report to DCGI (Drug Controller General of India). DCGI is a provide license and authority of Licensing of India that approves and give permits a new drug product manufacturing and production and also marketing in India. To start the marketing business in India with import or developing a new drug or new medicine in industry, it must require fill out FORM 44 and transfer the data that needed under Schedule Y of Drug and Cosmetics Act 1940 and rules 1945.(Rule 122A , 122B , and 122D with appendix I, IA, and VI).

Following are some provisions of the Drug and Cosmetics Rule1945

- In Rule 122A involve a request for a new drug approval
- In Rule 122B involve application of import permission of new drug or new medication
- In Rule 122D Fixed Dosage Combination permission to import and export
- In Rule 122DA involve request to approval to perform clinical trials for IND (Investigational New Drug)
- In Rule 122 involving majorly DAB that include compensation of injuries /death during clinical trials.

CDSCO: Central Drug Standard Control Organization

It under Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India .It is National Regulatory Authority (NRA) of India.

CDSCO Headquarter located at FDA Bhawan, Kotla Road, New Delhi. It has 6 Zonal offices, 4 sub Zonal offices, 13 port office and 7 Laboratories allover in India.

Role of CDSCO

1. For approval of new drug.
2. Processing and conducting the clinical trials.
3. Licensing and import registration.
4. Also approving license for blood banks, r-DNA Vaccine, LVPs vaccine, and some medicinal device and products.
5. New drug testing.
6. Drug and cosmetics banning.
7. Market surveillance through inspectorate center and state Authority.

Drug Approval Process in India

It is given in three phase

First phase

1. Applicant is filling the application of IND (Investigational New Drug) with their informational studies to CDSCO headquarters.
2. All the information is examined by new drug division.
3. Then detailed review by IND committee.
4. With proper information of CDSCO – Recommendation to DCGI (Drug Controller General Of India).
5. Then IND application is approved.

Second phase

1. Application is given one copy of IND information to ethical committee with application.
2. Then ethical committee report the application of IND.
3. This process taken within 12 Weeks.

Third phase

1. In 1st phase, IND application is approved and in 2nd phase, ethical committee report is positive then 3rd phase is started.
2. In 3rd phase, clinical trials is started.
3. Then again give application for new drug registration to CDSCO.
4. Then finally review by DCGI.
5. If Review is positive or complete then LICENSE IS GRANTED.
6. If Review is not complete then refused to grant license.

Requirement of Drug Approval Process in India

- Registration process of New drug approval is one time.
- Approval timeline is 2-18 months.
- Approval presentation format - paper.
- Process validation is required.
- Batch size is Pilot scale batch.

RESULTS

1. The Regulatory Affairs (RA) department of the pharmaceutical industry is in responsibility or functioning of obtaining permission for new pharmaceutical medicine or drug that ensuring the approval maintenance process for as desiring firm or for as long.
2. Right from the start of a product development, regulatory affairs experts provide technology and strategic guidance to quality control, R and D, production department, among other contributing significantly both financially and scientifically to the advancement of a development initiative and the enterprise.
3. Keep in touch with customer practices, guidelines and international legislation.
4. Ensure that a company's product comply with the current regulation.
5. Keep up to the date with a company's product range.
6. Manage review audit reports and compliance, regulatory and customer inspections.
7. The Regulatory Affairs professional role is to keep track of the ever changing legislation in all the region in which company wishes to distribute to it's product with the advice on the legal and scientific restrains and requirements, and collect also evaluate the scientific data that their research and colleagues are generating.
8. Regulation is a binding instruction issued by an agency that tells how to clarify and comply with the law, failures to follow regulation many end up into the "issued warning letter "sections of the FDA website, which is a fair for pharma industry.
9. Maintain approved application and the record of registration fees paid against submission of DMF's (Drug Master File) and other documents.

Regulatory affairs professional help company that avoid problem caused by badly kept records and inappropriate scientific thinking or poor presentation of data.

- A good Regulatory Affairs professional will have 'right first time' approaches and will play a very major and important part in coordinating scientific end with regulatory demand throughout the life of the products, helping to maximize the cost - effective use of the company resources.
- Also in the role to provide physician and other healthcare professionals with accurate and complete information about the safety, quality and effectiveness of the products.

Role of CDSCO

1. For approval of new drug.
2. Processing and conducting the clinical trials.
3. Licensing and import registration.
4. Also approving license for blood banks, r-DNA Vaccine, LVPs vaccine, and some medicinal device and products.
5. New drug testing.
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Present Regulatory Issues in the Indian Pharmaceutical Industry[10]

- According to a survey reported by *The Economic Times*, the pharmaceutical sector is one of the most dynamic industries in India. However, its regulatory compliance framework is highly complex, as the drug approval process requires coordination among multiple regulatory authorities and government departments.
- Key challenges related to industrial policy include the regulation of patents**,** drug exports, and the level of government support extended to the pharmaceutical industry. Following the introduction of the Patents Act, pharmaceutical companies were permitted to patent drug manufacturing processes, significantly impacting innovation and market exclusivity.
- Large pharmaceutical companies have increasingly invested in research and development (R and D) facilities to discover novel drug molecules. However, frequent global updates and evolving standards related to Good Manufacturing Practices (GMP)**,** Good Clinical Practices (GCP), and Good Laboratory Practices (GLP) have created ongoing challenges in licensing and quality compliance.
- Issues related to marketing authorization and patent protection continue to affect the industry. For example, in 2017, the Indian Patent Office granted a patent to the U.S.-based pharmaceutical company Pfizer for Prevenar 13 (a pneumococcal vaccine). This authorization provided exclusive marketing rights in India until 2026, thereby restricting domestic manufacturers from producing generic versions of the vaccine for export.

FUTURE PROSPECTS AND OPPORTUNITIES

India operates one of the world's largest public healthcare programs, serving nearly 500 million citizens, as announced in the Union Budget 2018. The flagship healthcare initiative, "Ayushman Bharat (formerly referred to as Namocare)", covers approximately 40% of the Indian population, significantly expanding access to healthcare services. To support this initiative, the Government of India has proposed major reforms in the Drug Price Control Order (DPCO) and is expected to introduce a new comprehensive pharmaceutical policy. This policy aims to support the successful implementation of national missions such as PHARMA 2020 by integrating and harmonizing critical components including manufacturing, research and development, financing, quality assurance, drug regulation, price control, and medical devices. Indian pharmacists and regulatory professionals remain committed to prioritizing patient safety and public health. They continue to advocate for stronger, more transparent, and patient-centric regulatory frameworks to ensure the sustained growth and global competitiveness of the Indian pharmaceutical industry[11,12].

CONCLUSION

Drug Regulatory Affairs (DRA) is a rapidly evolving and stable field that plays a crucial role in pharmaceutical and healthcare product development. It supports the safe, effective, and timely introduction of medicines to the market while contributing to industrial growth. Regulatory authorities worldwide, including CDSCO and DCGI in India, ensure that drugs comply with established standards of quality, safety, and efficacy through strict regulatory guidelines, thereby protecting public health.

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RESEARCH ARTICLE

Stability Indicating Simultaneous Method Development and Validation of Pregabalin and Etoricoxib in Bulk and Pharmaceutical Formulation by RP-HPLC

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Received: 06 Dec 2025 Revised: 12 Jan 2026 Accepted: 20 Jan 2026

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ABSTRACT

A simple, selective RP-HPLC method was developed for the simultaneous estimation of the Pregablin & Etoricoxib in bulk and its pharmaceutical dosage form. The method was developed on Waters X-Terra RP-C18 column capacitate 150X4.6mm, 3.5µm particle size, wavelength was fixed at 214 nm with PDA detector. The mobile phase was composed with Acetonitrile: 1% TEA in the ratio of 50:50 V/V and flow rate of mobile phase was fixed 1 mL/min. The retention times of Pregablin and Etoricoxib were found to be 2.9 and 3.8 min. The method was statistically validated with concern of selectivity & specificity, linearity, precision, accuracy, LOD & LOQ and robustness. The linearity concentration of the solution from 18.75 µg/mL – 112.50 µg/mL and R^2 value was found to be 0.999. The method was afforded excellent % recovery were found to be 98 %- 98.8 % for Pregablin & 100.01 % -101% for Etoricoxib respectively. The % RSD values of precision study were found to be <2. The LOD and LOQ values are 2.25µg/mL – 7.5 µg/mL for Pregablin & 1.8 µg/mL - 6 µg/mL for Etoricoxib. The method was proved as robust after slight changes to method parameters. The acid, base, peroxide, thermal, and hydrolytic forced degradation studies were conducted on the drugs, and the method proved stable.

Keywords: Pregabalin, Etoricoxib, Triethanol amine, RP-HPLC Method

INTRODUCTION

Etoricoxib (5-chloro-2-[6-methyl pyridine -3-yl]-3-[4-methyl sulfonyl phenyl] pyridine) is a potent COX-2 inhibitor and non-steroidal anti-inflammatory medication that is taken orally as an analgesic and anti-inflammatory(1-5). Etoricoxib (Fig.1) is a highly selective COX-2 inhibitor (coxib) that has been licensed in Europe for the treatment of acute gouty arthritis, rheumatoid arthritis, and osteoarthritis (OA) (4,5). The only coxib authorized for the treatment of acute gouty arthritis is etoricoxib, a potent analgesic medication that has demonstrated some enhanced efficacy over conventional NSAIDs (6,9). COX1 activity in circulating platelets and stomach biopsies is unaffected by the administration of therapeutic doses of etoricoxib to healthy individuals. Antidepressants (5,12), different anticonvulsants, opioids, and cannabinoids are used to treat central neuropathic pain (central pain), however these treatments are frequently ineffective and come with a number of side effects (12-15). Pregabalin (Fig.2), also referred to as (S)-2(aminomethyl)-5-methylhexanoic acid, is a neurotransmitter and anticonvulsant (15-17). The anticonvulsant pregabalin, a novel therapy for neuropathic pain (18&19). Similar to gabapentin, pregabalin is an antiepileptic medication that works by attaching itself to the voltage-gated calcium channels' alpha2-delta ($\alpha 2\delta$) subunit (20-22). Stability analysis of a medicine can be used to estimate the impact of temperature and humidity variations that may arise during drug product transportation (41-42). Different RP-HPLC methods, were reported on pregabalin & etoricoxib, individuall and few combined dosage forms with other drugs (23-37). The combined formulation of pregabalin & etoricoxib (38-40) estimated by the simultaneous RP-HPLC method and validated according to ICH guidelines.

MATERIALS AND METHODS

The PBL and ETC gift samples were kindly supplied by Mumbai, India-based Ajanta Pharma LTD. We purchased methanol, acetonitrile, and triethanolamine of High-Performance Liquid Chromatography (HPLC) quality from Rankem Chemicals in Mumbai. Furthermore, we purchased analytical grade hydrogen peroxide (H_2O_2), sodium hydroxide (NaOH), and hydrochloric acid (HCl) from Rankem Chemicals. We bought the tablet dosage form under the brand name Presidio from the neighborhood pharmacy. It contains 75 mg of PBL and 60 mg of ETC, according to the label. A Millipore Milli Q water purification system was used to provide high-purity water. Every chemical employed in this investigation was either LC or analytical grade.

Instrumental Conditions of HPLC

Data was collected utilizing an Alliance HPLC machine from Waters e 2695, based in Milford, MA, USA. The system has a model 2996 PDA detector and used Empower software for operation and analysis. The Waters C18 Column (150 mm×4.6 mm inner diameter, 3.5 µm particle size) was used for HPLC separation of the two drugs. The mobile phase was an isocratic mixture of Acetonitrile: 1% TEA (in the ratio of 50:50 v/v) and flowed at 1.0 ml/min. The column was run at ambient temperature. The PDA detector was used to monitor both drugs at an isosbestic wavelength of 214 nm. Before use, the solvents underwent filtration through a 0.22 mm membrane filter and were degassed using an ultrasonic bath.

Preparation of standard solutions

A carefully prepared mixed stock solution containing 75 µg/ml of PBL and 60 µg/ml of ETC was used to create the standard solutions. 75 mg of PBL and 60 mg of ETC had to be precisely weighed before being added to a 100 ml volumetric flask. The contents of the flask were then completely dissolved by adding 20 ml of solvent (acetonitrile:1%TEA (50: 50 V/V)) and using sonication. Using the same solvent, the flask's capacity was meticulously adjusted to the mark. Consequently, a stock solution containing 750 µg/ml of PBL and 600 µg/ml of ETC was present in the flask. Aliquots of this mixed standard solution were put into 100 ml volumetric flask. Further, 5 ml of the stock solution was pipetted out and transferred into a 50 ml volumetric flask, and the volume was made up to the mark. The concentrations of PBL & ETC acquired were75 µg/ml & 60 µg/ml.

Preparation of sample solution

Weigh and transfer 228 mg of pregabalin and etoricoxib to a 100 mL clean, dry volumetric flask. Add diluent and sonicate for 30 minutes to dissolve the sample completely. Fill the flask to the mark with solvent. The fluid is then filtered using a 0.45 micron injection filter (stock). Pipette 5 mL of the aforementioned stock solutions into a 50 mL volumetric flask and dilute to the mark with diluents. (75 µg/mL of pregabalin and 60 µg/mL of etoricoxib)

Method Validation

The chromatographic method was validated in accordance with the ICH Guidelines, Q2 (R1) 2005. (41,42)

System suitability

The system performance was confirmed through evaluation of suitable parameters. Six injections of the same standard preparation were used to evaluate precision, focusing on peak area, resolution, and theoretical plate number.

Accuracy

Recovery studies were undertaken at three levels to ensure accuracy: 50%, 100%, and 150% of the target concentration. The method accuracy was evaluated by analyzing chromatograms.

Precision

Six replicate injections of optimum concentrations of pregablin andetoricoxib were used to validate the analytical technique of intraday and interday precision levels. The chromatograms were used to generate averages and percentage RSD (Relative Standard Deviation) for peak area and assay.

Specificity

The method's specificity was tested by introducing a placebo solution (blank) without PGL and ERC, as well as a standard solution with concentrations of 75 µg/ml for pregabalin and 60 µg/ml for Etoricoxib, into the HPLC system. Formulations were evaluated, and chromatograms were generated to assess specificity.

Linearity

Linearity was validated by producing and evaluating pure analytical standards at five concentration levels. The new approach shown high linearity in concentration ranges of 18.75, 37.50, 56.25, 75.00, and 93.75 µg/ml for PGL and 15.00, 30.00, 45.00, 60.00, and 75.00 µg/ml for ERC.

LOD and LOQ

The LOD and LOQ for PGL and ERC were determined using the response's SD and slope. The limit of detection (LOD) was calculated as 3.3 times the SD divided by the slope, whereas the LOQ was 10 times the SD divided by the slope.

Robustness

The method's robustness, defined as its capacity to survive slight but purposeful changes in chromatographic conditions, was evaluated. The research assessed the influence of minor changes in the mobile phase flow rate (±0.2 units), organic phase (±5 ml), and wavelength (±2%).

Stress studies

We conducted stress testing to assess the stability of active compounds in accordance with ICH standards for novel medical substances and products. As part of this project, stress degradation studies on PGL and ERC were carried out using the described approach.

Acidic degradation studies

A technique was employed to investigate how acidic conditions influenced PGL and ERC. 5ml of the primary stock solution was initially put into a 50ml flask. To create an acidic atmosphere, add 1mL of 0.1N HCl to one of the standard flasks. The contents of the flask were then brought up to the mark with the mobile phase and refluxed at 70°C for 3 hrs. After cooling, 1ml of 0.1N NaOH was added to neutralize the acidic solution. The resulting solution was filtered through a 0.22mm syringe filter before being injected into the HPLC system for analysis.

Alkaline degradation studies

A 5ml of the primary standard solution was combined with 3ml of 0.1N NaOH in a 50ml volumetric flask to investigate the effect of alkaline condition. The mobile phase was then used to adjust volume. These standard flasks were heated twice, once at 60°C and again at 50°C. After the final solution had cooled to room temperature, 3ml of 0.1NHCl was added to neutralize the base. After being filtered using a 0.22mm syringe filter, the solution was loaded into vials for analysis in the HPLC system.

Peroxide degradation studies

A 5ml of the primary stock solution and 1ml of 3% (w/v) hydrogen peroxide were combined in a 25ml standard flask to conduct oxidative degradation investigations. Diluents were added to achieve concentrations of 75 µg/ml for PGL and 60 µg/ml for ERC. After that, the flask was stored at room temperature for six hours. The resulting solution was filtered using a 0.22mm syringe filter before being introduced into the HPLC machine for analysis.

Thermal induced degradation

To study thermally induced deterioration, 5ml of the primary stock solution was transferred to a 50ml standard flask and refluxed at 80°C for 9 hours. The sample was diluted with diluents (mobile phase) and adjusted to a total volume of 50 ml, yielding concentrations of 75 µg/ml for PGL and 60 µg/ml for ERC.After cooling to ambient temperature, the solution was filtered through a 0.22mm syringe filter before being fed into the HPLC system for analysis.

Photo degradation

A 5ml of the primary stock solution was pipetted into a 50ml standard flask to assess the effects of photodegradation.The concentrations of PGL and ERC were 75 µg/ml and 60 µg/ml respectively.These samples were exposed to 1.2 million lux and 200 Wh/m 2 of UV radiation for 30 minutes in a photostability chamber.The solution was then filtered through a 0.22mm syringe filter and placed in vials for HPLC system analysis.

RESULTS AND DISCUSSION

System suitability studies

A system suitability test was performed to ensure the analytical method's accuracy and validity. We carefully examined numerous essential parameters, such as theoretical plate number (N), resolution, retention time (Rt), and tailing factor. Table 1 summarises the findings of this analysis. To test the method's specificity, several solutions were added to the HPLC system, including a blank solution,PGL , and ERC standards at concentrations of 75 and 60 µg/ml, respectively, as well as the formulations under examination. During this study, no visible peaks were found in the blank solution, and the Rt values for the standards and samples were consistent. Representative chromatograms of these results are shown in Figures

Linearity

To establish the method linearity, linearity curves were generated by graphing peak area on the X-axis versus drug concentrations on the Y-axis. Regression equations were computed using these curves.The linearity of the techniques was found between 18.75 and 112.50 µg/ml for PBL and 15 and 90 µg/ml for TRC. Figures 3 shown visual presentations of the linearity curves for PBL and TRC, respectively.

Precision

The method precision was evaluated using intraday and interday changes with concentrations of 75 µg/ml for PBL and 60 µg/ml for TRC. This assessment required six replicate injections at each concentration level. The inter- and intraday accuracy of PBL were found to be 1.05% and 0.34%, respectively. In contrast, TRC inter and intraday precision were 1.06% and 0.32%, respectively.

Accuracy

The approach was evaluated at three distinct levels of accuracy: 50%, 100%, and 150%. Table 2 provides a summary of the results.At these levels, the average percentage recoveries for PBL & TRC were 100.29%, 99.62%, and 99.78%, respectively. This suggests that the approach can yield consistent results at a variety of concentrations.

Limit of detection (LOD) & Limit of quantification (LOQ)

Calculating the LOD (Limit of Detection) and LOQ (Limit of Quantification) values helped us assess the method sensitivity. The LOD and LOQ for PBL were found to be 2.25 and 7.5 µg/ml, respectively. The ERC has LOD and LOQ values of 1.8 µg/ml and 6 µg/ml, respectively.

Robustness

The robustness investigation revealed negligible differences in chromatograms when compared to optimum conditions. The study findings are reported in Table 3.

Assay

The proposed approach successfully quantified analytes in tablet formulations. The average assay (Table 4) for PBL and TRC was 99.22% and 100%, respectively.

Forced degradation studies

Forced degradation studies were conducted to evaluate method specificity in the presence of degradation products, including bulk and pharmaceutical dose forms. These studies investigated five distinct stress conditions. The analyte's ionizable groups may have catalyzed the degradation. Several degradation products were detected in both acidic and alkaline environments, but no further peaks were seen within the Rt of PBL and TRC. Both drugs shown considerable deterioration in acidic and alkaline environments. Oxidative degradation investigations discovered three degradation products, although none were found in the Rt of PBL and TRC. Photolytic stress can lead to deterioration by photooxidation or free radical processes. The Arrhenius equation can describe degradation under hydrolytic stress conditions. Table 5 summarizes the outcomes of various stress conditions. The PBL and TRC are subject to stress conditions, but remain stable with the proposed approach for a given period.

DISCUSSION

Using the Acquity HPLC system in this investigation resulted in significant cost savings and time efficiencies. The development of a simple, cost-effective, and precise HPLC approach for concurrent quantification in pharmaceutical formulations is crucial given the growing global demand for these drugs. This technology improves productivity and reduces costs in pharmaceutical quality control labs by making routine drug analysis easier. The HPLC approach was extended to investigate drug degradation under various stress situations. This detailed analysis confirms the method's specificity and provides insights into drug stability profiles, ensuring the safety and efficacy of pharmaceutical products. This aligns with drug production and quality control laws, improving overall quality assurance standards in the pharmaceutical business. The goal of this research was to create an analytical method for measuring PBL and TRC using HPLC-PDA chromatography. The approach was meticulously optimized, resulting in much lower Rts of 2.931 min for PBL and 3.883 min for TRC. The optimization procedure resulted in high sensitivity, well defined peak forms, and appropriate resolution. The PDA detector, with a particular wavelength of 285 nm,

improved detection sensitivity across all analytes. The sensitive equipment significantly reduced analysis time to as little as 6 minutes. These optimized conditions were used in validation experiments. The current approach is accurate, with all analytes recovering within acceptable ranges. The method's precision was confirmed by achieving % RSD values of less than 2% in both intra and interday precision studies. The high Performance liquid chromatography system is suitable for assessing all medicines, as shown in the system suitability study (Table1), with %RSD values < 2% across all parameters. The LOD and LOQ studies highlighted the method's high sensitivity, while the robustness study found that deliberate changes to factors such as flow rate and organic phase had no significant impact on the results. The marketed formulation's % assay yielded values of 99.10% for PBL and 100.10% for ERC, validating the efficiency of the test procedure.

This method is unique and provides benefits in terms of speed and cost-efficiency, as supported by empirical evidence. By decreasing analysis time to 6 minutes and replacing expensive acetonitrile with tri ethanol amine, this solution is cost-effective. Furthermore this approach is highly sensitive, with low detection and quantification limitations. The validation parameters provided findings within the ICH Q2B guidelines, indicating reliability and suitability for pharmaceutical analysis.

CONCLUSION

The HPLC method is reliable, reproducible, accurate, and specific for measuring pregabalin and etoricoxib in bulk and tablet formulations. This newly validated approach meets regulatory standards for accuracy, precision, and sensitivity. Therefore ,this method is suitable for routine analysis of selected pharmaceuticals in Quality Control laboratories.

ACKNOWLEDGEMENTS

The authors thank Ajanta Pharma LTD, Mumbai, India, for generously supplying gift samples of the active pharmaceutical components. The authors are grateful to Dattakala Institute of Pharmaceutical Science & Research, Bhigwan, for providing necessary equipment and resources for this study.

Conflicts of interest

There are no potential conflicts of interest

Abbreviations

PBL: Pregabalin, ERC: Etoricoxib, LOD: Limit of Detection, LOQ: Limit of Quantification

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Table:1 Data for system suitability

Parameter	Pregabalin	Etoricoxib
Theoretical Plate Count	3487	5321
Average Peak Area	3581428	2064821
Retention time (min)	2.938	3.886
Tailing	1.24	0.91
Resolution	--	4.48

Table:2 Results of Accuracy

% Concentration (at specified level)	Area	Amount added (µg/mL)	Amount founded (µg/mL)	% Recovery	Mean Recovery
Pregabalin					
50%	1754840	37.5	36.74	98.0	98.83
100%	3571578	75.0	74.78	99.7	
150%	5305895	112.5	111.1	98.8	
Etoricoxib					
50%	1046142	30	30.50	101.7	100.97
100%	2076921	60	60.55	100.9	
150%	3094817	90	90.23	100.3	

Table:3 Results of Robustness

Parameter	Condition	Pregabalin		Etoricoxib	
		Peak Area	% Assay	Peak Area	% Assay
Flow rate	0.8 mL/min	3671852	102	2094712	101.94
	1 mL/min	3581428	100	2054821	100
	1.2 mL/min	3499954	97.7	2019040	98.02
Organic Phase change	45: 50 (Low)	3460614	96.4	2015023	98.11
	50: 50(Actual)	3586572	100	2053837	100
	55: 45(High)	3660612	102	2092738	101.89

Table:4 Results of Assay

Brand Name	Drug	Average Sample area (n=5)	Standard Weight (µg/mL)	Labled Amount (mg)	Amount found (µg/mL)	Standard Purity	% Assay
Presidio	Pregabalin	3549854	75	75	74.33	99.80	99.10
	Etoricoxib	2060423	60	60	60.07	99.90	100.10

Table: 5 Results of Stress study

Condition	Pregabalin			Etoricoxib		
	Peak Area	% Assay	% Degradation	Peak Area	% Assay	% Degradation
Acid	3085241	86.1	13.9	1801240	87.5	12.5
Alkaline	3042147	84.9	15.1	1782027	86.6	13.4
Peroxide	2994625	83.6	16.4	1701129	82.6	17.4
Photolytic	3551247	91.1	0.9	1830687	88.9	11.1
Hydrolytic	3557642	91.3	0.7	2042097	91.2	0.8

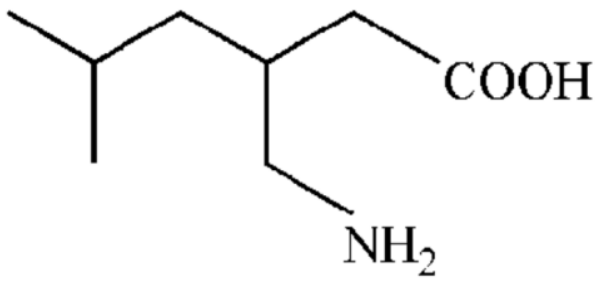


Fig (1)

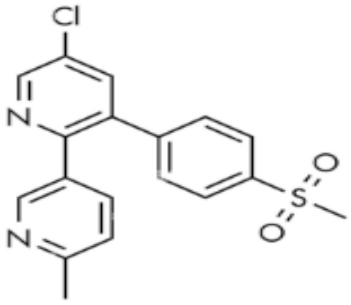
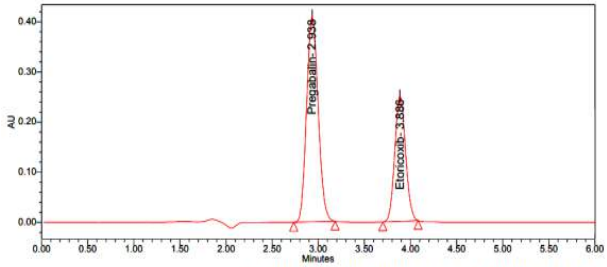
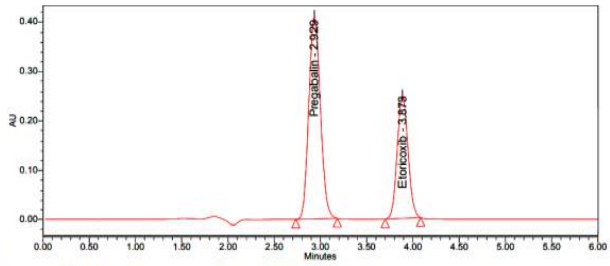


Fig (2)

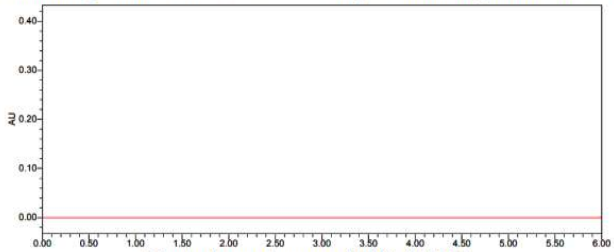
Figure: 1 & 2 Structures of Pregabalin & Etoricoxib



Standard chromatogram of PBL & ERC

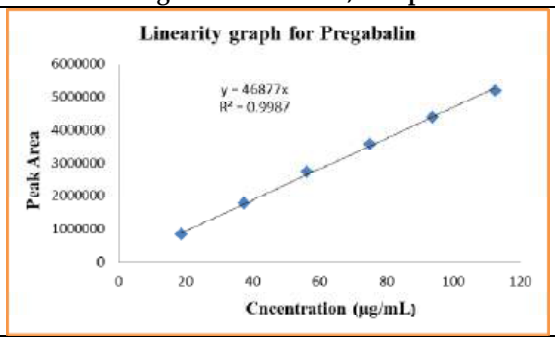


Sample Chromatogram of PBL & ERC



Blank chromatogram of PBL & ERC

Figure: 3 Standard, Sample and Blank Chromatograms of Pregabalin & Etoricoxib



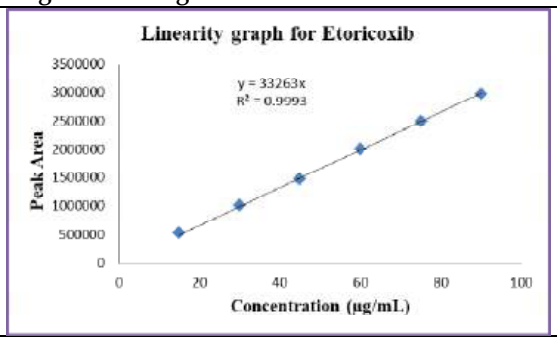


Figure: 4 Linearity curves of Pregabalin & Etoricoxib

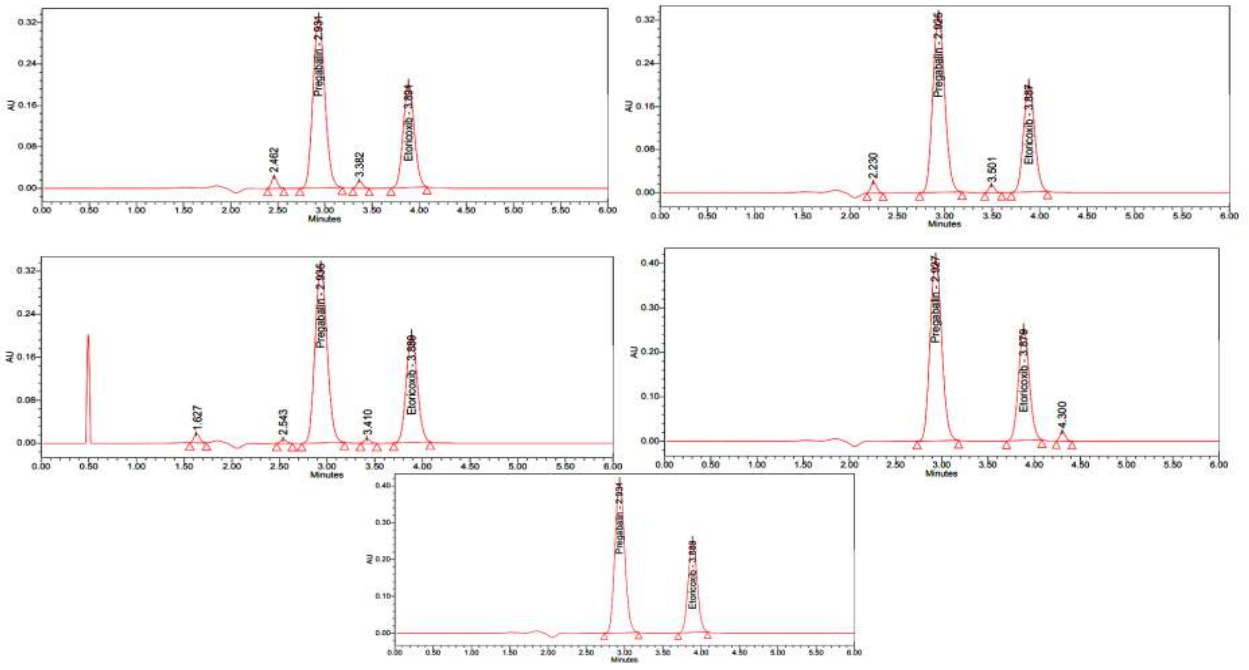


Figure: 5. Stress indicating chromatograms of acid, alkali, peroxide, photolytic & hydrolytic conditions

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Integer Solutions of Non-Homogeneous Fifth Degree Equation with Five Unknowns $3(x^4+y^4) = 26(z^2-w^2)^3$ and its Application

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Received: 31 Oct 2025 Revised: 28 Nov 2025 Accepted: 11 Dec 2025

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ABSTRACT

The non-homogeneous fifth degree Diophantine equation with five unknowns$3(x^4+y^4)=26(z^2-w^2)m^3$ is consider and analyzed for its non-zero distinct integer solutions. "If its perceive that by applying the linear transforms x=u+v, y=u-v z= 12u+v, w = 12u-v ($u\neq 0 v\neq 0$)in the stated equation one may get infinitely many non-zero integer solutions. similarly, one can introduce some other transforms to obtained different non zero integer solutions. Further, we explain an idea of linear Diophantine equations are applied to get the chemical equation.

Keywords: Non-homogeneous fifth degree equation, Polygonal number, pyramidal number, integer solutions, Diophantine equation, Chemical equations, input, output, reactants, products.

INTRODUCTION

The fifth degree Diophantine equation offer an limitless area of research due to this variety [1-3,12,13], for an huge of many problems on fifth degree equation with three unknows one may refer [4 and 5]. In [6,9,7] fifth degree equation with five unknows equation with are consider Chemical equations is chemistry are used as illustrative representations of chemical Reactions in which the reactants and the products are wrote down in terms of the relevant chemical formulae. In [8] studied the chemical using Diophantine equation and [9, 10 and 11] find solution for various applications.

Notations

Pr_n = Pronic integer number of order n.
CS_n= centered integer square number of order n
CH_n=centered hexagonal integer number of order n.
J_n = Jacobsthal integer number of order n.
j_n=Jacosthal lucas integer number of order n.
M_n = Mersenne integer number of order n.
P_n^5 =Pentagonal pyramidal integer number of order n
HG_n= Hexagonal integer number of order n
OH_n = octahedral integer number of order n
PP_n = Pentagonal pyramidal integer number of order n
SO_n=Stella octangular integer number of order n
$T_{7,n}$ =Heptagonal integer number of order n
$T_{8,}$ = Octagonal integer number of order n
$T_{9,n}$ = Nanogonalinteger number of order n
$T_{17,n}$ =Heptradecagonal integer number of order n
GnO_n = Gnomonic integer number of order n
$T_{3,n}$ = Triangular integer number of order n

METHODS OF ANALYSIS

The non-homogeneous fifth degree equation with five unknowns under consideration is $3(x^4+y^4)=26(z^2-w^2)m^3$…….(1)

Pattern 1

The substitutions of the linear transforms

$x=u+v$
$y=u-v$
$z=12u+$ u …….(2) (u≠v ≠ 0)
$w=12u-v$

In (1) leads to

$u^2+v^2=52m^3$ …….(3)

Assume $m = m(a, b)=a^2+b^2$ …….(4)

Where a and bare non-zero distinct integers.

Choice 1

Write 52 as (4+6i)(4-6i) …….(5)

Equation (3) becomes

$(u+iv)(u-iv)=(4+6i)(4-6i)(a+ib)^3(a-ib)^3$ ……..(6)

Let positive generate,

$(u+iv)=(4+6i)(a+bi)^3$

Equating both the real and imaginary parts in (6) we get,

$u=4a^3+6b^3-18a^2b-12ab^2$
$v=6a^3-4b^3+12a^2b-18ab^2$

The employing value of u and v in equation (2), we get

x (A, B)$=10a^3+2b^3-6a^2b-30ab^2$
y (A, B)$=-2a^3+10b^3-30a^2b+6ab^2$
z (A, B)$=54a^3+68b^3-204a^2b-162ab^2$
w (A, B)$=42a^3+76b^3-228a^2b-126ab^2$

m (A, B)=a^2+b^2

PROPERTIES

1. $x(a,a+1)+48PP_a^{\,5}+12T_{4,a}+24Pr_a-2=0$
2. $y(a,2a-1)-63OH_n+69T_{4,a}+90T_{3,a}+10=0$
3. $z\,(a,3a-2)+360PP_a+380CH_a\equiv 164(mod660)$
4. $w(a,a+1)+44T_{7,a}+252T_{4,a}\equiv 76(mod36)$
5. $m(a,13a-12)-85T_{6,a}\equiv 144(m0d227)$
6. $x(a,3a-1)+36OH_a+220cubic-132T_{4,\,a}+2=0$
7. $y(a,7a-5)-1518OH_a+1582T_{4,\,a}+1144T_{6,\,a}-1250CC_a=0$
8. $z\,(a,a+1)+278PP_a+122T_{4,\,a}+126P^7-68=0$
9. $w(a,2a-1)-459\,OH_a-27\,T_{4,\;a}+330a-76w(a,2a-1)+45OH_a+27T_{4,a}\equiv 76(mod330)$
10. $m(a,3a-2)-3CH_a-T_{4,\,a}\equiv 1(mod3)$

CHOICE 2

Write 52 as (6+4i)(6-4i) …….(7)

Equation (3) becomes

$(u+iv)\,(u-iv)=(6+4i)\,(6-4i)\,(a+ib)^3(a-ib)^3$ …….(8)

Let positive generate,

$(u+iv)=(6+4i)\,(a+bi)^3$

Equating both the real and imaginary parts in (8) we get,

$u=6a^3+4b^3-12a^2b-18ab^2$

$v=4a^3-6b^3+18a^2b-12ab^2$

Substituting u and v in (2), we get,

x (A, B)=$10a^3-2b^3+6a^2b-30ab^2$

y (A, B)=$2a^3+\mathbf{10}b^3-30a^2b-6ab^2$

z (A, B)=$76a^3+42b^3-126a^2b-228ab^2$

w (A, B)=$68a^3+54b^3-162a^2b-204ab^2$

m (A, B)=a^2+b^2

PROPERTIES

1. $x\,(a^2,\,a+1)-(120F_{4,a)T_{4,a}}-(3SO_a\,)T_{4,a}+14T_{4,a^2}+23cubic+72P_{5,a}=0$
2. $y\,(a,7a-5)=-428O_a+1326T_{4,a}+568T_{8,a}-1250CC_a=0$
3. $z(a,2a-1)=24So_4+(352GNO_4)T_{4,a}+42=0$
4. $w\,(a,a+1)+488PP_a+164T_{4,a}\equiv 54(mod42)$
5. $m(a,19a-17)-48T_{17,\,a}-2T_{4,a}\equiv 289(mod334)$
6. $x(a,5a-3)+960cubic-252T_{4\,,a}-540HG_a-M_5-23=0$
7. $y\,(a,3a-1)-128cubic+76T_{4,a}64T_{6,a}=10HG$
8. $z(a,2a^2+1)-(112T_{8,\,a})\,T4,\,a2+(168T_{7,a})cubic+(402OH_a)T_{4,a}+702cubic-126T_{4,a}\equiv 42(m0d228)$
9. $w(a,13a-11)-123186OH_a+241032T_{4,a}\equiv 71874(mod189080)$
10. $m(a,17a-15)-72TT_a-17T_{4,a}\equiv 105(mod186)$

Pattern 2

Write 52 as $\frac{(12+34i)(12-34i)}{25}$ ……..(9)

Equation (3) becomes

$(u+iv)(u-iv)=\frac{(12+34i)(12-34i)}{25}(a+ib)^3(a-ib)^3$ …….(10)

Let positive generate,

$(u+iv) = \frac{(12+34i)}{5}(a+ib)^3$

Equating both the real and imaginary parts in (10) we get,

$u = \frac{1}{5}(12a^3 - 102a^2b - 36ab^2 + 34b^3)$

$v = \frac{1}{5}(34a^3 + 36a^2b - 102ab^2 - 12b^3)$

The employing value of u and v in (2),we get

$x = \frac{1}{5}(46a^3 - 66a^2b - 138ab^2 + 22b^3)$

$y = \frac{1}{5}(-22a^3 - 138ab^2 + 66ab^2 46b^3)$

$z = \frac{1}{5}(178a^3 - 1188a^2b - 534ab^2 + 396b^3)$ ...……(11)

$w = \frac{1}{5}(110a^3 - 1260a^2b - 330ab^2 + 420b^3)$

$m = a^2 + b^2$

As our aim, we made choicea=5A,b=5B in (11), we obtain the non -zero integer solution to (1) as

x (A, B) $=1150A^3 - 1650A^2B - 3450AB^2 + 550B^3$

y (A, B)$= -550A^3 - 3450A^2B + 1650AB^2 + 1150B^3$

z (A, B)$= 4450A^3 - 29700A^2B - 13350AB^2 + 9900B^3$

w (A, B)$= 2750A^3 - 31500A^2B - 8250AB^2 + 10500B^3$

m (A, B)$= 25(A^2 + B^2)$

PROPERTIES

1. $x(A,A+1) + 21600TH_A - 5000PP_A - 1700T_{4,A} + j_9 + 39 = 0$
2. $y(A,2A-1) - 1150CC_A + 9000T_{5,A} - 1800OH_A - 4850cubic = 0$
3. $z(A,3A-1) - 62500cubic + 51300T_{4,A} + 30450T_{8,A} + 9900CT_A = 0$
4. $w(A,5A-3) - 475750SO_A + 1599800T_{4,A} + 120200T_{9,A} - 283500GNO_A = 0$
5. $m(A,21A-19) - 850S_A - 2380T_{7,A} \equiv 50 (mod 11280)$
6. $x(A,2A-1) + 23100PP_A + 7200T_{4,A} \equiv 550 (mod 150)$
7. $y(A,7A-5) - 143750CC_A - 163100cubic + 84715T_{4,A} + 213785\ T_{6,A} = 0$
8. $z(A^2,A+1) - (1780T_{7,A})T4,A2 + (27030PP_A)T_{4,A} + T4,A2 + 16800cubic \equiv 9900 (mod 29700)$
9. $w(A,A+1) + 13250SO_A - 16500T_{4,A} \equiv 10500 (mod 10000)$
10. $m(A,15A-13) - 2825HG_A - M_{12} \equiv 130 (mod 6925)$

Choice 1

Write 52 as $\frac{(34+12i)(34-12i)}{25}$ ……(12)

Equation(3)becomes

$(u+iv)(u-iv) = \frac{(34+12i)(34-12i)}{25}(a+ib)^3(a-ib)^3$ ……(13)

Let positive generate,

$(u+iv) = \frac{(34+12i)}{5}(a+ib)^3$

Equating both the real and imaginary parts in (13) we get,

$u = \frac{1}{5}(34a^3 - 36a^2b - 102ab^2 + 12b^3)$

$v = \frac{1}{5}(12a^3 + 102a^2b - 36ab^2 - 34b^3)$

The employing value of u and v in (2), we get

$x = \frac{1}{5}(46a^3 + 66a^2b - 138ab^2 - 22b^3)$

$y = \frac{1}{5}(22a^3 - 138\ a^2b - 66ab^2 + 46b^3\ )$

……..(14)

z =$\frac{1}{5}(420a^3 - 330a^2b - 1260ab^2 + 110b^3)$

w = $\frac{1}{5}$ $(396a^3 - 534a^2b - 1188ab^2 + 178b^3)$

$m=a^2+b^2$

As our aim, we made choicea=5A,b=5B in (14),we obtain the non zero integer solution to (1) as

x (A, B)=$1150A^3+1650A^2B-3450AB^2-550B^3$

y (A, B)=$550A^3-3450A^2B-1650AB^2+1150B^3$

z (A, B)=$10500A^3-8250A^2B-31500AB^2+2750B^3$

w (A, B)=$9900A^3-13350A^2B-29700AB^2+4450B^3$

m (A, B)=$25(A^2+ B^2)$

PROPERTIES

1. x $(A,3A-2)+597000O_A-8400T_{4,A}\equiv 4400(mod 13700)$
2. y$(A,7A-5)-143750CC_A-76200OH_A+69550T_{4,A}+105850HG_A=0$
3. $z(A,2A-1)=15000OH_A+160000PP_A-181250T_{4,A}+3J_{11}+701=0$
4. w $(A,3A-1)+10350SO_A+(71400GNO_A)T_{4,A}+13800cubic+j_{12}+353=0$
5. $m((A^2+A),(A^2+5A+6))=m((A^2+A),(A^2+5A+6))-100PT_A-160CP_A\equiv 740(mod 1070)$
6. $x(A,5A-3)+218400O_A-222300T_{4,A}\equiv 14850(mod 32500)$
7. y $(A,A+1)+5100P^6+750T_{4,A}\equiv 1150(mod 950)$
8. z $(A,3A-2)+223500cubic-13500T_{8,A}-205500T_{4,A}\equiv 22000(mod 27000)$
9. w $(A,2A-1)+100000PPA+58850T4,A\equiv 4450(mod 3000)$
10. $m(A,7A-5)-625T_{6,A}\equiv 25(mod 125)$

Pattern 3

$u^2+v^2=52m^3*1$ ……(15)

Write 1 as$\frac{(12+5i)\ (12-5i)}{169}$ ……(16)

Using (4), (5) and (16) in (15) and applying in method of factorization, we made define

Equation(3)becomes

$(u+iv)(u-iv)=(6+4i)(6-4i)\frac{(12+5i)(12-5i)}{169}\ (a+bi)^3(a-ib)^3$ ……..(17)

Let positive generate,

$(u+iv)=(6+4i)\ \frac{(12+5i)}{169}\ (a+bi)^3$ ……..(18)

*E*quating both the real and imaginary parts in (17) we get,

u =$\frac{1}{13}(52a^3 - 234a^2b - 156ab^2 + 78b^3)$

v =$\frac{1}{13}(78a^3 + 156a^2b - 234ab^2 - 52b^3)$

The employing value of u and v in (2), we get

x =$\frac{1}{13}(52a^3 - 234a^2b - 156ab^2 + 78b^3)$

y=$\frac{1}{13}(-26a^3 - 390a^2b + 78ab^2 + 130b^3)$ ……(19)

z=$\frac{1}{13}(702a^3 - 2652a^2b - 2106ab^2 + 884b^3)$

As our aim, we made choice a=13A,b=13B in (19), we obtain the non zero integer solution to (1) as

x(A,B)=$21970A^3-13182A^2B-65910AB^2+4394B^3$

y (A, B)= $-4394a^3 - 65910A^2B - 13182AB^2 + 21970B^3$

z (A, B) =$118638A^3-448188A^2B-355914AB^2+149396B^3$

w (A, B)=$92274A^3-500916A^2B-276822AB^2+166972B^3$

$m=25(A^2+B^2)$

PROPERTIES

1. $x(A^2,A+1)-(263640FN^4)T_{4,A}+(39546SP_A)T_{4,A}-83556T_{4,A^2}+(120905Pr_A)T_{4,A}+52728T_{4,A}\equiv 4394(\mathrm{mod}13182)$
2. $y(A,A+1)+17576SO_A-13182CS_A\equiv 8788(mod87880)$
3. $z(A,3A-1)+197730SO_A+725010HG_A+M_{17}\equiv 18325(mod65910)$
4. $w\,(A,2A-1)+790920P^7+10985SO_A\equiv 166972(mod450385)$
5. $m(A,23A-21)-2000T_{15,A}-100T_{7,A}\equiv 11025(mod13000)$
6. $x(A,7A-5)+896376SO_A+553644T_{4,A}\equiv 54920(mod659100)$
7. $y(A,3A-2)-509704cubic+210912T_{4,A}+158184T_{8,A}+175760CH_A=0$
8. $z\,(A,2A-1)+503113SO_A-79092T_{4,A}\equiv 149396(mod37349)$
9. $w\,(A,A+1)w(A,A+1)+518492cubic-224094Pr-329550T_{4,A}-M_{17}-35901=0$
10. $m\,((A^2+A),(A+2))-25T_{4,A^2}-100P_{A^5}\equiv 100(mod100)$

APPLICATION

Balancing chemical equations:

Example: 1

Consider the chemical reaction,

$aHgcl_2+bkI\rightarrow a'HgI_2+\ b'kcl$ ……(1)

Which leads to the equations

$2a=b'$ for k
$b=b'$ for H } ……(2)

In an earlier part system of equations could be easily reduced is $2a-b=0$, is a linear Diophantine equation with a Solutions $[a,b]=[1,2]$

Hence, $[a,b,a',b']=[1,2,1,2]$

As a result, equation (1) be becomes

$Hgcl_2+2kI\longrightarrow HgI_2+2kcl$

Example: 2

Consider the chemical reaction,

$aCH_3COOH+bkNO_2\rightarrow a'CH_3COOk+b'HNO_2$ …… (3)

Which leads to the equations

$2a=2a'$ for C
$4a=3a'+b'$ for H
$2a+2\,b=2a'+2b'$ for O } ……..(4)
$b=a'$ for k

In an earlier part system of equations could be easily reduced is $a-b=0$, is a linear Diophantine equation with a Solution $[a,b]=[1,1]$

Hence, $[a,b,a',b']=[1,1,1,1]$

As a result, equation (3) be becomes

$CH_3COOH+kNO_2\rightarrow\ CH_3COOk+HNO_2$

Example: 3

Consider the chemical reaction,

$aBr_2+bH_2O\rightarrow a'HBr$ ……(5)

Which leads to the equations

$2a=a'$ for Br
$2b=a'$ for H } ……(6)
$b=1$ for O

$a - b = 0$, is a linear Diophantine equation with a solution $[a, b] = [1,1]$
Hence, $[a, b, a'] = [1,1,2]$
As a result, equation (5) he becomes
$Br_2 + H_2O \rightarrow 2HBr$

Example: 4
Consider the chemical reaction,
$aNi + bCO \rightarrow a'NiCO_4$ ……(7)
Which leads to the equations
$a = a'$ for Ni
$b = a'$ for C
$b = 4a'$ for O } ……(8)
In an earlier part system of equations could be easily reduced is $b - 4a = 0$, is a linear Diophantine equation with a Solutions $[a, b] = [1,4]$
Hence, $[a, b, a'] = [1,4,1]$
As a result, equation (7) be becomes
$Ni + 4CO \rightarrow NiCO_4$

Example: 5
Consider the chemical reaction,
$aCOCl_2 + bkNO_2 \rightarrow a'CO(NO_2)_2 + b'kCl$ ……..(9)
Which leads to the equations
$a = a'$ for C
$a + 2b = 5a'$ for O
$2a = b'$ for Cl
b=b' for k
$b = 2a'$ for N } ……(10)
In an earlier part system of equations could be easily reduced is $b - 2a = 0$, is a linear Diophantine equation with a Solutions $[a, b] = [1,2]$
Hence, $[a, b, a', b'] = [1,2,1,2]$
As a result, equation (9) be becomes
$COCl_2 + 2kNO_2 \rightarrow CO(NO_2)_2 + 2kCl$

CONCLUSION

In this paper the order to get distinct integer" solutions, set of transformations and patterns have been taken into consideration. Io find different integer solutions, one may of some other set of transformation and patterns. And also in this paper, we assume that the linear Diophantine equation in chemical equation significant role in chemical equation.

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Indian Journal of Natural Sciences www.tnsroindia.org.in ©IJONS

Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Innovative Technologies Transforming Library Operations and User Services

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Received: 21 Nov 2025 Revised: 18 Dec 2025 Accepted: 02 Feb 2026

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ABSTRACT

In the modern era, information seeking behaviour is increasing day and day. The ancient or traditional library management and services are not enough to satisfy the knowledge sector of the user. So the emerging of new technological innovations are necessary to provide the right information to the right users in the right time. This paper deals with the recent emerging innovations in the information technology and how they are useful to provide the effective services of the library.

Keywords: Information Seeking Behaviour; Technology;Network Services; Innovative Methods.

INTRODUCTION

In the emerging knowledge society, libraries have faced many challenges in satisfying users' needs over the past few decades. New technologies are being used to improve library services and management, as well as to preserve library materials for the long term, because libraries contain the living records of human civilization. These records are treasures for future generations. In this changing scenario, Information and Communication Technology (ICT) has become the most instrumental factor in providing effective library services.

Innovation

The concept of innovation involves creating or identifying meaningful ideas to solve problems. In other words, it is a significant problem-solving technique. The Online Dictionary of Library and Information Science describes best innovative practices as the application of theory to real-life situations through procedures that, when properly applied, consistently yield superior results and therefore serve as reference points in evaluating alternative methods of accomplishing the same task.

According to Peter Drucker, the father of modern management science, innovation is the specific instrument of entrepreneurship. It is the act that endows resources with a new capacity to create wealth.

Need of Innovative Service

Information seeking is a natural and necessary mechanism of human existence (Marchionini, 1995). It involves personal reasons for seeking information, the kinds of information being sought, and the methods and sources used to obtain the required information. Changes in information-seeking behavior have led to the emergence of innovative technologies in library management and services. The changing needs of users have also transformed the role of the librarian into that of an information professional. Information professionals must act as intermediaries between knowledge sources and information seekers. Common obstacles in the information-seeking process identified by respondents include lack of time, uncertainty about the existence of relevant information, retrieval of excessive information, and difficulties in navigation and searching.

Emerging Innovations

Many innovative technologies are emerging in library management and services in the present era. Libraries adopt technologies according to their infrastructure, type of library, specific needs, geographical location, and the amount of funding allotted by the government.

Some of the specific technological innovations are:

Staff Management
Training Programmes
Resource Sharing and Networking
Library Automation
Open Source Software
Internet Search Engines – Semantic Web
World Wide Web
E-Learning
Web 2.0
Digitalization

Staff Management

For effective and innovative library services, librarians and library staff members should possess high-level skills and updated knowledge of technological advancements in library science. They should understand users' requirements and strive to meet their expectations. Librarians are also responsible for resolving problems faced by staff members due to technical inexperience and ensuring that services remain user-friendly. They should promote portable qualifications aligned with nationally recognized competency standards within a competency-based assessment system. It is recognized that learning can occur through various sources, both on-the-job and off-the-job, and through formal as well as informal methods. System management defines how different systems within the library are interconnected with one another and with external networks.

Training Programmes

The goal of training programmes is to motivate professional staff and learners to enhance their skills and update their knowledge. These programmes help learners improve their information-seeking behavior, understand the number of volumes available in a particular library, know the working hours, identify the type of library, and become aware of the services provided. Such initiatives help create a user-friendly environment and enable users to obtain the right information at the right time.

Resource Sharing and Networking

Resource sharing refers to the sharing of library resources in terms of documents, manpower, services, and equipment among participating libraries based on the principle of cooperation. Networking involves connecting information centers or libraries to function cooperatively. The objectives of resource sharing are to create an environment in which libraries can provide better services and more materials at the same cost. The main objectives are:

To improve the utilization of resources among users
To minimize costs
To maximize accessibility of resources
To extend the availability of resources

Library Automation

According to Webster's Dictionary, automation is the technique of making an apparatus, process, or system operate automatically. In other words, it refers to machinery that systematically stores, selects, processes, presents, and records input data or internally generated data. Automation is used to perform technical processes automatically.
Library automation is necessary due to:
Information explosion
Increase in library collections
Users' inability to explore vast amounts of literature and information
Advances in computer and communication technologies
Wastage of user and staff time in locating information
The need to provide wide access to resources within and beyond the library
Proper planning is essential for successful library automation.

Open Source Software

Open Source Software (OSS) is computer software whose source code is made available to users. Users can read, modify, and redistribute the software as they wish.
Open source software satisfies the following criteria:
The source code can be adapted to individual requirements, modified, and shared with others.
The software source code must be openly and easily accessible.
Anyone may use open source software as they desire.

Most projects initially began as classical open source software (OSS) initiatives developed by individual programmers. OSS has made library management and services more effective and efficient.

The Semantic Web – Internet Search Engine

Semantics is the study of linguistic meaning. The term "Semantic Web" was coined by Tim Berners-Lee, the inventor of the World Wide Web and Director of the World Wide Web Consortium. He defined the Semantic Web as a "web of data that can be processed directly and indirectly by machines." The Semantic Web is concerned with the meaning of words, sentences, and other linguistic elements rather than merely their syntactic structure. It promotes open access to information and follows web resource policies aimed at improving information retrieval. Its objectives include:

* Providing relevant information with minimal time spent filtering irrelevant or outdated data sources.
* Helping users obtain required information with accurate linguistic meaning.
The Semantic Web enhances the internet environment and supports web-based learning systems.

World Wide Web

The Web, popularly known as the World Wide Web (WWW), is a major component of the Internet and online communication. The Internet and its "publishing arm," the WWW, play a significant role in the communication process. The Web is a client-server system used to access various kinds of information available on the Internet. This information may be in the form of text, hypertext, images, audio, Usenet newsgroups, and other types of data. Web services provide a distributed information system that allows information sharing among users at any time.

The World Wide Web provides

* A distributed information system
* Receipt and delivery of electronic publications and access to data stored on remote computers
* Online, real-time interaction with other network users
* Equal opportunity of access for all types of users

E-Learning

E-learning is a continuous learning process, especially beneficial for learners who are unable to attend traditional classroom-based education. In earlier distance education models, students learned through nearby libraries or materials sent by course organizers. Modern media such as radio and television were also used in distance learning, though they had certain limitations. The distance learning process has been further strengthened through video conferencing. In this method, a nodal center is equipped with a studio where experts assemble and deliver lectures. This technique creates a classroom-like environment and enables direct interaction between teachers and learners.

E-Documents

There are certain information sources categorized as non-documentary sources, where data is transferred in electronic form rather than in printed format. CDs, DVDs, microfilms, and audiovisual materials are called electronic documents or e-documents. Books available in electronic form are called e-books, and journals available in electronic form are called e-journals. These resources are very useful to users because they can be accessed anytime and anywhere using a computer or digital device. Moreover, they can be preserved for a long period.

Web 2.0 Technology

Web 2.0 has become an important and central concept in the information world. Libraries worldwide are increasingly using various Web 2.0 applications. Librarians use these technologies to promote services, share information, engage with users, and network with colleagues globally. Many libraries use blogs as effective communication tools. Blogs serve as excellent sources of information and provide a platform where librarians can express their opinions and share updates with users.

Digitalization

A library in which data is stored in digital form is called a digital library. The process of converting information into digital format is known as digitalization. This process ensures long-term storage and preservation of information. Digitalization includes retrieving metadata from data files, interpreting the retrieved data in a decoded format, and rendering the data for human access. It is a significant method that enables easy access for users and ensures long-term accessibility of information resources.

CONCLUSION

The successful operation of any library largely depends on the selection of library collections, effective management, and quality services. Therefore, librarians must be well aware of the needs of the user community connected to library resources. Emerging innovative techniques play a vital role in providing the right information to the right user at the right time.

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Table 1. No of OSS software have different versions used depends upon the type of library.

S.NO	OSSSOFTWARE	VERSION
1.	Avanthi	1.0
2.	Emilda	1.2.1
3.	Koha	2.2.0
4.	Gnutcea	1.5
5.	LearningAccessILS	-
6.	Obiblio	0.5.1
7.	Openbible	2.0.3
8.	PhpmyBibli	2.0.3

RESEARCH ARTICLE

AI in Multiple Sclerosis: Revolutionizing Diagnosis, Monitoring, and Treatment

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Received: 10 Jan 2026 Revised: 16 Jan 2025 Accepted: 18 Jan 2026

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ABSTRACT

Multiple sclerosis (MS) is a complex autoimmune disease that affects the central nervous system, resulting in neurodegeneration and disability. Artificial intelligence (AI) has revolutionized MS research with its innovative approaches to computer-assisted diagnosis, disease monitoring, and customized treatment. This review highlights the use of AI in MS, including deep learning for MRI lesion segmentation, machine learning for biomarker integration, digital twins for disease simulation, and wearable technology for symptom monitoring. By facilitating early diagnosis and individualized treatment plans, AI-driven algorithms transform clinical practice and enhance patient outcomes. AI has shown a lot of promise in the diagnosis of multiple sclerosis, particularly in the areas of MRI lesion segmentation and biomarker integration. Deep learning frameworks like convolutional neural networks (CNNs) have achieved high accuracy in lesion segmentation, while multimodal models created with AI can accurately read difficult biomarker panels, distinguishing multiple sclerosis from other neuroinflammatory diseases. AI-based simulations that use clinical, imaging, and genomic data to predict treatment responses and relapses enable personalized disease modeling and early intervention. In order

to track MS-related mobility impairment and enable timely interventions and early rehabilitation, AI has also been integrated with wearable technology and gait analysis. AI-powered cognitive evaluation and speech recognition tools are evolving into non-invasive MS monitoring methods that enable the early detection of neurodegeneration. AI-driven customized treatment approaches, such as nanotechnology-mediated drug delivery and reinforcement learning-based treatment selection, may enhance the management of multiple sclerosis. However, ethical and regulatory concerns must be addressed prior to broad clinical use. The future of AI in MS research depends on sophisticated AI computations, collaborative multispecialty teamwork, and data-sharing infrastructures that optimize global patient benefit. As this review explores the potential advantages and disadvantages of AI in MS, more research and development are needed to fully realize the benefits of AI in MS diagnosis, monitoring, and treatment. AI has the potential to transform clinical practice and improve patient outcomes, which could have a substantial impact on MS research and treatment in the future.

Keywords: Multiple sclerosis; Artificial intelligence; Biomarker integration; Digital twins; Wearable technology; Personalized medicine; Machine learning

INTRODUCTION

Multiple sclerosis (MS) is a long-lasting autoimmune disorder that impacts the central nervous system (CNS), resulting in neurodegeneration and disability [1]. The intricacy of diagnosing, tracking, and managing MS requires sophisticated computational methods for precision medicine [2]. Artificial intelligence (AI) has become a transformative force in MS research, providing innovative approaches for computer-assisted diagnosis, tracking disease advancement, and tailoring treatments to specific patients [3,5]. The use of AI in MS is reviewed here, with a focus on machine learning for biomarker incorporation6 and deep learning for MRI lesion segmentation [7,10,18], wearable technology for symptom monitoring[22], and digital twins for disease simulation[14,19,31], as well as AI-powered customized therapies[20,32]. The article addresses challenges such as ethical issues[13,27], requirements for algorithmic transparency[10,29], and frameworks for data-sharing[7,30]. New developments in MS research through artificial intelligence are anticipated to improve patient outcomes and transform clinical practice[6,24]. Multiple sclerosis (MS), which affects over 2.8 million individuals globally, poses substantial challenges for diagnosis and treatment due to its diverse spectrum of symptoms and unpredictable progression[25]. MRI and biomarker analysis are examples of classic diagnostic methods whose accuracy and cost-effectiveness are often inadequate[9]. The use of AI, especially machine learning (ML) and deep learning (DL), has enabled novel approaches to improve MS diagnosis, monitoring, and treatment[12]. The automation of processes like biomarker analysis, MRI lesion segmentation, and predictive model construction by AI-powered algorithms enables early diagnosis and customized treatment plans[30]. While outlining significant developments in its application, this study explores the potential advantages and disadvantages of AI in MS[5].

AI in MS Diagnosis MRI and Lesion Segmentation

MRI is still the gold standard against which all MS diagnostics are measured because it gives essential information about lesion development and neurodegeneration. However, lesion segmentation is labor-intensive and susceptible to observer variation. Computer-assisted methods have significantly enhanced lesion detection performance, but deep learning frameworks like convolutional neural networks (CNNs) have been even more significant[8]. State-of-the-art models such as U-Net and Mask R-CNN have segmented with accuracy above 92% and lessened manual labour[15,36]. Recent research has proven that hybrid AI methods, where deep learning is combined with traditional image processing, also enhances lesion characterization[28]. Transfer learning and ensemble models have also been used with success to enhance prediction power[37,38]. Reinforcement learning is also on the horizon for optimizing MRI scan protocols and maximizing lesion visibility with lower scan time[34].

Biomarker Integration

Biomarker-Based Models (Logistic Regression and SVM): Subclinical changes can be detected more easily when biomarker indicators like oligoclonal bands, cytokines, GFAP, and NfL are combined with AI algorithms. This strategy opens up new avenues for preventive measures and early diagnosis[21]. Beyond imaging, AI enhances biomarker-guided diagnosis by combining genomic signatures, oxidative stress markers, and serum neurofilament light chain (SNFL) to expedite MS classification[18,39]. Multimodal models built with AI have the ability to accurately read difficult biomarker panels, distinguishing MS from other neuroinflammatory diseases at better than 90% accuracy[11,40]. Identification of early relapsing-remitting and progressive types of MS subtypes has also been incredibly revolutionized by AI-supported classification approaches[34,41]. Predicting novel biomarkers of disease progression and treatment response is becoming more and more common with machine learning algorithms[42]. Such computer programs search through real-world patient information in huge MS registries to give a better, sooner regimen of disease management[43].

AI-Based Discrimination of MS and Mimics

Multimodal analysis based on artificial intelligence, e.g., MRI, cerebrospinal fluid (CSF) biomarkers, and clinical history, has enhanced the differential diagnosis of MS from Neuromyelitis Optica Spectrum Disorder (NMOSD) and small vessel disease considerably[9,44]. Robust diffusion tensor imaging (DTI) algorithms identify microstructural changes in the CNS typical of MS, and differential diagnoses can be established more accurately[27,45].

AI in Monitoring Disease Progression

Digital Twins for Personalized Disease Modelling

Digital twins, computer models of patients built from big data sets, have been demonstrated to monitor MS disease progression in real time[14]. AI-based simulations using genomic, imaging, and clinical data and integrating it to forecast relapses and treatment response[19,46]. New evidence indicates that digital twin models are able to predict long-term disability progression accurately and allow for earlier intervention[26,47].

Wearables and Gait Analysis

Wearable technology allows for timely monitoring of MS-associated mobility impairment. Smart sensors powered by artificial intelligence track motor function, balance, and gait to spot minute alterations before they become clinical symptoms[31,48]. Machine learning algorithms have facilitated the establishment of predictive models for mobility impairment, allowing for early rehabilitation[16,49].

Speech and Cognitive Analysis in Disease Monitoring

Speech recognition and cognitive testing programs using AI are emerging as a non-invasive method of MS monitoring. Speech patterns, cognitive reaction times, and voice modulations are processed by AI algorithms to identify cognitive impairment, usually a neurodegeneration of disease advancement[37,50]. Large-scale clinical studies demonstrate that AI-augmented cognitive testing is superior to conventional testing for the detection of early neurodegeneration.

AI in MS Treatment Optimization Personalized Treatment Regimens

Personalized AI models that take into account the genetic, clinical, and imaging characteristics of each patient may improve prognosis prediction and disease classification, opening the door to more specialized treatment approaches[23]. AI models scan clinical, genetic, and biomarker data to tailor DMT choice[32]. Reinforcement learning can forecast long-term treatment responses to optimize therapy planning with minimal off-target activity[20].

Nanorobotics and AI-Based Drug Delivery

Drug delivery targeting improvements in MS therapy are being studied using nanotechnology. Artificial intelligence (AI)-powered nanorobotics may improve blood-brain barrier penetration for targeted neuroprotective medication

delivery[17]. AI-driven simulations are crucial to producing the best nanoparticles and forecasting their therapeutic efficacy in preclinical models[33].

Challenges and Future Directions Ethical Considerations and AI Transparency

Data privacy, algorithmic bias, and clinical interpretability are among the ethical concerns brought up by its use in MS research[13]. Models of explainable AI (XAI) are being developed to increase clinician confidence and transparency[10].

Data Sharing and Global Collaboration

Federated learning makes it possible for institutions to securely share data without compromising patient privacy[29]. International partnerships such as the Multiple Sclerosis Data Alliance are essential for combining data sets to create stronger AI models[7].

CONCLUSION

More accuracy, efficiency, and personalization in MS diagnosis, monitoring, and treatment are being made possible by artificial intelligence. A previously unheard-of understanding of the evolution of disease is made possible by wearable technology, biomarker multispecialty, and high-resolution imaging. Nanotechnology-mediated drug delivery and reinforcement learning-based treatment selection are two AI-driven personalized treatment strategies that could be extremely valuable in improving MS treatment. Before widespread clinical use, regulatory and ethical issues must be resolved[24]. The future relies on collaborative multispecialty teamwork, advanced AI computations, and data-sharing infrastructures that optimize global patient benefit[6].

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CASE STUDY ARTICLE

Effectiveness of Herbal Medicine in Controlling the Normal HbA1c Levels in a Diabetic Patient : A Case Study

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Received: 02 Jan 2026 Revised: 10 Jan 2025 Accepted: 18 Jan 2026

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ABSTRACT

Diabetes mellitus (DM) is a major non-communicable disease with a prevalence rate of 11.6%. India ranks second, after China, in the number of diabetic cases. This article highlights the seriousness of DM and its management using herbal medicine without complications. It presents a case study of a 57-year-old male patient with an HbA1c level of 7%. The patient was treated with a combination of herbal drugs mentioned in Ayurvedic Samhitas for 8 to 12 months, alongside a daily 45-minute walk. After one year of treatment, a significant improvement was observed, with the HbA1c level returning to the normal range.

Keywords: Diabetes Mellitus, Obese, Herbal, *Madhumeha*

INTRODUCTION

Diabetes mellitus(DM) is a metabolic disorder characterized by polyuria, polydipsia, polyphagia, weakness, and fatigue(1). It is a lifestyle disorder with a worldwide prevalence. The number of people suffering from diabetes symptoms is increasing daily. According to the International Diabetic Federation (IDF) in 2019, India has 77 million people with diabetes and 25 million who are prediabetic; type-2 DM constitutes 90% of these cases(2). The seriousness of this disease is compounded by its occurrence across almost all age groups. Major causative factors include a sedentary lifestyle, incompatible diet, and lack of physical activity, leading to low metabolism, obesity, and insulin resistance. DM is classified into two types: type-1 and type-2(3). The pathophysiology of type-1 DM involves insulin deficiency, while type-2 DM is primarily due to insulin resistance(4). In Ayurveda, DM is correlated with

Madhumeha, a type of *VatajPrameha. Madhumeha* is characterized by sweet, dry, astringent, and pale-colored urine(5). The principal Dosha involved is *Kapha*, and the major *Dushyas* (affected tissues) are *Meda* (fat), *Mansa* (muscle), *Kleda* (fluid), *Shukra* (reproductive tissue), Oja (vital essence), *Rakta* (blood), *Lasika* (lymph), *Rasa* (plasma), *Vasa* (muscle fat), and *Majja* (bone marrow)(6). Various herbal formulations and single drugs (*Ekal Dravya*) are described in Ayurvedic texts. Using these drugs alongside *Pathya Apathya* (dietary and lifestyle guidelines) and physical exercise can help control DM in patients who have not yet started modern medicine.

CASE STUDY

A 57-year-old male patient presented with complaints of weakness, fatigue, excessive thirst (polydipsia), excessive hunger (polyphagia), and frequent, increased volume of urination (polyuria). Detailed history-taking and general examination were conducted (details below). The patient had not taken any modern or Ayurvedic medicine for diabetes prior to this consultation. He was a known case of hypothyroidism for seven years, taking 125 mcg thyroxine daily. There was no history of hypertension, other major illnesses, past surgeries, or a family history of DM. He was advised to undergo fasting blood sugar and HbA1c tests.

Personal History
Diet: Vegetarian
Occupation: Office work (sedentary job)
Addiction: None
Sleep: Sound sleep
Bowel Habit: Twice daily, normal consistency
Micturition: 7-8 times a day, 2-3 times at night
Appetite: Increased
Sanitation: Good
Other: No significant stress

General Examination
Height: 170 cm
Weight: 75 kg
BMI: 26 kg/m² (Overweight/Obese)
Built: Obese
Icterus: Absent
Edema: Absent
Lymphadenopathy: No
Skin: Dry
Nails: Rough
Pallor: Absent
Speech: Normal

Vitals
Temperature: Afebrile
Blood Pressure: 140/90 mmHg
Pulse: 76/min
SpO2: 95%

Ayurvedic Assessment (*Ashtavidh and Dashvidh Pariksha*)
Nadi (Pulse): Manda Visham
Mutra (Urine): Increased quantity

Mala (Stool): Prakrit (Normal)
Jivha (Tongue): Lipta (Coated)
Shabda (Voice): Prakrit (Normal)
Sparsh (Touch): Ruksha (rough, dry), Anushnasheet (moderate temperature)
Drik (Eyes): Prakrit (Normal)
Akriti (Physique): Obese
Prakriti (Constitution): Kaphapittaj
Vikriti (Pathological State): Kapha Vataj
Saara (Tissue Quality): Madhyam (Moderate)
Samhanan (Compactness): Pravar (Good)
Praman (Proportion): Madhyam (Moderate)
Satva (Mind): Madhyam (Moderate)
Satmya (Adaptability): Madhyam (Moderate)
Aahar Shakti (Digestive Power): Pravara (Good)
Vyayam Shakti (Exercise Tolerance): Madhyam (Moderate)
Vaya (Age): Madhyamavastha (57 years)

Laboratory Investigation Before Treatment
HbA1c: 7% (Normal level <6.5%)(7)

Treatment Protocol(8)
A fresh juice formulation was prepared using equal quantities of the following herbs:
1. Amla (*Emblica officinalis*)
2. Kutki (*Picrorhiza kurroa*)
3. Jamun Seed (*Syzygium jambolanum*)
4. Vijayasara (*Pterocarpus marsupium*)
5. Gudmar (*Gymnema sylvestre*)
6. Bel Patra (*Aegle marmelos*)
7. Giloy (*Tinospora cordifolia*)
8. Methi (*Trigonella foenum-graecum*)
9. Neem (*Azadirachta indica*)

Dosage: 15 ml of the juice with an equal quantity of water, twice daily on an empty stomach (morning and evening).
Lifestyle Modification: A daily 45-minute walk on an empty stomach.

Dietary Advice
Morning: Light diet (e.g., 2-3 multigrain chapatis, green vegetables). Citrus fruits.
Afternoon: Dal, rice, chapati, vegetable curry (excluding high-carbohydrate options).
Evening: Roasted chickpeas (brown chana), puffed rice (murmura).
Night: 3 chapatis, vegetable curry, dal. Unsweetened milk at bedtime.

Results: Clinical Features and Investigation

CONCLUSION

Herbal medicines can be highly effective, particularly in patients who have not previously taken modern anti-diabetic drugs, as they may help stimulate and activate cells for regular metabolic function. Regular exercise enhances cellular adaptive capacity and increases metabolism. Adhering to a proper diet helps reduce the risk of disease progression. In this case, strict adherence to herbal treatment and a regular 45-minute daily walk proved

highly beneficial. The patient found it challenging to follow the dietary plan completely but managed to reduce meal portions while maintaining the medicinal and exercise regimen. This combined approach resulted in the normalization of HbA1c levels, demonstrating the potential of integrated Ayurvedic management in controlling type-2 diabetes.

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Table 1: Results: Clinical Features and Investigation

Clinical Feature	Before Treatment (15/05/23)	After Treatment (09/12/24)
Weakness	More	Less
Polyphagia	More	Less
Polydipsia	More	Less
Polyuria	More	Less
Fatigue	More	Less
HbA1c	7%	4.46% (Normal)

RESEARCH ARTICLE

Entropy Weighted Water Quality Index and Geo Indices Approach for Assessing Pollutants Level in Ground Water Resources

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Received: 09 Aug 2025 Revised: 18 Nov 2025 Accepted: 03 Jan 2026

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ABSTRACT

Globalization, industrialization and urbanization poses a big challenge on safe drinking water. Consumption of safe drinking water is most important for human being since unsafe drinking water consumption causes many water borne diseases namely typhoid, cholera etc. Ground water is the only primary source for the residents of Mayiladuthurai district. It is located in southern part of India. In this study, hydrochemical analysis were made on 20 samples and the samples were analysed and the analysed measures like pH, Electrical conductivity, Total dissolved solids content, chloride ion, sulphate ion, nitrate ion, fluoride ion, calcium, magnesium , total hardness, total alkalinity and heavy metals like zinc, iron, manganese, chromium and lead. Standard water quality analysing methodology recommended by APHA (1995) and BIS (1991) was used to get the results. The drinking quality was checked and studied using Entropy weighted water quality index (EWQI), Nemerrow's index (NPI) and heavy metals influence towards water quality was studied using Geo accumulation index (I geo). This type of multiple index oriented study was not undertaken in the study area so far. Results of EWQI showed that 85% of water samples were in poor category, 10 % of water samples were in extremely poor category and 5% of water samples were in medium category. Results of Nemerrow's Pollution Index

(NPI) revealed that most of the samples were in polluted state, required pretreatment and the results of I geo value indicating that heavy metal pollution came from the heavy loading of copper and lead in the water samples. The results of EWQI, NPI and I geo calculation indicate that application of these indices is identified the real nature of drinking water sources quality and highly supportive to the residents and water board authorities of Mayiladuthurai district for taking the required decision.

Keywords: Ground water, Mayiladuthurai, Entropy weighted water quality index (EWQI),Nemerow's Pollution Index(NPI), Geo accumulation Index.

INTRODUCTION

Water resources are the heart of the planet Earth.It is supporting in large scale for human being to their livelihood both for drinking and many domestic responsibilities.Development of economy,sustainability of environment also based on the quality of water available for the people.Increase in the size of population, modernization, urbanization, industrial activities and unscientific approach in handling water resources may cause the change of quality of ground water and it becomes global concern. Climatic change also deteriorates the quality.Now-a days , many human activities causing the deterioration of ground water resources. [6],[7],[1,4]. However, most of the human population is forced to drink the available slightly to moderately deteriorated water for their drinking purpose which in turn causes many diseases. The quality of water directly or indirectly affects public health, agricultural productivity, and industrial processes. Heavy metalsand their presence in water and also presence of nitrates, phosphates, and microbial pollutants can degrade water quality, making it unsuitable for human consumption and ecological balance. Water quality and its measured value are the most important one to ensureits quality while using it for drinking purposes, agriculture, and industrial use. Water quality assessment typically involves the measurement of multiple physicochemical and biological parameters, including multiple parameters like pH,DO(Dissolved Oxygen),BOD(**B**iochemical oxygen demand, TDS (Total Dissolved Solids) and concentrations of various chemical contaminants. However, interpreting these parameters individually can be complex and may not provide a thorough and clear understanding of the overall water quality because all the measured parameters were not in the same unit of measurement. To resolve this challenging problem, Water Quality Indices (WQIs) were proposed and developed as effective tools to sum up the contribution of variouswater quality measuresand all the water quality measures contribution converted into a whole number. This single numerical whole number giving the overall statusabout the quality and nature of water samples [5].

Traditional WQIs assign weights to different water quality parameters based on expert judgment or regulatory guidelines. Traditional water quality indices (WQIs) provide a numerical representation for water samples to represent its quality.The process involves collection of all physicochemical and biological measure's contribution and converting it into a single value[8][9][10]. This index calculation uses subjective evaluation technique. This evaluation method involved assigning weight for each and every parameter based on the experts opinion. Majorly WQI involved with evaluation procedure with more subjectivity based on experts opinion for parameter weights ofeach and every parameter to compute the WQI score. This creates the ambiguityin the originality in water quality of the studied sample[12] [13].However, conventional WQIs often rely on subjective weight assignments, which may introduce bias and reduce the reliability of the assessment[14].

While these approaches have been widely used, they introduce an element of subjectivity that may affect the reliability and accuracy of this water quality analysis. Many cases were reported, in that the assignment of parameter weights does not fully account for the inherent variability. Overall water quality determined by the contribution of given by each parameter. This has led researchers to explore more objective and data-driven methodologies for water quality assessment.

For resolving this issue, the Entropy Water Quality Index (EWQI) has emerged like a robust approach [2].In water quality assessment, it helps in identifying the most influential parameters without requiring subjective weight assignments. The entropy weighted water quality index, which applies entropy concept and its principles from information theory. It is used to identify the relative significance of these parameters based on their variability[3]. This method eliminates the need for subjective weight assignments and provides a more statistically rigorous approach to water quality evaluation. The usage of entropy is supporting here is to determine the relative significance of each parameter based on its variability across different sampling locations and time periods. Unlike conventional WQIs, which rely on fixed weights, the entropy-based method assigns dynamic weights to water quality parameters based on their statistical distribution, ensuring a more unbiased and data-driven evaluation.By considering the variability of each parameter, EWQI chooses the parameter which has greater heights of impact on the final water quality index in terms of improved accuracy. The method can be applied to different water quality datasets without requiring prior knowledge of local water conditions or predefined weighting schemes improving the flexibility and adaptability.

The concept EWQI utilizes entropy information theory to objectively for all the measures of water sample to measure their weight based on their variability. The subjectivity issue of water quality index is minimized by EWQI approach in the evaluation of this process, leading to a more data-driven calculation of analysis of groundwater samples for getting their quality . A study conducted in Mayiladuthurai district,southern part of India by applying the EWQI method to assess groundwater quality. The researchers collected samples from 20 locations and analyzed major anions and cations.

Secondly Nemerow's Pollution Index (NPI) was applied for assessment**.** Vales of NPI provides a comprehensive assessment of pollution by considering both the mean value of individual pollution indices and the maximum pollution index. This dual approach ensures that the evaluation reflects both average pollution levels and the most severe contamination, offering a balanced perspective on the quality determination part groundwater sources. The findings of this study highlighted variations in pollution levels.

Thirdly **g**eoaccumulation Index (I_geo) was also used. Originally developed to assess soil contamination. However, the I_geovalue has been adapted for groundwater studies to evaluate the accumulation of trace metals concentration.Comparing the obtained concentrations of trace metals with its pre-industrial levels, categorizing the degree of pollution and helping to identify anthropogenic influences. I geo values specially gives us the hidden contribution given by traces of heavy metals to judge the water quality. Which will in turn affects the ecology in terms of its risk. In this study, this study integrats the following indices namely Nemerow's Pollution Index (NPI) and geo accumulation index with EWQI for evaluating ground water quality of the studied samples. This study helps us to understand about the groundwater quality concerning with all level of pollution including heavy metal contamination which in turn, aids in identifying pollution sources and developing effective management strategies to protect this essential resource.No such types of studies were undertaken in this area.So to analyse the current status of the ground water in the proposed area ,the tools like Entropy weighted water quality Index(EWQI), Nemerow's Pollution Index and geo accumulation indices were used. Using these indices detailed study were undertaken to get real quality.By using the entropy weighted water quality approach, there contributing advanced research tool to assess the water quality.

Study area description

Groundwater samples from the twenty sampling points from in and around of Mayiladuthurai were collected. Mayiladuthurai district is recently separated from the Nagapattinam district for the purposes of administrative reasons in southern part of India. The district is largely supporting to agriculture as it receives water from the holy river the Cauvery particularly during rainy season. It is supporting to its residents by means its fast development. Ground water is the only major support for the residents of Mayiladuthurai for their drinking purpose.

From January 2024 to February 2024, totally 40 samples were collected and it is involved for measuring water quality measure during post monsoon season. The sampling stations details and their locations were presented in Fig .1 and Table.1.

MATERIALS AND METHODS

APHA (1995) [15]and BIS (1991)[16] recommended standard procedures to do the analysis. All the sample collection and its analysis were based standard methods prescribed by determined by APHA (1995) [15]and BIS (1991)[16]. In 5 Litre capacity pre cleaned plastics containers water samples were collected. After careful and thorough filteration, it was separated into two portions, one was preserved with nitric acid to pH < 2 (for trace metals). Preservation of both portions was maintained in refrigeration at 4°C. Water quality parameters like pH and electrical conductivity measurements were completed in the sample collection points itself using digital equipment's. Measurement of Total Dissolved Solids (TDS)was completed by digitalised TDS meter. Using EDTA method total hardness, calcium were measured. Magnesium was calculated through EDTA method's calculation. **U**sing flame photometric method measurement of sodium and potassium was completed**.** Using acid titration method alkalinity was measured. Chloride ion concentration was measured using argentometric titrations.Measurement of fluoride was completed using SPADNS spectrophotometric method. Presence phosphate ion concentration was measured by spectrophotometric method. Turbidity spectrophotometricmethodwas used to measure sulphate ion concentration. Nitrate by brucine sulphate spectrophotometric method**.** Trace elemental analysis - Atomic Absorption Spectrophotometric method for the estimation of chromium, copper, iron, manganese, zinc and lead.

Entropy-weighted water quality index (EWQI):

*Entropy-weighted water quality index (EWQI),t*he WQI utilized by [17]. Being an improved or enhanced model of index for measuring water quality, itis the mostly used model for checking the drinking water samples suitability. Developed form of WQI is EWQI[18].In WQI, each and every individual parameters is assigned with some weight as per experts judgement and this is completed minimized in EWQI calculation. Across the world ,EWQI is considered as the most reliable, justifiable and accurate method for calculating drinking water quality[19]. A five step calculation steps are involved in the computation of EWQI[20].Initially, the term the information entropy (ej) was determined as:

$$\mathbf{ej} = -\frac{1}{ln}\mathbf{n}\sum_{i=1}^{z} Pij\ ln\ Pij \quad \text{.....(1)}$$

Where total number of water samples is represented by n and Pij is the probability of normalized value of the parameter *j* [2] expressed as: $\mathbf{Pij} = \frac{Pij}{\sum Pij}$.....(2)

Here y represents individual samples of water *(i= 1, 2, 3…z) and* water quality measures were represented by x [3]. *(j = 1, 2, 3…n)* are to be tested to measure the water quality and the ratio between *j* and *i*is given as

$$Pij = yij/\sum_{i=1}^{z} yij \quad \text{.....(3)}$$

Using equation (4) the entropy weight was calculated (*w*j),

$$(wj) = \frac{1-ej}{\sum_{i=1}^{n}(1-ej)} \quad \text{.....(4)}$$

Here 1-ej is taken as equal to dj for convenient calculation. Each parameter's quality rating scale (qj) was expressed by

It should be $\mathbf{qj} = \frac{Cj}{Sj}$***100** .....(5)

Where concentration of each measured parameters were noted with Cj in mg/L and the respective parameters were represented by *Sj* in the samples, expressed in mg / L for drinking water quality [31,34] .
The entropy weighted water quality index (EWQI) which is an improved form is calculated as;

EWQI= $\sum_{j=1}^{n} Wj.qj$ ……(6)

Hydro chemical risk assessment by geo indices
Nemerow's pollution index (NPI)
Equation (7) was used to calculate the NPI values by referring Swathi and Umesh [20],[21].
NPI $= \frac{Ci}{wqs}$……(7)

where, concentration of each water quality analysing measure was reported as*Ci* and its standard limit is given as wqs.

Geoaccumulation index (I geo)
Geoaccumulation Index (I geo) is the most widely used index for assessing soil pollution status. However, the I geo index calculation is also supportive to judge the water quality in terms of trace metal content [22, 23, 24]. To calculate I geo values, Eq. (8) was used.

$I\ geo = Log2\frac{CHMS}{1.5*GBV}$……(8)

where, C HMS is concentration of heavy metal ion presentin water; geochemical background value is denoted in terms of GBV. The value 1.5 is used as a constant here to meet and analyse the variation of a given substance occurs naturally in the environment [25, 26, 27].

RESULTS AND DISCUSSION

The results of physico chemical parameter concentrations in terms of mean values used for the entropy weighted water quality index calculation were given in Table (2)and Table 2a. Table 3 is providing the results of Information weight (ej),dj and Entropy weight(Wj) values of the study area and Table 4 deals with the final result and categorization os water samples based on entropy weighted water quality.

Entropy weighted water quality Index
Results obtained from Information entropy(ej),dj and entropy weight (Wj) were tabulated in Table(3).The values of EWQI of this study for all samples based on WHO guidelines was tabulated in Table (4) and the Table (5) represented reference categorization score of EWQI. Fig:2 showed the final calculated of values of EWQI. Results of EWQI showed that it was ranged between 97.6162 and 430.1126. Out of 20 analysed samples, sample number eight secured EWQI score <100 (97.6162),falling in medium category. It showed that the sample 8 scored lowest value EWQI and reflects its highest quality among the analysed samples. Sample 2(EWQI Score 152.85) and 17 scored above 150 (EWQI Score 430.11) rated as the samples were in extremely poor category[33],this is due to heavy anthropogenic damage. These two samples 2 and 17 were scored highest EWQI score, indicating that they were in extremely poor quality. EWQI score of remaining water samples falling between >100 to<150 ,indicating that water samples were poor in quality. 85% of water samples were rated as in poor category, 10 % of water samples were in extremely poor category and 5% of water samples were rated as medium category. The above results of EWQI showed that it reduced subjectivity of WQI method. This has been achieved by the application entropy-based weights for the analysed parameters, demonstrating that objective-weighting systems like EWQI provide more accurate and dependable results [30,12,28,29]. Samples which received low quality area may be due to the low

ground water level availability or agricultural activities practices [4,6,32]. The results supported as more informative in decision-making processes for environmental monitoring and sustainable water resource management.

Hydro-environmental pollution risk evaluation by geo indices

Nemerow's Pollution Index (NPI)

The Nemerow's Pollution Index (NPI) providing a comprehensive evaluation of environmental contamination by integrating multiple pollution indicators. The Nemerow's Pollution Index serves as a valuable tool in environmental risk assessment, offering a balanced approach by considering both the worst pollutant and the overall pollution level. Nemerow's index criteria for classification score was tabulated in Table(6).

Nemerow's pollution Index is one of the most powerful tool to identify the quality of water [31].It identifies the priority contaminants for treatment of water samples and also the level of pollution contribution given by each and every parameter in a particular sample water [31]. Nemerow's pollution Index values were calculated as per the method discussed in the methodology Section [27] for all the analysed samples, and the results of NPI was provided in the Table (7). The samples whose NPI score exceeding 1 indicates that it was polluted and requires prior purification treatment before consumption. All salts which in dissolved form is the combination of all inorganic salts present in dissolved form and small amount of organic substance. Results of NPI in this study for Total dissolved Solids was more than 1 for all the samples indicating that the water is not fresh in quality [21]. NPI score of pH, chloride, sulphate, nitrate, zinc, iron and manganese were less than 1 for all the samples indicating that the is not polluted according to these parameters.NPI score of fluoride ion, calcium ion, magnesium ion and heavy metals like lead, total hardness were also crossed one. NPI score for Electrical conductivity of all samples were greater than one except sample 8. Chromium's NPI value was crossed the limit 1 except sample number 13. From the results of NPI showing that all of the studied water samples were not advisable for direct consumption for drinking without prior treatment. For sites with **NPI > 3**, immediate remediation strategies such as wastewater treatment, soil rehabilitation, or stricter emissions regulations should be enforced. It was observed that the samples with NPI score between 1 and 2 indicating that slight level of pollution was identified. Samples with their NPI score between 2 and 3 indicates that moderate pollution for the studied water samples. Samples which has NPI score 2 to 3 required continuous monitoring and pollution control measures to prevent deterioration. The results indicate that sites with high NPI values require urgent intervention, while areas with moderate contamination demand continuous monitoring. The NPI helps identify which specific contaminants are most significantly impacting water quality, allowing for targeted remediation efforts. In this the Mayiladuthurai district study, the NPI results indicated that most water samples were classified as polluted, necessitating pretreatment before consumption. By integrating NPI with other environmental indicators, policymakers and researchers can develop more effective pollution control and management strategies.

Geo accumulation index

Classification criteria for geo accumulation index (I geo accumulation value) values were in Table 8 and its results for this study was given in Table 9.It is pictorially given in Figure 3 . The obtained values of I geo accumulation value fluctuated from 1to 2. According to I geo accumulation value values, the quality of water was divided into seven types based on the presence of pollutants level. According to[20] the classification I geo values was made, it was given in the Table 8.I geo accumulation value results of this study area revealed that the scores ranged between 0 and 6. 15% of the samples were falling in($0 <$ I geo accumulation value ≤ 1) range representing that 15% of samples were in the uncontaminated to contaminated state. accumulation value 3% of samples were in the range of ($2 <$ I geo accumulation value ≤ 3) revealing that those samples were moderately to heavy contamination stage.1% of the sample was in the range of (I geo accumulation value ≥ 5) indicting that in extremely polluted stage, sampling station- 17 received this score and it may be due to anthropogenic activities. The remaining 65% of samples were in the range of (I geo accumulation value ≤ 0) revealing that they were in uncontaminated pure stage. Results of I geo values of all samples indicating that trace metal pollution was slightly impacted in the studied water samples. From the results, it was observed that heavy metal pollution came from the higher loading of copper and lead. This may be due to anthropogenic activities[20].

CONCLUSION

The entropy weighted water quality index and geoindices tools were applied to evaluate the pollutants level in ground water resources of Mayiladuthurai region. Results of EWQI showed that 85% of water samples were rated as in poor category, 10 % of water samples were in extremely poor category and 5% of water samples were rated as medium category. The above results showed that EWQI reduced subjectivity which arises in the water quality index tool by taking into account of entropy-based weights for water quality measures, demonstrating that objective weight scale systems like EWQI provide more accurate and dependable results. NPI revealed that most of the samples were in polluted required pretreatment and the results of *I geo* value indicating that heavy metal pollution came from the heavy loading of copper and lead in the samples of study area. This finding of NPI aligns with the poor water quality assessment from other indices used in the study such as the entropy weighted water quality index (EWQI) and the geo-accumulation index (I geo). The present study recommends requirement of pretreatment for water for purifying before its consumption.

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Table 1 - Details of ground water sampling station locations in the study area

Sl. No	Water sample collection points		
1	Kuthalam (P-1)	11	Tiruvazhundur (P -11)
2	Sethrabalapuram (P-2)	12	Coconut tree street (P-12)
3	Arayapuram (P-3)	13	Chenthangudi (P -13)
4	Malliyam (P -4)	14	Nagangudi (P-14)
5	Mahadhanapuram(P -5)	15	Lakshmipuram (P -15)
6	Moovalur (P -6)	16	Uluthukuppai (P -16)
7	Sitharkadu (P -7)	17	S.S. Nallur (P -17)
8	Pukadai Mayiladuthurai (P -8)	18	Thirunanriyur (P -18)
9	Kora nadu (P -9)	19	KeezhaAthukudi (P -19)
10	Mahadana street (P-10)	20	Mela Athukudi (P -20)

Table (2) : Results of physico chemical parameter concentrations for the study area

Sampling Station locations	TDS	pH	Electrical Conductivity	Chloride	Sulphate	Nitrate	Fluoride	Calcium	Magnesium
P-1	806	7.615	1.26	162	99	0.12	5.125	115	67
P -2	925	7.635	1.445	185	110	0.16	4.9	138.5	74.5
P -3	845	7.72	1.32	165	95	0.16	4.895	120.7	65.8
P -4	864	7.735	1.35	176	100	0.145	4.925	134.6	67
P -5	1005	7.68	1.57	170	95	0.15	4.915	129	70
P -6	742	7.605	1.16	190	85	0.075	3.185	123	65
P -7	755.5	7.485	1.18	180.5	85.4	0.05	3.31	120	70.5
P -8	621	7.61	0.97	160.5	80.2	0.105	3.31	110.5	61.2
P -9	665.5	7.39	1.04	136	72.5	0.105	3.375	100.3	56.5
P -10	832	7.5	1.3	156.9	74.9	0.1	3.325	115.3	64.6
P-11	892.5	7.795	1.395	160.7	100.7	0.085	3.29	117.9	65.9
P -12	793.5	7.54	1.24	156	81.5	0.105	3.035	109.9	59.8
P -13	832	7.535	1.285	165.5	95.6	0.14	3.055	120	67.1
P-14	819	7.59	1.28	154	70	0.08	2.9	105.9	55.7
P -15	851	7.765	1.33	155.4	112.3	0.075	2.975	125	67.8
P -16	828.5	7.605	1.295	185.9	120.9	0.085	3.405	168.4	55.9
P -17	832	7.52	1.3	150.8	95.9	0.105	3.48	109.7	59.9
P -18	848	7.5	1.325	173	97	0.055	3.44	120.8	68.9
P-19	960	7.525	1.5	175.9	105.9	0.08	3.55	120.6	65.2
P -20	880	7.57	1.375	167.9	88.9	0.06	3.39	130.6	75.3

Table (2a) : Results of physico chemical parameter concentrations for the study area

Sampling Station locations	Zn	Cu	Fe	Mn	Cr	Pb	TH*	TA*
P -1	0.015	0.015	0.05	0.025	0.14	0.13	563.061	247
P -2	0.02	0.02	0.055	0.025	0.23	0.17	652.6255	280
P -3	0.02	0.02	0.04	0.025	0.1	0.17	572.3523	245.8
P -4	0.035	0.03	0.05	0.035	0.21	0.15	612.0022	276
P -5	0.015	0.025	0.05	0.04	0.09	0.12	610.373	260
P -6	0.025	0.015	0.03	0.015	0.08	0.1	574.801	300
P -7	0.035	0.015	0.035	0.02	0.06	0.09	589.959	280.5
P -8	0.02	0.01	0.035	0.015	0.06	0.06	527.94	210
P -9	0.025	0.01	0.045	0.02	0.12	0.26	483.11	202.5
P -10	0.02	0.01	0.055	0.01	0.09	0.07	553.92	248.8
P -11	0.01	0.01	0.05	0.02	0.18	0.21	565.77	240.6
P -12	0.01	0.01	0.035	0.015	0.09	0.11	520.67	223.5
P -13	0.02	0.02	0.04	0.015	0.03	0.07	575.95	221.9
P -14	0.02	0.03	0.045	0.015	0.06	0.08	493.80	208.5
P-15	0.015	0.04	0.035	0.03	0.09	0.2	591.32	265.4
P -16	0.02	0.015	0.05	0.01	0.09	0.07	650.69	245.7
P -17	0.02	0.01	0.03	0.01	0.08	7	520.58	265.5
P -18	0.02	0.01	0.03	0.02	0.11	0.19	585.36	270.6
P -19	0.015	0.01	0.055	0.01	0.16	0.13	569.63	275.9
P -20	0.02	0.01	0.04	0.01	0.13	0.15	636.19	270.8

- TH-Total hardness, TA-Total alkalinity

Table : 3 Results showing Information weight (ej),dj and Entropy weight(Wj) values of the study area

Parameters	ej	dj=1-ej	Wj=$\frac{1-ej}{\sum_{i=1}^{n}(1-ej)}$
TDS	8.957601	-7.9576	0.06162
PH	8.974148	-7.97415	0.061748
Electrical conductivity	8.957594	-7.95759	0.06162
Chloride	8.96501	-7.96501	0.061677
Sulphate	8.944136	-7.94414	0.061516
Nitrate	8.813604	-7.8136	0.060505
Fluoride	8.916108	-7.91611	0.061299
Calcium	8.955208	-7.95521	0.061601
Magnesium	8.963813	-7.96381	0.061668
Zinc	8.830569	-7.83057	0.060636
Copper	8.640007	-7.64001	0.059161
Iron	8.913107	-7.91311	0.061275
Manganese	8.704455	-7.70446	0.05966
Chromium	8.673356	-7.67336	0.059419
Lead	4.009334	-3.00933	0.023303
Total Hardness	8.964657	-7.96466	0.061675
Total Alkalinity	8.957343	-7.95734	0.061618

Table. 4 Results and categorization score EWQI for the analysed samples for the study area.

SSL*	P -1	P -2	P -3	P -4	P -5	P -6	P -7	P -8	P -9	P -10
∑Wj.Qj	131.10	152.85	128.46	146.77	133.11	110.65	109.56	97.612	111.99	108.97
Category	4	5	4	4	4	4	4	3	4	4
Quality of water	Poor	Extremely Poor	Poor	Poor	Poor	Poor	Poor	Medium	Poor	Poor
SSL	P -11	P -12	P -13	P -14	P -15	P -16	P -17	P -18	P -19	P -20
∑Wj.Qj	129.36	105.40	102.67	100.20	121.66	116.54	430.11	121.80	127.42	125.17
Category	4	4	4	4	4	4	5	4	4	4
Quality of water	Poor	Poor	Poor	Poor	Poor	Poor	Severe	Poor	Poor	Poor

***SSL-Sampling station locations**

Table (5) : Classification criteria reference used for EWQI ground water quality

EWQI score	Category	Quality of water	Number of ground water samples	Percentage of samples
<25	1	Excellent	0	0
>25 to <50	2	Good	0	0
>50 to <100	3	Medium	1	5
>100 to <150	4	Poor	17	85
>150	5	Extremely Poor	2	10

Table: 6 -Nemerow's index criteria for classification scores

NPI Score	Nature of pollution
≤ 1	Not polluted
1< NPI ≤ 2	Slightly affected by pollution
2< NPI ≤ 3	Moderately affected by Pollution
NPI>3	Heavily affected by Pollution

Table: 7 -Results of NPI score for the analysed samples in the study area

Parameters/Sampling station locations	P-1	P -2	P -3	P -4	P-5	P -6	P -7	P -8	P -9	P-10
TDS (mg/l)	1.61	1.85	1.69	1.73	2.01	1.48	1.51	1.24	1.33	1.66
pH	0.90	0.90	0.91	0.91	0.90	0.89	0.88	0.90	0.87	0.88
EC	1.26	1.45	1.32	1.35	1.57	1.16	1.18	0.97	1.04	1.30
Chloride	0.65	0.74	0.66	0.70	0.68	0.76	0.72	0.64	0.54	0.63
Sulphate	0.50	0.55	0.48	0.50	0.48	0.43	0.43	0.40	0.36	0.37
Nitrate	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Fluoride	5.13	4.90	4.90	4.93	4.92	3.19	3.31	3.31	3.38	3.33
Calcium	1.53	1.85	1.61	1.79	1.72	1.64	1.60	1.47	1.34	1.54
Magnesium	2.23	2.48	2.19	2.23	2.33	2.17	2.35	2.04	1.88	2.15
Zinc	0.00	0.00	0.00	0.01	0.00	0.01	0.01	0.00	0.01	0.00
Copper	0.30	0.40	0.40	0.60	0.50	0.30	0.30	0.20	0.20	0.20
Iron	0.17	0.18	0.13	0.17	0.17	0.10	0.12	0.12	0.15	0.18
Manganese	0.25	0.25	0.25	0.35	0.40	0.15	0.20	0.15	0.20	0.10
Chromium	2.80	4.60	2.00	4.20	1.80	1.60	1.20	1.20	2.40	1.80

Lead	2.60	3.40	3.40	3.00	2.40	2.00	1.80	1.20	5.20	1.40
Total Hardness	1.88	2.18	1.91	2.04	2.03	1.92	1.97	1.76	1.61	1.85
Total Alkalinity	1.24	1.40	1.23	1.38	1.30	1.50	1.40	1.05	1.01	1.24

Table: 7a -Results of NPI score for the analysed samples in the study area

Parameters/location points	P-11	P -12	P -13	P-14	P -15	P-16	P -17	P -18	P -19	P-20
TDS	1.79	1.59	1.66	1.64	1.70	1.66	1.66	1.70	1.92	1.76
pH	0.92	0.89	0.89	0.89	0.91	0.89	0.88	0.88	0.89	0.89
EC	1.40	1.24	1.29	1.28	1.33	1.30	1.30	1.33	1.50	1.38
Chloride	0.64	0.62	0.66	0.62	0.62	0.74	0.60	0.69	0.70	0.67
Sulphate	0.50	0.41	0.48	0.35	0.56	0.60	0.48	0.49	0.53	0.44
Nitrate	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Fluoride	3.29	3.04	3.06	2.90	2.98	3.41	3.48	3.44	3.55	3.39
Calcium	1.57	1.47	1.60	1.41	1.67	2.25	1.46	1.61	1.61	1.74
Magnesium	2.20	1.99	2.24	1.86	2.26	1.86	2.00	2.30	2.17	2.51
Zinc	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Copper	0.20	0.20	0.40	0.60	0.80	0.30	0.20	0.20	0.20	0.20
Iron	0.17	0.12	0.13	0.15	0.12	0.17	0.10	0.10	0.18	0.13
Manganese	0.20	0.15	0.15	0.15	0.30	0.10	0.10	0.20	0.10	0.10
Chromium	3.60	1.80	0.60	1.20	1.80	1.80	1.60	2.20	3.20	2.60
Lead	4.20	2.20	1.40	1.60	4.00	1.40	140	3.80	2.60	3.00
Total Hardness	1.89	1.74	1.92	1.65	1.97	2.17	1.74	1.95	1.90	2.12
Total Alkalinity	1.20	1.12	1.11	1.04	1.33	1.23	1.33	1.35	1.38	1.35

P-Water sample collection points, EC expressed in (dS/m) * pH-no unit *other variables presented in (mg/l)

Table 8: Geo Accumulation Index score criteria for classification of water quality based on (Muller,1969)

Index class	I geo Accumulation value	Level of contamination
0	I geo accumulation value < 0	Pure
1	0<I geo accumulation value < 1	pure to reasonable (medium range) contamination
2	1<I geo accumulation value < 2	reasonable (medium range) contamination
3	2<I geo accumulation value < 3	reasonable (medium range) to strong contamination
4	3<I geo accumulation value < 4	Strong contamination
5	4<I geo accumulation value < 5	strong contamination to extremely contamination
6	I geo accumulation value < 5	Extremely contamination

Table 9: Results of geo accumulation index for the studied samples

Parameters	Geo accumulation Index *(I geo)*																			
	P -1	P -2	P -3	P -4	P -5	P -6	P -7	P -8	P -9	P -10	P -11	P -12	P -13	P -14	P -15	P -16	P-17	P-18	P -19	P -20
Fe	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mn	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Zn	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Cu	2	2	2	3	2	2	2	1	1	1	1	1	2	3	3	2	1	1	1	1
Pb	1	2	2	2	1	1	1	0	2	0	2	1	0	0	2	0	6	2	1	2

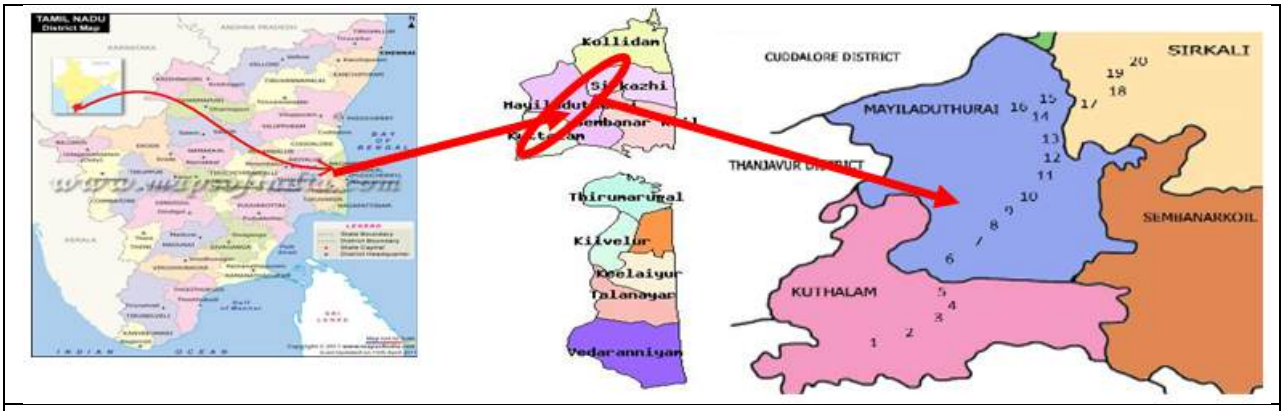

Fig. 1.Geological locations for study area

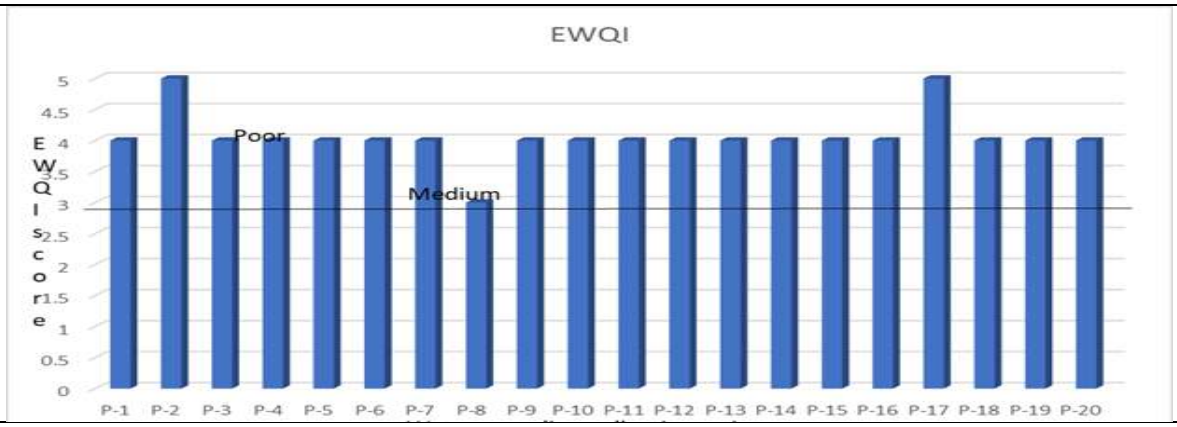

Fig: 2 : Results of Entropy Weighted Water Quality Index values for the study area

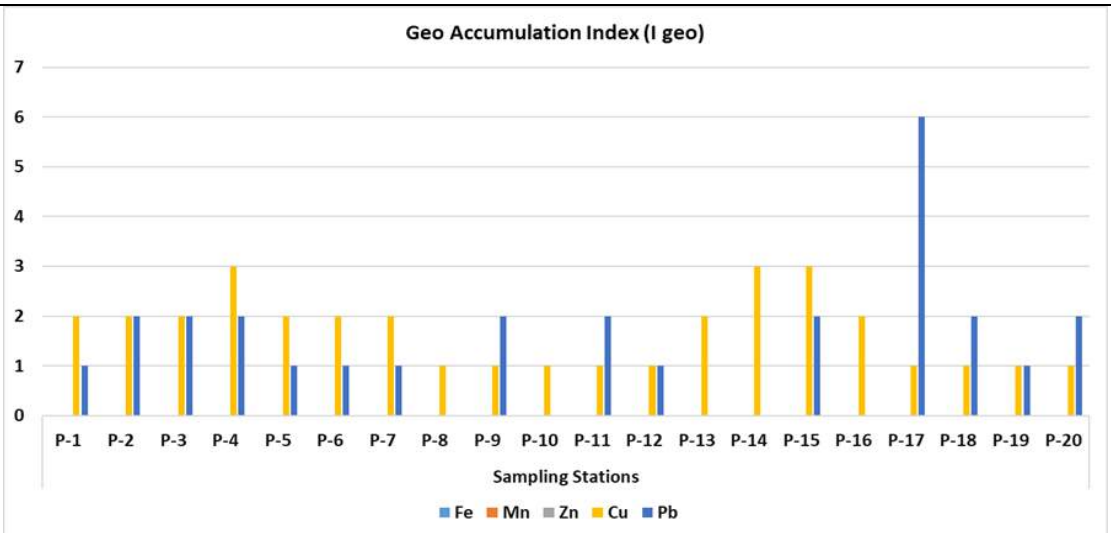

Fig: 3- Results of Geo accumulation Index values for the study area

Indian Journal of Natural Sciences www.tnsroindia.org.in ©IJONS

Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

REVIEW ARTICLE

Phytosociological Study of Surrounding Area of Botad District, Gujarat : A Review

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Received: 08 Oct 2025 Revised: 12 Nov 2025 Accepted: 23 Dec 2025

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ABSTRACT

Gujarat's forests, predominantly deciduous in nature, harbour rich biodiversity, supporting a wide variety of plant and animal species. The Saurashtra region, located in the southwestern part of Gujarat, is characterized by a rocky tableland ranging from 300 to 600 meters above sea level, bordered by coastal lowlands. Botad District, positioned within this region, experiences a hot semi-arid climate and lies between approximately 22°N latitude and 71°E longitude. This review focuses on the phytosociological profile of Botad and its surrounding areas, emphasizing the study of vegetation structure, species composition, and ecological relationships within Plant communities. Phytosociology provides critical insights into the interactions between local climatic and edaphic (soil) factors and plant diversity. Previous studies conducted in regions adjacent to Botad consistently highlight the dominance of the *Fabaceae* family among dicots and *Poaceae* among monocots. These patterns reflect the adaptive strategies of these families to arid and semi-arid environments. The findings underscore the ecological importance of these dominant families and the need for continued vegetation monitoring to support biodiversity conservation and sustainable land management in Saurashtra.

Keywords: Botad, Ecosystem, Phytosociology, Saurashtra,Vegetation

INTRODUCTION

Gujarat, a western state of India, is geographically positioned between 20°07′N to 24°43′N latitudes and 68°10′E to 74°29′E longitudes. Following the bifurcation of the Bombay State, Gujarat was established on 1 May 1960. The total area of the state is approximately 196,024 km² (or 9.67%) is classified as forest cover, accounting for about 7.72% of India's total forested area (Gujarat Forest Department, 2024). The state exhibits a diverse ecological landscape, ranging from the Rann of Kutch's saline deserts to grasslands, wetlands, and India's longest coastline. This varied topography and climate contribute significantly to the biodiversity of the region. Gujarat is administratively and ecologically divided into five regions: North Gujarat, South Gujarat, Central Gujarat, Saurashtra, and Kutchh. Gujarat's forests are broadly categorized into Tropical deciduous, Drydeciduous, and Mangrove Forests, each supporting unique floral and faunal communities. Studies on the state's floristic diversity report 2205 species of angiosperms, representing 905 genera and 156 families (Uma Devi, 1988; Kumar *et al*., 2014). Among these, 748 species have recognized medicinal value. A detailed assessment by the Gujarat Forest Department further identifies 915medicinal plant species distributed across different forest types and agroclimatic zones (Kumar *et al*., 2014).

Vegetational and Geographic Characterization of the Saurashtra Region

Saurashtra, also historically referred to as Kathiawar, is a prominent peninsula located in the southwestern part of Gujarat. Covering an area of approximately 47,000 km², it lies between latitudes 20°50′N and 23°5′N and longitudes 69°20′E and 72°10′E. The region is bounded by the Gulf of Khambhat to the southeast, the Arabian sea to the south and west, the alluvial plains of Bhavnagar to the east, and the Gulf of Kutch and coastal plains to the north. The Saurashtra peninsula is primarily a rocky tableland, elevated between 300 to 600 meters above sea level, surrounded by coastal lowlands. Its interior landscape comprises undulating plains interspersed with low hill ranges and dissected by rivers flowing in various directions, reflecting the region's complex geomorphology (Hiremath & Shiyani, 2012). The climate is predominantly hot and dry, and the natural vegetation is chiefly composed of thorn forests, which are disjunctly and sparsely distributed due to the arid conditions. Administratively, Saurashtra includes eleven districts: Rajkot, Jamnagar, Porbandar, Junagadh, Amreli, and Bhavnagar, As well as the more recently formed districts of Morbi (from Rajkot), Botad (from Bhavnagar), Devbhumi Dwarka (from Jamnagar), and Gir Somnath(from Junagadh), which were established in 2013 (Mehta, 2015). The floristic diversity of the region is well-documented. According to a comprehensive checklist by Santapau and Janardhan (1966), the flora of Saurashtra comprises approximately 1,136 plant species, belonging to 591 genera and 126 families. An earlier compilation by Santapau (1953) recorded 980 species, highlighting the region's botanical richness and ecological significance.

Geographical and Climatic Overview of Botad District

As per the Gujarat State Portal (2024), Botad District is situated in the Saurashtra region and was officially formed from parts of Bhavnagar and Ahmedabad districts. The administrative headquarters is in Botad town, which is approximately 92km from Bhavnagar and 133 km from Ahmedabad by road. Botad is geographically bounded by Surendranagar District to the northeast, Rajkot District to the west, Bhavnagar and Amreli Districts to the south, and Ahmedabad District to the east. The district lies roughly between 22°N latitude and 71°E longitude and spans an area of 2,564 km². Climatically, Botad experiences a hot semi-arid environment with an average annual rainfall 620mm. The major river flowing through the district include the Sukhbhadar River, which forms the northern boundary in Ranpur Taluka, and the Kalubhar River, which traverses the southern region in Gadhada Taluka. Other important river includes the Ghelo, Utavali, and Goma, which play essential roles in the district's ecology and agriculture.

Phytosociology: A Quantitative Approach to Understanding Plant Community Structure and Conservation Needs

Phytosociology is the systematic analysis of the composition, structure, distribution, and classification of plant communities (Kumar & Desai, 2016). A standard phytosociological survey records mot only the floristic inventory but also key structural attributes- vertical stratification, basal area, canopy cover and species abundance- thereby offering a quantitative portrait of vegetation organization. Such information is indispensable for biodiversity conservation and ecological-restoration planning, because community architecture regulates the fluxes of energy,

water and nutrients that underpin ecosystem functioning (Conant & Risser, 1974; Chavda, 2017). During the past century, tropical forest has declined precipitously owing to large-scale deforestation, settlement expansion, agricultural conversion, pollution, infrastructure development and biological invasions. These pressures have eroded biodiversity, altered local climates, reduced ecological services, and undermined rural livelihoods (Kumar & Desai, 2016). Robust, site specific data on plant-community composition and structure are therefore a prerequisite for sustainable management. Species richness and turnover vary markedly along climatic, edaphic and altitudinal gradients; teasing apart the influence of these factors is a central goal of phytosociological research (Gairola *et al*., 2011; Malik & Bhatt, 2015). Linking vegetation patterns to local environmental drivers also provides the historical context needed to anticipate future change and set sound conservation priorities (Patel& Patel, 2016).

Dominant plant families around the Botad district:

According to earlier research conducted by Santapau and Janardhan (1966) in the broader Saurashtra region, the most dominant plant families identified were *Fabaceae*, *Poaceae*, *Asteraceae*, *Malvaceae*, and *Acanthaceae*. In a more localized study, Sodha (20008) reported from the Hingolgadh Nature Education Sanctuary that the *Poaceae*, *Fabaceae*, *Asteraceae*, *Euphorbiaceae*, and *Convolvulaceae* were the five major dominant families. Similarly, Patel's (1982) investigation of Victoria Park in Bhavnagar found *Fabaceae*, *Poaceae*, *Euphorbiaceae*, *Asteraceae*, and *Malvaceae*- as dominant. A more recent study by Chavda (2017) on the Bhandariya Forest of Bhavnagar also recognized *Fabaceae*, *Poaceae*, *Euphorbiaceae*, and*Asteraceae* among the leading families, with the*Caesalpinaceae* subfamily (under *Fabcaeae*) also highlighted as a major group. At the state level, Shah (1978), in the Flora of Gujarat State, listed *Fabaceae*, *Poaceae*, *Cyperaceae*, *Asteraceae* and *Acanthaceae* as the most prevalent families.

Overall, across these diverse studies and locations, the families *Fabaceae*, *Poaceae* and *Asteraceae*, consistently appear as the most dominant, followed by *Euphorbiaceae* and *Malvaceae*, indicating a strong ecological representation and adaptability of these groups in the semi-arid and dry deciduous ecosystem of Saurashtra.

CONCLUSION

The phytosociological review of Botad surrounding districts within the Saurashtra region reveals a remarkable consistency in floristic composition across diverse ecosystems, including dry deciduous forests, coastal zone, canal command areas, scrublands, and protected sanctuaries. Across all examined studies-from the early observations of Santapau and Janardhan (1966) to recent works by Chavda (2017), Sodha (2008), and Suthar *et al*., (2021)- certain plant families prominently recur, especially *Fabaceae*, *Poaceae*, *Asteraceae*, and *Euphorbiaceae* these families exhibit exceptional ecological adaptability, occupying a wide range of habitats and dominating both herbaceous and woody vegetation layers. Dominant species such as *Acacia Senegal*, *Prosopis juliflora*, *Cynodon dactylon*, *Cassia auriculata* frequently appear, indicating their resilience and ecological importance in the semi-arid to sub-humid zones of Saurashtra. The recurrence of these species and families not only highlights a core floristic structure in the region but also reflects common anthropogenic pressures and climatic patterns that shape vegetation distribution. Collectively, these findings underscore the ecological significance of the Saurashtra region's vegetation and support the need for region-specific conservation and management strategies. Future studies should focus on long term monitoring, species vulnerability assessments, and the role of invasive species like *Prosopis juliflora*. Which, while dominant, can alter Native biodiversity patterns. The convergence of historical and contemporary data provides a robust foundation for biodiversity planning, restoration ecology, and sustainable land use in the region.

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Table 1. Quantitative indices to be used

Community attribute	Derived indices	Refrences
Presence/ absence	Frequency (F), Relative Frequency	(Curtis & Mcintosh, 1950; Grieg-Smith, 1957; Kersaw, 1973; Misra, 1968; Muller-Dombois & Ellenberge, 1974; Samant *et al*., 2002; Wani and Pant, 2023).
Number of individuals	Density (D), Relative Density	
Spatial distribution	Abundance (A), Relative Abundance	
Size of individuals	Basal area (BA), Relative Basal Area	
Integrated dominance	Importance Value Index (IVI)	
Community diversity	Shannon-Wiener index (H), Simpsons's index (1-D)	

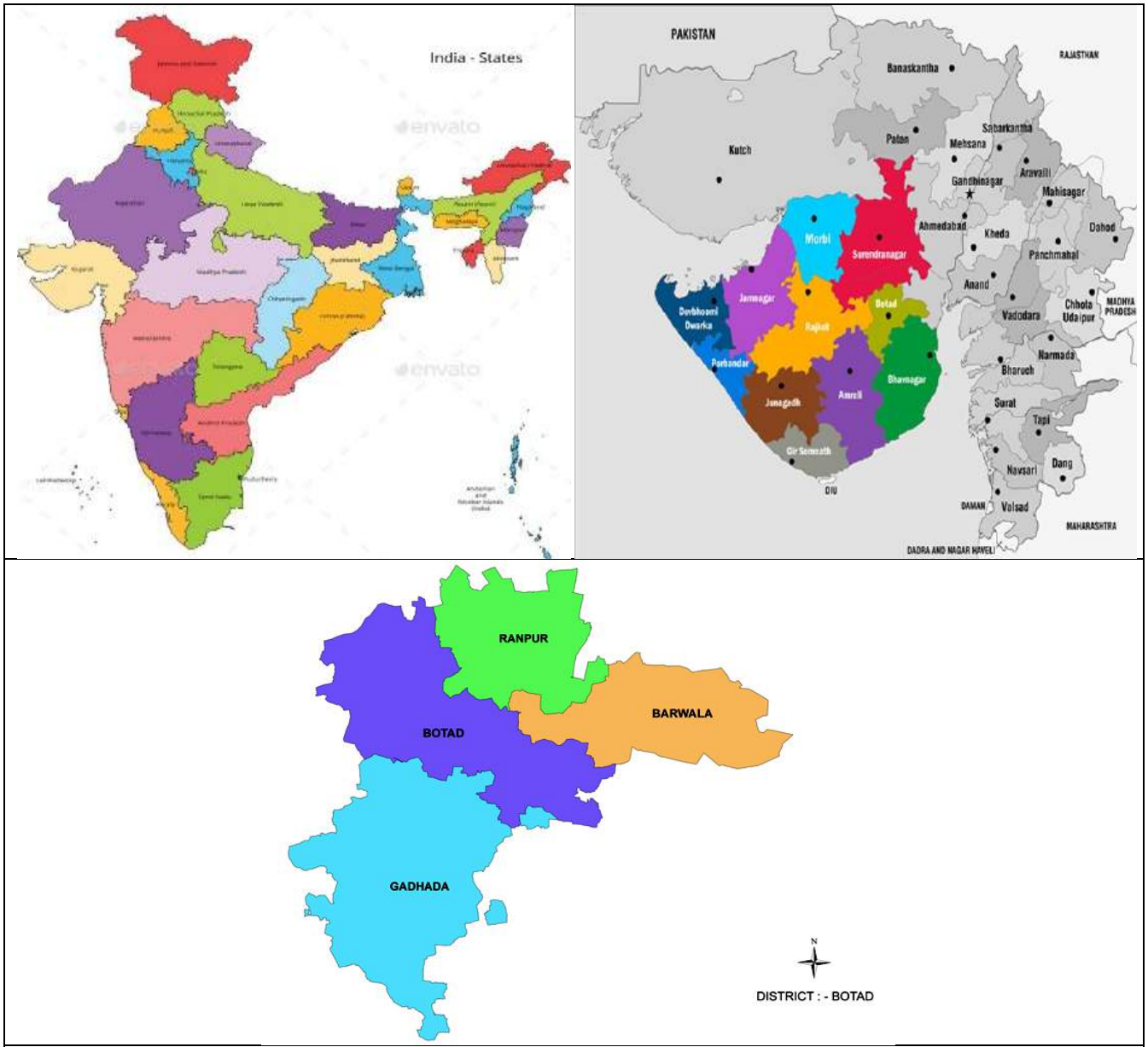
Table-2 Vegetation study of Surrounding area of Botad district

AREA	VEGETATION	METHODS	MAJOR PLANT	MAJOR FAMILY	REFRENCES
Hingolgadh Sanctuary, Rajkot (Dry Deciduous Forest)	Total 313 Species, 224 genera, belonging to 98 family. 49 tree species from 29 family, 38 shrubs species from 22 family, 40 species of grasses, Climbers 42 species from 11 family, Herbs 144 species from 37 family	Quantitative analysis: Density, frequency, abundance, relative frequency, relative density, Important Value Index, Basal area Diversity indices: Shannon Diversity index, Simpson's Diversity index, Simpson's index of Diversity, Simpson's Reciprocal index, Evenness index	*Aristida adscensionis, Spermacoce stricta, Rhus mysurensis, Maytenus emarjinata, Acacia senagal* are dominant plants.	Dicot: *Fabaceae* and *Asteraceae* Monocot: *Poaceae*	Sodha, 2008
Barda hills (dry deciduous forest)	368 species belonging to 268 genera and 80 families of Angiosperms were counted in the study. Most dominant type is herbs followed by trees, shrubs, and climbers.	Phytosociological parameter: Density, frequency, abundance, Diversity index: Shannon Diversity index and simpson Diversity index.	The plants that dominated the area were *Manilkara hexandra, Cassia auriculata, Lantana camara,* and *Acacia senegal*.	*Fabaceae* and *Euphorbiaceae* were the two most represented families among Dicotyledons. *Poaceae* and *Cyperaceae* were the two most represented families among Monocotyledons.	Raviya, 2020.
Naramada canal command area	premonsoon season: 201 plant	Transect and Quadrate method.	Highest Density Herbaceous	Postmonsoon: *Poaceae* most	Suthar *et al*., 2021

(NAAC) Bhavnagar, Botad, Surendranagar, Morbi.	species from 43 families. 156 herb species and 45 grass species. Post monsoon season: 259 species of herbaceous plants (208 species of herbs and 51 species of grasses) belonging to 49 families.	1 m x 1 m quadrat was placed at a regular 500 m interval on each transect. Quantitative analysis done by Phytosociological parameter: Density, frequency, abundance, Diversity index: Simpson Diversity index. Menhinick index of species richness.	plant (Premonsoon): *Cynodon dactylon* followed by *Schoenefeldia gracilis, Aristida funiculate,* and *Dichanthium annulatum*. Highest Density Herbaceous plant (Postmonsoon): *Cynodon dactylon* Followed by *Aristida funiculata, Cyperus bulbosus*, and *Indofera linnaei*.S	dominant. Followed by *Asteraceae, Fabaceae, Malvaceae, Amaranthaceae, Acanthaceae, Cyperaceae, Euphorbiaceae, Lamiaceae,* and *Solanaceae*. Premonsoon: Poaceae most dominant. Followed by *Asteraceae, Fabaceae, Amaranthaceae, Malvaceae, Acanthaceae, Lamiaceae, Solanaceae, Cyperaceae*, and *Euphorbiaceae* families	
Rampara forest, Morbi/Vankaner (Dry Deciduous Forest)	-	Randomly placed 10m x 10m quadrates. Phytosociological parameter: Density, frequency, abundance, relative frequency, relative density. Diversity Mean basal cover (MBC) Total Basal cover (TBC) Importance value index (IVI). index: Shannon Diversity index, Simpson Diversity index and Sorenson's similarity index	Three tree species dominated the area: *A. nilotica, A.flabellifer*, and *A. senegal*. At the forest's areas, there were just five or seven different species of trees.	Some dominant tree family: *Fabaceae, Arecaceae*	Panchal and Pandey, 2004.
Ghogha Coastal area, Bhavnagar	Angiospermic plant species in	-	Dicots were dominating over	With a total of 8 sp, the *Poaceae*	Chavda *et al*., 2023

	the region, about 54 species are classified into 42 genera and 28 families. In these 39 species from 31 genera and 24 families are classified as dicots, whereas 15 species from 11 genera and 4 families are classified as monocots.		monocot	family was determined to be dominating. *Fabacea, Cyperaceae, Chinopodiaceae, Malvaceae* were also dominating plant families found in this area.	
Bandiyabedi forest, Surendranagar district	-	For trees or shrubs, 10 × 10 m quadrates were laid, and for herbs, 1 x 1 m. Phytosociological parameters: Density, frequency, abundance, A/F ratio, basal cover and importance value index. index: Shannon Diversity index, simpson Diversity index and Sorenson's similarity index	Dominant tree species were *Acacia Senegal, Acacia catechu, Prosopis specigera*	*Fabaceae* family dominating this area	Parejiya *et al*., 2013
Bhandariya forest area, Bhavnagar (Tropical dry deciduous forest and Dry deciduous thorn forest)	Total 432 Angeospermic plant species plants-282 genera and 91 families. Monocot: 58 species, 42genera and 13 family. Dicot: 374 species, 240 genera and 78 families.	Random 20m × 20m quadrates for trees, shrubs and climbers. And 4m × 4m for herbaceous species. Phytosociological parameter: Density, frequency, abundance, Relative frequency,	*Cassia, Ipomea, Euphorbia, Cyperus, Acacia, Corchorus, Alysicarpus, Ficus, Indigofera, Amaranthus, Sida, Commelina* etc. are dominant plant genera.	*Fabaceae, Poaceae, Euphorbiaceae, Asteraceae, Caesalpiniaceae, Mimosaceae, Convolvulaceae, Acanthaceae* and *Cucurbitaceae* are Dominant plant family found in this area.	Chavda, 2017

		Relative density, Relative abundance, importance value index. Alpha Diversity indices: Shannon diversity index, Simpson reciprocal index for species richness, Pielou's index for species evenness. Beta diversity indices: jaccard's index, Sorenson index			
Reserved forest, Victoria Park near, Bhavnagar. (Semi-arid forest) (Thorny and Scruby vegetation).	Total 422 species: 96 angiosperm Family. Dicot: 350 Monocot: 72	Quadrate size: 7m × 7m Phytosociological parameter: Density, Basal cover, Frequency, average height of tree.	*Cassyth*a and *Cuscuta* are dominant climbers. *Prosopis juliflora* and *Acacia senegal* like thorny plant are dominant.	*Leguminosae* is largest family of dicot and *Poaceae* is largest family of monocot. *Asteraceae* and *Euphorbiaceae* also are the dominant family of this area.	Patel, 1982
Chotila taluka, Surendranagar district. (Dry moist deciduous forest).	Total 380 plant species. Family 84 Genera 279 Herbs 175, Shrubs 37, Tree 110, Climber 58.	-	Dominant tree species, *Prosopis juliflora, Acacia Senega*l and *Butea monosperma.*	*Fabaceae* 27 was most dominant plant family, followed by *Poaceae* 18, *Caesalpiniaceae*16, *Mimosaceae* 14, *Asteraceae* 20, *Apocynaceae* 19, *Euphorbiaceae* 18, *Malvaceae* 20, *Convolvulaceae* 19 and *Amaranthaceae* 13.	Popatbhai, 2023



Georaphical map of Botad District (Saurashtra), Gujarat (India).
(Image Source: wikimedia.org/wiki/File:Botad_Gujarat_map.svg)

Indian Journal of Natural Sciences www.tnsroindia.org.in ©IJONS

Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Artificial Intelligence in the Pharmaceutical Industry: Applications, Challenges, and Future Perspectives

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Received: 10 Jan 2026 Revised: 15 Jan 2025 Accepted: 18 Jan 2026

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ABSTRACT

Artificial Intelligence (AI) has emerged as a transformative force in the pharmaceutical industry, enabling innovation across drug discovery, development, manufacturing, regulatory affairs, and post-marketing surveillance. By leveraging machine learning, deep learning, and advanced data analytics, AI has significantly reduced drug development timelines, improved decision-making, and enhanced operational efficiency. This review highlights the key applications of AI throughout the pharmaceutical product lifecycle, including drug discovery, clinical trials, manufacturing, regulatory affairs, and pharmacovigilance. Furthermore, current challenges related to data quality, regulatory acceptance, and ethical considerations are discussed, along with future perspectives on the role of AI in personalized medicine and adaptive regulatory systems. Overall, AI represents a powerful tool for accelerating pharmaceutical innovation while ensuring patient safety and regulatory compliance.

Keywords: Artificial Intelligence, Pharmaceutical Industry, Drug Discovery, Clinical Trials, Regulatory Affairs, Pharmacovigilance

INTRODUCTION

The pharmaceutical industry is characterized by high research costs, long development timelines, and strict regulatory requirements. The development of a new drug typically requires 10–15 years and substantial financial investment, with a high risk of failure. Artificial Intelligence (AI), encompassing machine learning (ML), deep learning (DL), and data-driven analytics, has gained prominence as a solution to these challenges. AI enables the efficient analysis of large and complex datasets, thereby supporting faster and more accurate decision-making across pharmaceutical research and development [1,2]. In recent years, AI has been increasingly integrated into multiple stages of the pharmaceutical value chain, reshaping traditional approaches to drug development and regulation.

Role of Artificial Intelligence in Drug Discovery and Development

AI has revolutionized early-stage drug discovery by enabling rapid identification of potential drug candidates. Machine learning algorithms analyze chemical, biological, and genomic datasets to predict drug–target interactions and optimize lead compounds. AI-driven techniques such as virtual screening, molecular docking, and quantitative structure–activity relationship (QSAR) modeling have significantly reduced the dependence on conventional trial-and-error methods [3,4]. These approaches not only shorten discovery timelines but also improve the probability of identifying effective and safe drug candidates. Artificial Intelligence (AI) has significantly transformed the drug discovery and development process by enabling faster, more cost-effective, and data-driven decision-making. Traditional drug discovery is a lengthy and expensive process, often requiring more than a decade and billions of dollars to bring a single drug to market, with a high rate of attrition. AI technologies, including machine learning (ML), deep learning (DL), and neural networks, offer powerful tools to address these challenges by efficiently analyzing large and complex biological and chemical datasets.

AI in Target Identification and Validation

One of the earliest applications of AI in drug discovery is target identification and validation. AI algorithms analyze genomic, proteomic, and transcriptomic data to identify disease-related targets and predict their therapeutic relevance. Machine learning models can uncover hidden patterns in biological networks, enabling the identification of novel drug targets with higher precision compared to conventional approaches [3, 4].

AI in Lead Discovery and Optimization

AI plays a crucial role in lead discovery by accelerating virtual screening of large chemical libraries. AI-driven virtual screening and molecular docking techniques predict drug–target interactions and binding affinities, significantly reducing the need for extensive wet-lab experiments. Additionally, AI-based quantitative structure–activity relationship (QSAR) models assist in optimizing lead compounds by predicting their pharmacological activity and toxicity profiles [1,5].

AI in De Novo Drug Design

De novo drug design is another rapidly advancing area where AI is used to generate novel chemical structures with desired biological properties. Deep learning models, such as generative adversarial networks (GANs) and recurrent neural networks (RNNs), can design new molecules by learning from existing chemical databases. These AI-generated compounds often exhibit improved potency, selectivity, and drug-like properties [4, 6].

AI in Preclinical Development

During preclinical development, AI assists in predicting pharmacokinetic (ADME) and toxicological properties of drug candidates. AI-based in silico models help identify potential safety issues early in development, thereby reducing late-stage failures. Predictive toxicology models enhance decision-making by estimating organ toxicity, genotoxicity, and cardiotoxicity before animal or human testing [2, 7].

AI in Clinical Development

AI has also demonstrated significant impact in clinical drug development. Machine learning models improve clinical trial design by predicting patient response, optimizing dosing strategies, and identifying suitable patient populations. AI-driven analytics reduce trial duration, improve success rates, and support personalized medicine approaches [8].

Advantages and Limitations

The key advantages of AI in drug discovery include reduced development time, lower costs, improved success rates, and enhanced innovation. However, challenges such as data quality, model interpretability, regulatory acceptance, and ethical concerns remain. Addressing these limitations through explainable AI models and standardized regulatory frameworks is essential for broader adoption [7, 9].

Artificial Intelligence in Clinical Trials

Clinical trials are among the most time-consuming and expensive stages of drug development. AI enhances clinical trial efficiency by improving protocol design, patient recruitment, and monitoring. Predictive analytics help identify suitable patient populations and reduce recruitment delays, while AI-based tools enable real-time monitoring of patient safety and adherence [10]. The application of AI in clinical research has demonstrated potential in reducing trial failures and accelerating regulatory decision-making.

AI in Pharmaceutical Manufacturing and Quality Control

AI applications in pharmaceutical manufacturing focus on process optimization, predictive maintenance, and real-time quality assurance. Advanced AI models monitor critical process parameters, detect deviations, and ensure compliance with Good Manufacturing Practices (GMP). The implementation of AI-driven quality systems has resulted in improved batch consistency, reduced production failures, and enhanced operational efficiency [2,4]. These advancements support the industry's transition toward smart manufacturing and continuous production models. The pharmaceutical manufacturing sector is increasingly adopting Artificial Intelligence (AI) to enhance process efficiency, ensure consistent product quality, and maintain regulatory compliance. Conventional manufacturing and quality control approaches often rely on fixed process parameters and retrospective quality testing, which can lead to batch failures, increased costs, and delayed product release. AI technologies, including machine learning (ML), deep learning (DL), and advanced data analytics, provide predictive and real-time control solutions that support the principles of Quality by Design (QbD) and Process Analytical Technology (PAT) [11].

AI in Process Optimization

AI-based models are widely used for optimizing manufacturing processes by analyzing large datasets generated during production. Machine learning algorithms can identify relationships between critical process parameters (CPPs) and critical quality attributes (CQAs), enabling real-time adjustments to manufacturing conditions. This results in improved yield, reduced variability, and enhanced process robustness [12].

AI in Predictive Maintenance

Predictive maintenance is a key application of AI in pharmaceutical manufacturing. AI algorithms analyze equipment performance data to predict potential failures before they occur, thereby minimizing unplanned downtime and maintenance costs. This approach improves equipment reliability and supports continuous manufacturing operations [13].

AI in Quality Control and Assurance

AI significantly improves quality control by enabling automated inspection and real-time monitoring of product quality. Computer vision systems and deep learning models are used for visual inspection of tablets, capsules, and packaging to detect defects such as cracks, discoloration, or labeling errors. AI-driven quality systems reduce human error, enhance inspection accuracy, and accelerate batch release [14].

AI in Process Analytical Technology (PAT)

AI enhances the effectiveness of PAT by enabling real-time analysis of in-process data collected from sensors and analytical instruments. Machine learning models interpret spectroscopic and process data to predict CQAs during manufacturing, supporting real-time release testing (RTRT). This aligns with regulatory expectations for continuous quality assurance and improved process understanding [15].

Regulatory Considerations and Compliance

Regulatory agencies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) encourage the adoption of advanced manufacturing technologies, including AI, provided they comply with GMP requirements. However, challenges related to model validation, data integrity, and explainability of AI algorithms must be addressed to ensure regulatory acceptance [8].

Artificial Intelligence in Regulatory Affairs

Regulatory affairs is a critical domain where AI has shown increasing potential. Natural language processing (NLP) and data analytics tools assist regulatory professionals in managing regulatory submissions, tracking global regulatory updates, and ensuring compliance with evolving guidelines. AI also supports pharmacovigilance activities by enabling rapid detection of safety signals from adverse event databases. Regulatory agencies, including the U.S. Food and Drug Administration (FDA), have recognized the growing role of AI and are developing frameworks to regulate AI-based tools used in healthcare.

AI in Regulatory Intelligence

Regulatory intelligence involves continuous monitoring and interpretation of evolving regulatory guidelines across different regions. AI-powered NLP tools automatically scan regulatory agency websites, guidance documents, and legislation to identify updates and assess their impact on existing and pipeline products. This reduces manual effort, minimizes compliance risks, and enables proactive regulatory planning [4, 9].

AI in Regulatory Submissions and Dossier Management

AI significantly improves the preparation and management of regulatory submissions such as Investigational New Drug (IND), New Drug Application (NDA), Abbreviated New Drug Application (ANDA), and Marketing Authorization Applications (MAA). AI-based systems assist in document authoring, data validation, cross-referencing, and version control. Machine learning algorithms help identify inconsistencies, missing data, and formatting errors, thereby improving submission quality and reducing review cycles [17].

AI in Compliance and Audit Management

AI tools are increasingly used to monitor compliance with Good Manufacturing Practices (GMP), Good Clinical Practices (GCP), and Good Pharmacovigilance Practices (GVP). Predictive analytics identify potential compliance risks before inspections, while AI-driven audit systems analyze historical inspection data to improve inspection readiness and corrective action planning [15].

AI in Pharmacovigilance and Safety Reporting

Pharmacovigilance is a major regulatory function where AI has demonstrated significant benefits. AI algorithms analyze adverse event reports, literature, and real-world data to detect safety signals more efficiently than traditional methods. Natural language processing enables automated case intake, triage, and coding, leading to faster signal detection and regulatory reporting [18, 19].

Regulatory Acceptance and Ethical Considerations

Despite its benefits, the use of AI in regulatory affairs raises concerns regarding data integrity, transparency, and accountability. Regulatory authorities such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) emphasize the need for model validation, explainability, and robust data governance.

Ethical considerations, including algorithmic bias and decision accountability, must also be addressed to ensure trust in AI-driven regulatory systems [16].

AI in Post-Marketing Surveillance

Post-marketing surveillance is essential for ensuring the long-term safety of pharmaceutical products. AI algorithms analyze real-world data from electronic health records, spontaneous reporting systems, and social media platforms to identify potential adverse drug reactions. Compared to traditional methods, AI-based pharmacovigilance systems offer improved sensitivity and faster signal detection, supporting proactive risk management strategies [4,7].

Challenges and Future Perspectives

Despite its numerous advantages, the adoption of AI in the pharmaceutical industry faces challenges such as data quality issues, lack of transparency in algorithmic decision-making, ethical concerns, and regulatory uncertainty. The development of explainable AI models and standardized regulatory guidelines is essential to address these limitations. In the future, AI is expected to play a key role in personalized medicine, digital therapeutics, and adaptive regulatory frameworks, further transforming the pharmaceutical landscape [2,7,8].

CONCLUSION

Artificial Intelligence has emerged as a powerful enabler of innovation in the pharmaceutical industry. Its applications across drug discovery, clinical trials, manufacturing, regulatory affairs, and pharmacovigilance have demonstrated significant potential to improve efficiency, reduce costs, and enhance patient safety. While challenges remain, continued advancements in AI technologies and regulatory frameworks are expected to further integrate AI into pharmaceutical research and development, shaping the future of healthcare delivery.

FUTURE PERSPECTIVES

The future of AI in drug discovery lies in its integration with systems biology, real-world data, and precision medicine. As regulatory agencies increasingly recognize AI-based approaches, AI is expected to become an indispensable component of pharmaceutical research and development, enabling faster translation of scientific discoveries into effective therapies [2,4].

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Role of Sleshmadhara Kala in Sandhivata: A Case Report with Clinical and Radiological Correlation

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Received: 19 Oct 2025 Revised: 18 Nov 2025 Accepted: 31 Dec 2025

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ABSTRACT

Acharya Sushruta described *Kala* as specialized membranes separating *Dhatu* from their *Ashaya*. Among the seven *Kala*, *Sleshmadhara Kala* is located in the joints and plays a vital role in maintaining joint integrity and smooth movements. Its structure and function closely resemble that of the synovial membrane described in contemporary anatomy. Degenerative joint disorders such as *Sandhivata* are increasingly prevalent in the elderly and contribute significantly to disability. To evaluate the role of *Sleshmadhara Kala* in joint degeneration and to assess the efficacy of Ayurvedic *Shodhana* and *Shamana* therapies in the management of *Sandhivata* through clinical and radiological assessment. A 74-year-old male diagnosed with *Sandhivata* affecting both knee joints was treated with a comprehensive Ayurvedic treatment protocol, including internal medications and *Panchakarma* procedures. MRI findings were used to assess changes in the synovial membrane. MRI findings revealed synovial membrane involvement, highlighting its role in joint pathology. The findings support the correlation of *Sleshmadhara Kala* with the synovial membrane. The treatment effectively restored joint function and reduced symptoms. Significant improvement was observed in pain, stiffness, swelling, and difficulty in walking. Ayurvedic interventions targeting *Vata Dosha* and joint lubrication proved effective in managing *Sandhivata* and preventing disability.

Keywords: *Sleshmadhara Kala*, Synovial membrane, *Sandhivata*, Osteoarthritis

INTRODUCTION

Kala is a fundamental anatomical concept uniquely described by Acharya Sushruta. It refers to specialized membranous structures that separate *Dhatu* from their respective *Ashaya*. Sushruta elaborated seven types of *Kala* in the fourth chapter of *ShariraSthana*: *Mamsadhara*, *Raktadhara*, *Medhodhara*, *Sleshmadhara*, *Pureeshadhara*, *Pittadhara*, and *Shukradhara Kala*[1]. *Sleshmadhara Kala* is situated within the joints, where it retains and regulates *Sleshma* (lubricating fluid), ensuring smooth, frictionless joint movements. Acharya Sushruta compares its function to oil applied to the axle of a wheel, enabling effortless rotation[2]. Structurally and functionally, this description closely parallels the synovial membrane in modern anatomy, which lines synovial joints, bursae, and tendon sheaths and secretes synovial fluid essential for lubrication, nutrition of cartilage, and joint protection[3]. *Sandhivata*, a degenerative disorder described under *VatajaNanatmajaVyadhi* by Acharya Charaka, manifests with pain, stiffness, swelling, crepitus, and restricted joint movement[4]. Sushruta emphasized degenerative changes in joints as the hallmark of this disease[5]. Clinically, *Sandhivata* can be correlated with osteoarthritis. The World Health Organization reports that symptomatic osteoarthritis affects approximately 9.6% of men and 18.0% of women over the age of 60 globally. Among individuals with osteoarthritis, nearly 80% experience restricted mobility, and about 25% are unable to carry out routine daily activities. Epidemiological data indicate that the prevalence of osteoarthritis in India ranges from 22% to 49%. Radiological signs of osteoarthritis are observed in the majority of individuals by the age of 65 and in nearly 80% of people older than 75 years[6]. Modern management of osteoarthritis offers symptomatic relief but has limitations in halting disease progression. Hence, understanding the role of *Sleshmadhara Kala* in joint health and exploring effective Ayurvedic interventions is essential. This case report highlights the significance of synovial membrane pathology in *Sandhivata* and demonstrates the therapeutic potential of Ayurvedic treatment.

MATERIALS AND METHODS

The study aims to explore the role of *Sleshmadhara Kala* in the development of degenerative joint disorders and to evaluate the efficacy of Ayurvedic treatment in the management of *Sandhivata*. MRI was used to evaluate synovial membrane changes in a patient diagnosed with *Sandhivata*. Based on clinical findings and radiological evidence, a tailored Ayurvedic treatment protocol comprising *Shodhana* and *Shamana* therapies was administered.

Case Presentation

History of Present Illness

A 74-year-old male patient with bilateral knee joint pain for three years consulted our hospital. The pain aggravated by prolonged standing, walking, and stair climbing. He noticed mild outward bending of both knees over the past eight months. The patient was admitted for detailed evaluation and treatment(Personal History Table: 1). (Examination of Locomotor System Table: 2)

MRI Findings

- Degenerative osteoarthritic changes in the knee joint
- Moderate to gross synovial effusion
- Mild synovial thickening suggestive of synovitis

Diagnosis - *Sandhivata* (Osteoarthritis of knee joints)

Treatment Protocol

Internal Medications(Tamil: 3)

Panchakarma Procedures

(Table: 4)

RESULTS

The patient showed marked improvement in joint mobility, pain relief, and functional ability(Table: 5).

DISCUSSION

Sushruta's description of *Sleshmadhara Kala* emphasizes its role in joint lubrication and protection. MRI findings in this case revealed synovial membrane thickening and effusion, directly supporting the concept that impairment of *Sleshmadhara Kala* leads to degenerative joint changes. This case highlights the significant role of *Sleshmadhara Kala* in maintaining joint health and its correlation with the synovial membrane. Degeneration of this structure contributes to *Sandhivata*. The administered Ayurvedic therapies possess *Vatahara*, *Shothahara*, *Vedanasthapana*, and *Brimhana* properties. *Shodhana* procedures remove obstructed *Dosha*, while *Shamana* medicines nourish joint tissues and restore lubrication. Together, they help in reducing inflammation, improving circulation, and restoring joint function[7]. Ayurvedic management using *Shodhana* and *Shamana* therapies was effective in reducing symptoms and improving quality of life, suggesting its potential in preventing disability due to osteoarthritis.

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Table 1: History of Present Illness. Personal History

Personal History	
Parameter	**Observation**
Bowel	Regular
Appetite	Normal
Micturition	Within normal limits
Sleep	Sound
Allergy	Not reported
Diet	Mixed

Table 2: History of Present Illness.
Examination of Locomotor System

Examination of Locomotor System	
Parameter	**Findings**
Inspection	Oedematous
Palpation	Crepitus present, tenderness present
ROM	Flexion, extension possible with pain
Gait	Antalgic

Table 3: Internal Medications

Medicine	Dose	Duration
Rasnerandadi kashayam	15 ml BD	52 days
Kanchanara guggulu	2 BD	26 days
bonetone	1 BD	52 days
Septec tab	1 BD	47 days
Yogaraja guggulu	2 BD	26 days

Table 4: Panchakarma Procedures

Procedure	Duration
Dhanyamla dhara	7 days
Knee bandha with Murivenna	5 days
Abhyanga with murivenna	2 days
Patra potali sweda	5 days
Pizhichil with murivenna	7 days
Jambeera panda sweda	7 days
Sastika panda swedam	7 days
Matravasti – Sahacharadi tailam	7 days

Table 5: Results - The patient showed marked improvement in joint mobility, pain relief, and functional ability.

Symptom	Before Treatment	After Treatment
Pain	+2	0
Difficulty walking	+2	0
Stiffness	+2	0
Swelling	+2	0

Fig.1: MRI Images of Left Knee Joint

Indian Journal of Natural Sciences www.tnsroindia.org.in ©IJONS

Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

An Explainable and Calibrated Deep Learning Framework for Satellite - based Tropical Cyclone Detection

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Received: 20 Nov 2025 Revised: 11 Dec 2025 Accepted: 26 Dec 2025

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ABSTRACT

One of the most destructive forces of nature on the Earth is tropical cyclones, disasters that can wipe out all human possessions and infrastructure in minutes. Besides the Earth, only India lives through 10% of the world's tropical cyclones, about 5-6 times a year, 2-3 of them being severe and causing significant disasters. Early prediction and warning plays a crucial role in reducing risks. Reliable detection of tropical cyclones is vital for early warning, risk mitigation, and forecasting of operational disasters through the integration of data from satellites. Despite the deep learning models having made a significant progress in the automatic recognition of cyclone, effectively all of the existing methods used deterministic outputs as their main consideration and provide a limited understanding of prediction uncertainty or internal representational mechanisms. This work demonstrates a method that is explainable and calibrated for deep learning-based tropical cyclone image recognition in a way that it uses EfficientNetB0 pre-trained model as the backbone. The model is trained on the TC-Satellite-DataSet, and various tools for probabilistic verification, such as the Brier score and reliability diagrams, are used for the evaluation alongside the standard metrics for classification. Besides looking at the overall classification accuracy, the framework examines the internal representations of the features with the help of principal component analysis and K-means clustering, thus revealing the particular morphological regions that the architecture is able to catch. Another thing that we did is using the model-agnostic occlusion sensitivity mapping which shows us that the classifier relies on the physically recognizable cyclone, these models use features that are inherently a part of the earth's atmosphere ('deep convection, spiralbands and organized cloud structures). Together, these components improve the transparency, interpretability, and credibility of the cyclone identification models. The proposed method establishes the fact that incorporation of

explanation, calibration, and representation-space analysis along with the deep learning methods will give very practical solutions for the hazard monitoring on a global scale.

Keywords: Tropical Cyclone, Satellite Imagery, Explainable Deep Learning, EfficientNet, Probabilistic Calibration, Brier Score, Reliability Diagram, PCA Embeddings, Occlusion Sensitivity, Cyclone Morphology Analysis.

INTRODUCTION

Tropical cyclones, also known as hurricanes or typhoons, are natural disasters that negatively impact humanity, producing very extreme winds, excessive rains and the associated flooding. Each year cyclones contribute a huge loss of life, extensive damages to Infrastructure, and even complete stoppage of socio-economic activities, mainly in the vicinity of the coastline. Such disastrous effects are fully realized in the high production and low lying areas since both the Bay of Bengal and the Arabian Sea present complicated environmental conditions that are likely to lead to a sudden increase in the cyclone's power and unexpected alterations of its course. Therefore, the issue of cyclone-related disasters' mitigation depends on efficient, timely, and reliable availability of now-casting and forecasting techniques based on numerical weather prediction (NWP) models and reanalysis. Although substantial progress has been achieved in the development of these tools over the last few decades, performance is still limited due to the inherent chaotic nature of the atmosphere, the inadequacies in physical parameterizations, the insufficiencies of spatial resolution, and the high cost of running frequent global forecasts. These limitations galvanize the usage of data-driven methods particularly deep learning (DL) which will further advance the science and practice of weather forecasting. This change in technology is in line with the experience of a number of other scientific areas,' in that DL has proven to be a very successful tool for a number of tasks including computer vision, spatiotemporal modelling, and of course, pattern recognition.

The natural disaster monitoring functions can significantly be improved by the use of the provision of satellite imagery, where the involved factors include: the observation of the cloud structure, the identification of the thunderstorm formation, the measurement of humidity patterns, and the capturing of the large-scale dynamical features. Geostationary satellites that monitor from a fixed point in the sky give regular timely updates of the weather conditions whereas polar-orbiting ones give high-resolution multispectral information. A cyclone's current power and future course are often important morphological characteristics of a cyclone, such as a thick cloud formation in the center, an eye wall starting to show, or the occurrence of asymmetric convection points'. Visual signs have traditionally been subject to the manual interpretations of industry experts using techniques such as the Dvorak method. Manual interpretation, while being very productive, is always time-consuming, subjective, and irregular. Deep learning comes to the market as a great change in this space as it could entirely automate the interpretation process and also bring many enhancements through the learning of structural patterns from raw imagery. In the last 10 years, a lot of the research has focused on using machine learning and deep learning methods to track the tropical cyclones and estimate their intensity. CNNs have been the main networks that have been used for this purpose with very good results, detecting the cyclonic circulation patterns as well as the clouds with cyclone-like shapes. Some of the articles have gone as far as using CNNs for the classification of cyclone intensity categories with the help of infrared cloud-top temperatures.

Moreover, there are of course other deep learning experts who have taken a different path and have suggested using recurrent neural networks (RNNs) like Long Short-Term Memory (LSTM) and Convolutional LSTM (ConvLSTM) to capture temporal dependencies and predict the future cyclone routes or rainfall. The scientists are also focusing on GANs for climate track prediction, super-resolution enhancement of climate model outputs, and providing more detailed forecasts of the cyclone boundary. In addition, some new combined models have been developed, which employ deep learning and NWP-provided meteorology. These models are generally more accurate in the prediction

of track and intensity. Yet, there are still several scientific and operational issues that need to be tackled. The main issue that needs to be addressed first and foremost is that the majority of the current deep learning studies on hurricanes are focused on one single task. For instance, a model could identify whether a hurricane was present or not, but it could not pinpoint the storm's center. One model could estimate the storm's power or intensity but ignore the entire storm's convective environment. Yet, another model might predict the hurricane's path with some certainty but fail to note the diversity of morphological shapes or reflect the model's uncertainty.

This division among the models would then govern the restrictiveness of deep learning systems to the extent of useful applications on the operational side of the workflow where both the analysts or the automated systems need all the information at once, such as the presence, structure, intensity, expected landfall location, and precipitation potential, etc. The lack of an integrated multi-task framework implies that the knowledge from one domain (e.g., cloud morphology used for detection) does not get to another (e.g., intensity estimation). So, the gap promotes the design of multi-task architectures that are capable of concurrently learning the presence of cyclones, the localization of their centers, the characterization of the convective structure, and the accompanying indicators, like the potential for rainfall or the cloud organization metrics. The second difficulty is related to training with the knowledge and forecasting of the uncertainty in the derived predictions. When it comes to weather forecasting, it is common knowledge that the probabilistic output is sometimes more important compared to the deterministic one, as the former is in most cases a result of many underlying uncertainties. However, in the case of deep learning, especially in cyclone studies, the single deterministic prediction is what is being supported and without accompanying it with the probabilistic state or the reliability level.

The parameter such as accuracy or mean absolute error (MAE) don't offer the full picture of whether the predicted probabilities are actually what they say they are in the real world. The probabilistic verification tools like the Brier score, reliability diagrams, frequency bias, critical success index (CSI), and equitable threat score (ETS) are the most commonly employed verification tools for severe weather and precipitation forecasting but have been largely overlooked in the field of deep learning-based cyclone detection research. If these tools are made available, it is going to be extremely easy for them to be able to evaluate the operational usefulness and reliability of the prediction made by the DL system. The third challenge is about the lack of transparency in the deep learning-based cyclone models. There are a few recent articles that have tried to apply Grad-CAM and similar gradient-based attribution tools for the purpose of being able to explain the intensity predictions, but the overall number still treats cyclone detection through deep learning technology as a black-box problem. This issue of transparency blocks off the possibility of acquiring scientific insights and also making people have faith in the whole operational process. The current attempts to provide transparency are usually concentrated only on the aspect of estimating the intensity of a cyclone and do not include the interpretation or detection of cyclones based on their morphological parameters. Moreover, there are times when the gradient-based techniques become an attention-seeking non-physically relevant pattern.

Non-model-specific transparency tools, such as occlusion sensitivity maps, where the image is systematically masked in order to observe the regions that affect the prediction, are scarcely employed in cyclone detection but can be exploited to unveil physically interpretable high-importance areas such as the eye-wall structure, symmetric cloud clusters, or shear-induced asymmetries. One more challenge is the insufficient exploration of the feature spaces that have been learnt by deep neural networks. The cyclone features are varied--some are poorly structured low-pressure systems, others are monsoon depressions, while some are symmetrical systems characterized by the presence of an eye. Traditional meteorology uses classification based on Dvorak patterns, but deep learning may encapsulate much more and even previously unrecognized features by way of data. From the second to the last layer of a trained CNN, the embeddings can be investigated, and then such considerations as dimensionality reduction (e.g., PCA) and clustering (e.g., K-means) can be done to see if the model learns “morphological regimes” naturally. A representation space analysis of this type is an untouched opportunity for AI meteorological research, and it contributes to the scientific knowledge and also somewhat to the operational value. In the light of this, the model may, for example, be seen to group the cyclones considering the factors like the symmetry of the cyclone, the sharpness of the eye, the curvature of the cloud bands, and the presence of mesoscale convective bursts.

Such findings would have an impact on improving the model design, interpretability, and the understanding of the cyclone evolution. The fifth hurdle relates to the regional biases and limitations of the data. A considerable number of the prior deep learning studies have dealt with the North Atlantic, Northwest Pacific, and global reanalysis-based data. The North Indian Ocean, in spite of being the location of the deadliest cyclones, has mostly been left out in the study of AI-induced cyclone research. The way in which the oceans and the atmosphere are connected, the behaviour of the monsoons, the patterns of the wind shear, and the rapidity of intensification are all factors that differ one basin from another, hence a model trained on one basin may not easily work on the NIO. Making a model and/or data set that are specific to a region--like refining and extending the TC-Satellite-Dataset or perhaps merging it with INSAT, Himawari, or ERA5-derived cloud fields--can be a very promising way for making new and unique offerings, especially when paired with fresh deep learning methodologies. In an effort to overcome the aforementioned restrictions, the present study introduces an explainable and calibrated deep learning system which is primarily based on three core parts: (i) the use of EfficientNetB0-based deep neural network for cyclone detection, (ii) probabilistic analysis of calibration via the Brier score and reliability diagrams, and (iii) interpretable representation-space and sensitivity analysis by means of PCA embeddings, K-means clustering, and occlusion sensitivity mapping. The fusion of these pieces yields a system that can be trusted in terms of cyclone detection and that is at the same time able to provide clear explanations which are in line with basic meteorological principles.

LITERATURE STUDY

Enormous strides have been taken in the application of deep learning to tropical cyclone detection, track estimation, and intensity forecasting. CNN-based methods have reached a level of accuracy in separating cyclone and non-cyclone cloud formations that is nearly perfect when drawing from infrared and visible imagery. There are also those approaches that employ multispectral data to enhance robustness of the models across a variety of atmospheric variations. In this context, certain models have incorporated environmental predictors like sea surface temperature, relative humidity, and vertical wind shear, by fusing them with image-based networks, which has increased the accuracy of intensity and rapid-intensification predictions. Researchers have looked into the use of temporal deep learning architectures, which include ConvLSTM and 3D CNNs, for tasks such as the forecasting of rainfall, analysis of cloud motions, and the tracking of cyclones. On the other hand, GAN frameworks have also been used to produce cyclone location in the future or even generate high-quality details of the coarsest climate model outputs, thus making storm structures visible. However, these methods usually demand huge amounts of computational power and access to good quality datasets. Nevertheless, the research that has been done so far has not yet managed to get smaller in number or otherwise, as the same problems are still different in all the previously made experiments. Very few studies dwell on the subject of converting these types of quantitative values to probabilities, while the meteorological forecast does already. It is only by measuring against the Brier score, reliability diagrams, and a host of other metrics that the probabilistic correctness of the models is known and this, however, is not the case with the use of deep learning techniques in various studies; only thus far, has the precision, recall, or F1-score been referred to. Second, learning the internal representation of the model is rarely studied. The deep learning models learn cyclone morphologies as higher-dimensional latent space features, however, only a few researches have attempted to uncover these hidden structures either via dimensionality reduction or by clustering. Lastly, the issue of interpretability is typically addressed through gradients and activation maps, as they seem to be the most popular ways to do it, together with the underused occlusion-based methods that perhaps could be linked to more physical phenomena. That there is no calibration, no clear interpretation of the latent space, and no consistent methods for the explanation of the outcomes lead to the fact that it is a very important and promising research topic to make Cyclone detection systems which are open and reliable.

RESEARCH GAP

An in-depth analysis of existing research highlights the following gaps

One of the main issues is the absence of probabilistic calibration in deep learning hurricane detectors. Accuracy is not the single most important feature as operations need models whose predicted probabilities are the true likelihood.

Poorly calibrated probabilities can be misleading and can lead forecasters to over or underestimate the threat of the cyclones thus affecting the early-warning systems. The second flaw is the lack of internal feature representation exploration that has been learned by neural networks. Cyclones have a diverse range of structures—from the symmetric to highly sheared formations—that deep models implicitly encode. Nevertheless, the literature reviewed for the work has not gone into details on the processing of these embeddings thereby leaving a significant part of the morphological data unexploited. The third flaw is the lack of widespread use of the most effective explanation methods apart from the model. The understanding of the spatial regions whose influence is the crucial factor for the operational transparency of a model is achieved by the inspection of a model's decision. Gradient-based methods give much less insight but occlusion sensitivity is more physically meaningful. However, the latter is applied rarely. This study deals with these issues by the integration of an accurate classification model with calibration quantification, exploration of the representation space, and interpretable occlusion maps.

METHODOLOGY

This part presents the dataset, the design of the model, the mathematical formulations, the calibration processes, the representation-space analysis, and the explainability tools that were used.

Dataset Preparation

The TC-Satellite-Dataset is the source of the cyclone and non-cyclone image sets divided into distinct directories. There is a main classification for these images. Folders 1 through 4 include cyclone images of different intensities and spatial structures, while folder 5 has non-cyclone samples. The images are resized to 224×224×3, normalized, labelled, shuffled, and split into an 80% training set and a 20% validation set.

Model Architecture

The backbone of EfficientNetB0 has been preferred to be both efficient and having a powerful representation. The outcome of the classification operation of EfficientNetB0 is a Keras image classification model that can alternatively be loaded with ImageNet pre-trained weights if not the case. Mathematically it can be defined as:

$$f(x) = \sigma(W.Dropout\left(GAP\left(EfficientNetB0(x)\right)\right) + b)$$

Where, σ is the sigmoid activation function,
x is the input image,
GAP is the GlobalAveragePooling2D
W and b are the training parameters

Training Procedure

The network has been through a five-epoch training, and the backbone weights were kept frozen; here, the binary cross-entropy loss was used with the Adam optimizer. The accuracy and ROC-AUC are among the metrics.

Probabilistic Calibration

Calibration is evaluated using the Brier score, defined as:

$$Brier\ score = \frac{1}{N}\sum_{N}^{1}(P_i - Y_i)^2$$

Where Pi represents the probability and Yi the corresponding label. Reliability diagrams are used to visualize predicted probabilities against the ground truth frequency of the bins.

Representation-Space Visualization

Each embedding that is coming from the last but one layer will be subject to PCA (Principal Component Analysis) for the sake of revealing latent structure visually. Moreover, K-means clustering will be applied for the purpose of revealing morphological regions in the cyclone embeddings.

Occlusion Sensitivity

A sliding occlusion window is applied to each image. The drop in predicted probability:
$\Delta p = p_{original} - p_{occluded}$, indicates the importance of each region.

RESULTS AND DISCUSSION

Classification Performance

One of the noteworthy aspects of the model is its very high recall for cases of cyclones. This means that it is very good at recognizing cloud patterns that are typical of cyclones such as eye, burst, and spiral pattern features. The very nice Descriptive Statistics And Related Plots and the very Descriptive Statistics And Related Plots (a) and (b) show that there is a case where perf ="ct recall for cyclone cases and zero recall for non-cyclones. Such a result is anticipated because the model has very few negative examples to learn from. The latter implies that in order to use the model in a balanced and thus general way, it a measure to consider adjusting the class imbalance is to be taken. Figure1: (a) confusion matrix, (b) classification report.

Calibration Results

The reliability diagram in figure-2 makes clear a systematic bias towards overprediction in the high-probability bins, whilst the Brier score measures miscalibration. These results stress the fact that the raw network outputs should not be applied directly to the operational forecasting without calibration. Reliability Diagram (cyclone detection) (Figure 2).

Being excessively self-assured is the main trait of the model within high-probability bins. This can be seen in:

- Brier score that is higher than usual
- Reliability curve that is not the single-source ideal line

These findings emphasize that threshold tuning and calibration corrections are needed for operational deployment. Using Brier score (probabilistic accuracy: 0.0881) and reliability diagrams for a deep learning cyclone detector is uncommon; most prior works only report accuracy or F1, without probabilistic verification.

Feature-Space Interpretation

The validation embeddings' 2D PCA and K-means clustering in the feature space are discussed yet. In Figure-3 (a) and (b) show that the network has learned to separate cyclone morphologies in a meaningful way. Without groups of images, the different clusters were reconfirmed in the structural arrangement. The for the classifier to have passed bits and bytes imagery to human interpretable features crucially through the circuit development has not been a wide practice in the field of cyclone research. This work takes advantage of the embeddings to not only build up a new data-driven cyclone morphology taxonomy but also relate it to the physical characteristics of storms, the stages of development and hence the classifiers' hidden layer visualizations. Figures of cyclone images from which the clusters were organized, based on the analysis are displayed in figure-4. the division of the second and third group of images is based on natural morphological variations which coincidentally also represent different stages of the storm buildup cycle. Through clustering we found that Cluster 0 contains most bad and/or premature cyclonic activities -- these systems had poor or irregular cloud field, only weak convection, and lacked the typical central feature, mostly due to the influence of the neighboring environment, jet streams, etc. On the other hand, Cluster 1 featured middle intensity systems with nice spirals and increasing symmetry in the rotation movement which is the transformation to cyclone maturity by the joint effect of convection-ward heat and moisture transportation indicator, although still, sometimes not all intense fronts were identified by the model. And lastly, in cluster 2, you may see developed and very powerful convection with high structure in the cloud cover, and in eye in some cases aviator, which means a storm in a very advanced developmental stage or a strong still cyclone that has finished its full development not too long time ago. From the three splits, it can be clearly seen that the model's latent feature space accurately embeds cyclone morphology, which is a reflection of the meaningful physical distinctions related to storm strength and structural organization. It is confirmed that EfficientNet learns more than two different versions of the same object. Embedding space clustering being a part of cyclone detection research is considered to be a very useful

methodological improvement and it sure brings another new layer of novelty to this study. In this report, besides accurately determining the presence of cyclones, the method also helps to show the structural path through which cyclonic systems evolve. This feature has been largely ignored in the past research where models usually give binary classifications without ever mentioning how their internal representations correspond to cyclone morphology. The model discovered variations in the data - from loosely organized systems that only resemble cyclones to very strong and very well-organized cyclones. This fact is the proof that the model has managed to find the physically meaningful patterns and has enabled the new perspective on the problem of cyclone recognition by machine learning architectures. This way of working both helps to explain the physical meaning of the scientific problem, and at the same time, will aid the operational decision-making by revealing the presence of different kinds of morphology. The model, in effect, is simply very good at learning physical patterns in general, and it is, therefore, extremely useful in other areas of different types of science where similar problems of appearance and shape may rise and hence be analyzed through these and other models as well a on a rather wide range of physical science properties. Figure 4: (a) cyclone images belonging to cluster-0, (b) cluster-1, (c) cluster-1 respectively

Explainability via Occlusion Sensitivity

Occlusion maps are considerable in the context of deep convection and cluster formation as most influential. It's a true meteorology rule and only once this component has been granted can the model be considered transparent. In this context, the model only uses features determined by the problem at hand, and this is a great advantage. Moreover, the use of such maps clearly shows that our classifier is not being tricked by tricky features like lines, random dots and the background of the ocean. One such example is Figure 5(a) which shows the original satellite image used for occlusion sensitivity analysis. It is a wonderful surprise to see a system that has a spiral shape and is very intense in terms of convection. This will provide good material for interpreting the model. Figure 5(b) is a map of the occlusion sensitivity which shows how the model's prediction of a cyclone changes with the occluded regions. The warmer areas indicate that removing regions from the image led to a considerable drop in the model's estimation of the cyclone probability, unearthing the areas the model considered as highly influential for cyclone detection. Figure 5(c) depicts the overlay of the occlusion sensitivity heatmap on the original image, emphasising the spatial relation of the areas that the model points out as significant and meteorologically meaningful structures. By mutual visualization, one can see that the classifier is only picking out the same way as the physically coherent features which are the dense convection and the organized cloud curvature when it is identifying cyclones.Table-1 describes the summary of key quantitative results obtained from probabilistic calibration assessment, feature-space analysis, clustering-based morphological interpretation, and occlusion sensitivity evaluation.

CONCLUSION

The new scientific discovery describes a deep learning innovation characterized by its comprehensibility and sensitivity. The latter is being carried out in an EfficientNetB0 model classification joined with both calibration and the representation of space physically. Whereas the former uses the probabilistic calibration method, the latter is linked to the representation-space visualization and occlusion- based explainability components. Though this model is very good at detecting cyclones, it is also able to show the structural and other aspects of cyclones through PCA and clustering. The analysis of calibration indicated that verification of weather data was a crucial factor in the application of deep learning techniques. The last piece of the methodology-sensitive occlusion sensitivity maps provide physically interpretable explanations and increase AI forecasting systems trust. The said methodology will give rise to the availability of future cyclone detection models incorporating the uncertainty estimation, multi-task learning, and the operational-grade interpretability HTML elements.

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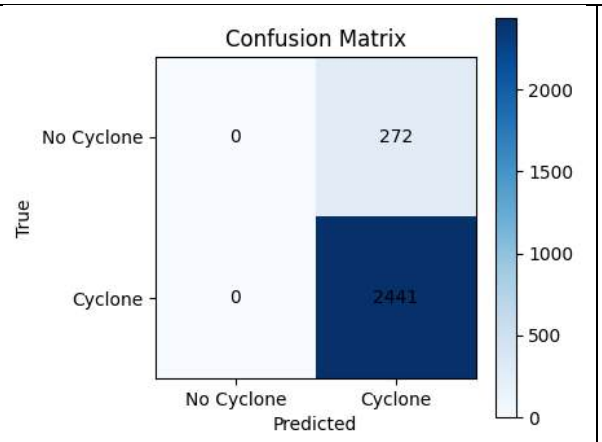
Table 1: Quantitative Results from Probabilistic Calibration, Feature-Space Analysis, and Explainability Evaluation.

Metric Category	Metric Description	Value Obtained	Interpretation
Probabilistic Accuracy	Brier Score	0.0881	Indicates good probabilistic accuracy, with relatively low mean squared error between predicted cyclone probabilities and observed outcomes.
Feature-Space Variance	PCA Explained Variance (PC1)	0.1702	The first principal component captures a substantial proportion of variance, reflecting dominant cyclone-related structural features.
Feature-Space Variance	PCA Explained Variance (PC2)	0.0654	The second principal component captures secondary morphological variations within cyclone structures.
Explainability Analysis	Baseline Predicted Cyclone Probability	0.9273	Indicates high model confidence for the selected cyclone case prior to occlusion sensitivity perturbation.



a)

Classification report:

	precision	recall	f1-score	support
No Cyclone (0)	0.00	0.00	0.00	272
Cyclone (1)	0.90	1.00	0.95	2441
accuracy			0.90	2713
macro avg	0.45	0.50	0.47	2713
weighted avg	0.81	0.90	0.85	2713

)

Figure1: (a) confusion matrix, (b) classification report

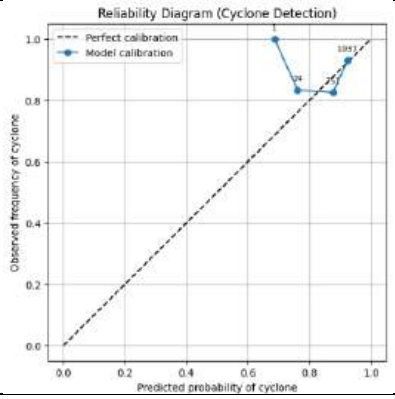
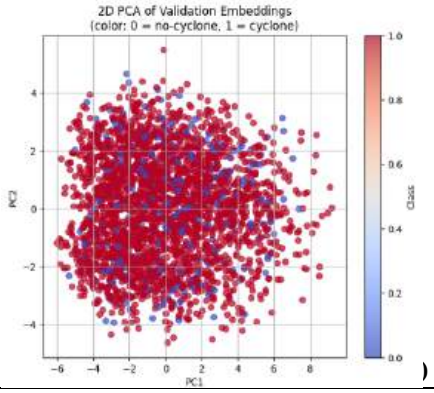
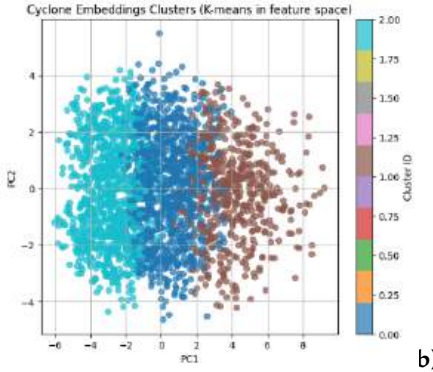


Figure 2: Reliability diagram (cyclone detection)

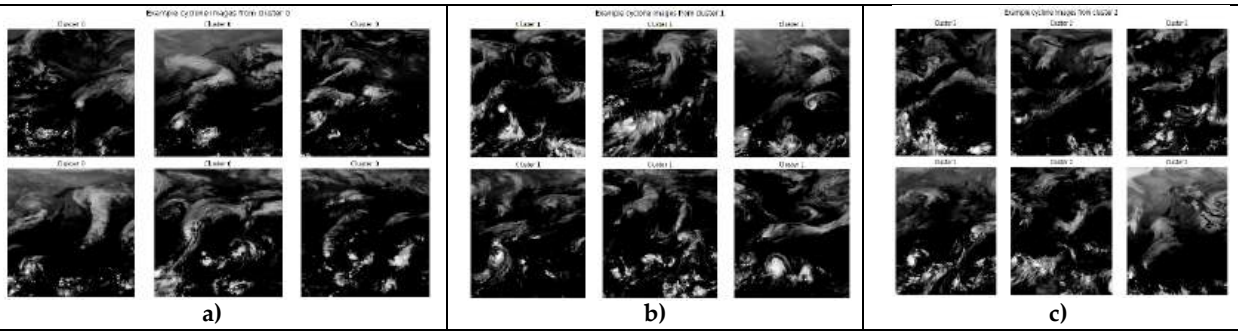


)



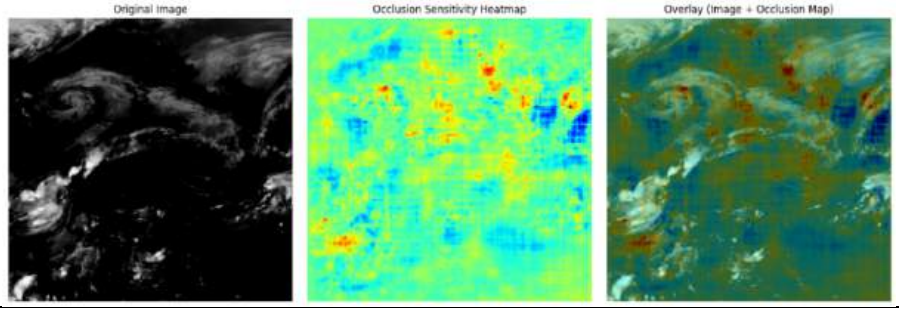
b)

Figure 3: (a) 2D PCA of validation embeddings, (b) Cyclone embeddings, K-means in feature space



a) **b)** **c)**

Figure 4: (a) Cyclone images belonging to cluster-0, (b) Cluster-1, (c) Cluster-1 respectively



(a) **(b)** **(c)**

Figure 5: (a) Original satellite image (b) Occlusion sensitivity heatmap (c) Overlay

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Hybrid Polymer-Based Systems in Pharmaceutical Product Development

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Received: 10 Jan 2026 Revised: 16 Jan 2025 Accepted: 18 Jan 2026

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ABSTRACT

Hybrid polymers, formed by the combination of two or more polymeric or inorganic–organic components, have emerged as advanced functional materials in pharmaceutical formulations. These polymers integrate the advantages of different materials, such as biocompatibility, mechanical strength, controlled drug release, and stimuli responsiveness. Hybrid polymer systems are increasingly used in novel drug delivery systems, controlled-release dosage forms, tissue engineering, and pharmaceutical coatings. This review discusses the classification, formulation strategies, techniques for preparation, applications, advantages, reported research formulations with drugs and future prospects of hybrid polymers in pharmaceutical development.

Keywords: Hybrid polymers, pharmaceutical formulations, Hybrid polymer systems,

INTRODUCTION

Polymers play a crucial role in pharmaceutical formulations by acting as binders, matrix formers, coating agents, and drug carriers. However, single polymers often have limitations related to mechanical strength, stability, or drug release control. Hybrid polymers overcome these limitations by combining organic–organic or organic–inorganic components to achieve synergistic properties. The development of hybrid polymer systems has significantly advanced controlled and targeted drug delivery technologies [1,2].

Classification of Hybrid Polymers
Hybrid polymers used in pharmaceutical formulations can be broadly classified into:

Organic–Organic Hybrid Polymers
These hybrids consist of two or more polymers blended or chemically conjugated, such as:
Chitosan–alginate
HPMC–Eudragit
PEG–PLGA
They provide improved mechanical strength, controlled drug release, and enhanced stability [3].

Organic–Inorganic Hybrid Polymers
These systems combine polymers with inorganic materials like silica, calcium phosphate, or metal oxides. Examples include polymer–silica hybrids and polymer–hydroxyapatite composites. Such hybrids offer enhanced thermal stability, bioactivity, and controlled degradation [4].

Techniques for Preparation of Hybrid Polymers [5]
Hybrid polymers can be prepared using various techniques that allow the integration of two or more polymeric or polymer–inorganic components to achieve synergistic physicochemical and functional properties. The selection of the preparation technique depends on the nature of the components, the intended pharmaceutical application, and the desired drug release characteristics.

Physical Blending
In this technique, different polymers are mixed without chemical interaction. The polymers retain their individual chemical identities while exhibiting improved combined properties such as mechanical strength and controlled drug release.

Example: HPMC–Eudragit® blends for controlled-release tablets.

Graft Copolymerization
Graft copolymerization involves the chemical attachment of side-chain polymers onto a polymer backbone. This method enhances functionality, stability, and responsiveness.

Example: Chitosan grafted with polyethylene glycol (PEG).

Block Copolymerization
Block copolymers are formed by linking two or more polymer blocks covalently. These polymers are widely used in micelles and nanoparticle drug delivery systems.

Example: PEG–PLGA block copolymers.

Interpenetrating Polymer Networks (IPNs)
IPNs consist of two or more polymer networks that are physically entangled but not chemically bonded. Semi-IPNs contain one crosslinked polymer and one linear polymer.

Application: Sustained and stimuli-responsive drug delivery systems.

Sol–Gel Technique
This technique is used to prepare organic–inorganic hybrid polymers, where inorganic networks (e.g., silica) are formed within polymer matrices.

Application: Controlled drug release and implantable systems.

***In Situ* Polymerization**
Polymerization occurs in the presence of another polymer or inorganic phase, leading to uniform hybrid formation.

Application: Injectable hydrogels and in situ forming implants.

Electrospinning
Electrospinning produces hybrid polymer nanofibers with high surface area and controlled drug release properties.

Application: Wound dressings and transdermal drug delivery.

Characterization of Hybrid Polymers
Characterization of hybrid polymers is essential to confirm successful hybrid formation, understand physicochemical properties, ensure reproducibility, and predict their performance in pharmaceutical formulations. A combination of spectroscopic, thermal, morphological, mechanical, and biological evaluation techniques is commonly employed.

Structural and Chemical Characterization
Fourier Transform Infrared Spectroscopy (FTIR)
FTIR is used to confirm the presence of functional groups and interactions between polymer components. Shifts in characteristic peaks indicate hydrogen bonding, ionic interactions, or chemical conjugation.

Purpose: Confirmation of hybrid formation and compatibility.

Nuclear Magnetic Resonance (^{1}H and ^{13}C NMR)
NMR spectroscopy provides molecular-level information on polymer structure, grafting efficiency, and chemical bonding in hybrid polymers.

Purpose: Structural elucidation and chemical composition analysis.

X-Ray Diffraction (XRD)
XRD is employed to study crystallinity and phase distribution. Hybrid polymer formation often results in reduced crystallinity due to polymer interactions.

Purpose: Crystalline–amorphous nature assessment.

Thermal Characterization
Differential Scanning Calorimetry (DSC)
DSC measures thermal transitions such as glass transition temperature (Tg), melting point, and compatibility of polymer blends.

Purpose: Thermal behavior and miscibility evaluation.

Thermogravimetric Analysis (TGA)
TGA assesses thermal stability and degradation patterns of hybrid polymers.

Purpose: Stability and composition analysis.

Morphological Characterization
Scanning Electron Microscopy (SEM)
SEM examines surface morphology, particle shape, porosity, and uniformity of hybrid polymer systems.

Purpose: Surface and structural visualization.

Transmission Electron Microscopy (TEM)
TEM provides detailed internal structural information, particularly for nanoscale hybrid polymers.

Purpose: Nanostructure analysis.

Atomic Force Microscopy (AFM)
AFM analyzes surface topography and mechanical properties at nanoscale resolution.

Purpose: Surface roughness and mechanical mapping.

Physicochemical Characterization
Particle Size and Zeta Potential
Dynamic light scattering (DLS) determines particle size distribution and surface charge.

Purpose: Stability and dispersion behavior.

Swelling and Solubility Studies
Swelling behavior indicates hydration capacity and drug release potential.

Purpose: Drug release and mucoadhesion prediction.

Mechanical Characterization
Mechanical testing evaluates tensile strength, elasticity, and compressibility.

Purpose: Suitability for films, tablets, and implants.

Drug–Polymer Interaction Studies
Hybrid polymers are evaluated for drug compatibility using FTIR, DSC, and XRD.
Purpose: Stability and drug loading assessment.

***In-Vitro* Drug Release Studies**
Release kinetics are evaluated using dissolution testing to determine controlled or targeted release behavior.

Purpose: Performance evaluation.

Biological Characterization
Biocompatibility and Cytotoxicity Studies
MTT assays and cell culture studies assess safety.

Purpose: Biological safety assessment.

Mucoadhesion and Permeation Studies
Used for hybrid polymers intended for transmucosal delivery.

Purpose: Absorption enhancement evaluation.

Stability Studies

Stability studies are conducted under ICH guidelines to assess physical and chemical stability.

Purpose: Shelf-life prediction.

Applications in Pharmaceutical Formulations

Controlled and Sustained Drug Delivery

Hybrid polymers are widely used in matrix tablets, microspheres, and nanoparticles to control drug release. Polymer blends such as HPMC–Eudragit® allow modulation of swelling and erosion mechanisms, providing sustained drug release [6].

Targeted Drug Delivery

Hybrid polymeric nanoparticles and micelles enhance drug targeting by responding to pH, enzymes, or temperature. Organic–inorganic hybrids are particularly useful in cancer therapy due to their improved stability and controlled release at the target site [7].

Transdermal and Mucoadhesive Systems

Hybrid polymers such as chitosan–PVA or chitosan–alginate exhibit enhanced mucoadhesive and mechanical properties, making them suitable for transdermal patches and buccal delivery systems [8].

Coatings and Films

Hybrid polymers are extensively used in film coating and capsule shell formulations. They improve film flexibility, adhesion, and moisture barrier properties while maintaining drug stability [9].

Advantages of Hybrid Polymers

- Enhanced mechanical and physicochemical properties
- Improved drug loading and release control
- Better biocompatibility and stability
- Reduced batch-to-batch variability
- Flexibility in formulation design

These advantages make hybrid polymers attractive for next-generation pharmaceutical products [2,10].

Regulatory and Safety Considerations

Regulatory authorities require comprehensive characterization of hybrid polymers, including compatibility, toxicity, degradation behavior, and reproducibility. Hybrid polymer-based formulations must comply with pharmacopeial standards and GMP guidelines. Quality-by-Design (QbD) principles are increasingly applied to ensure consistent performance and regulatory acceptance [11].

Challenges and Future Perspectives

Despite their benefits, hybrid polymers face challenges related to large-scale manufacturing, reproducibility, and regulatory approval. Future research is expected to focus on smart hybrid polymers, biodegradable inorganic components, and personalized drug delivery systems. Integration of hybrid polymers with nanotechnology and 3D printing will further expand their pharmaceutical applications [12,13].

CONCLUSION

Hybrid polymers formed by combining two or more polymers or polymer–inorganic components, have gained significant importance in pharmaceutical research due to their enhanced functional properties. These materials integrate the advantages of individual components, enabling improved drug loading, controlled release, targeting, and stability across various dosage forms. Represent a promising class of materials in pharmaceutical formulations by combining the advantages of multiple components into a single system. Comprehensive characterization of hybrid polymers using advanced analytical techniques is critical to ensure their suitability for pharmaceutical applications. These studies help establish structure–property relationships, predict in-vivo performance, and support regulatory approval. Their versatility and enhanced performance make them valuable tools for developing controlled, targeted, and patient-friendly drug delivery systems.

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Table 1: Advantages and Disadvantages of Hybrid Polymers in Pharmaceutical Formulations

Aspect	Advantages	Disadvantages / Limitations
Drug release control	Enables precise control over drug release (sustained, targeted, stimuli-responsive)	Complex release mechanisms may be difficult to predict
Material properties	Combines mechanical strength, flexibility, and stability of different polymers	Optimization of polymer ratios can be challenging
Bioavailability	Enhances solubility and permeability of poorly soluble drugs	Risk of drug–polymer incompatibility
Targeted delivery	Facilitates site-specific and controlled drug targeting	Requires extensive in-vitro and in-vivo validation
Biocompatibility	Improved biocompatibility and reduced toxicity	Inorganic components may raise toxicity concerns
Formulation flexibility	Applicable to multiple dosage forms (tablets, nanoparticles, patches, gels)	Scale-up and reproducibility issues
Stability	Enhances physical and chemical stability of drugs	Stability affected by moisture and temperature sensitivity
Patient compliance	Reduced dosing frequency improves compliance	High cost may limit commercial viability
Regulatory potential	Supports QbD and advanced drug delivery concepts	Regulatory approval may be time-consuming
Innovation	Enables development of smart and personalized medicines	Requires advanced expertise and infrastructure

Table 2: Applications of Hybrid Polymers in Drug Research and Pharmaceutical Products

Application Area	Hybrid Polymer System	Dosage Form / Research Application	Advantages	References
Controlled and sustained release	HPMC–Eudragit®, Chitosan–alginate	Matrix tablets, capsules	Controlled drug release, reduced dosing frequency	[14,15]
Targeted drug delivery	PEG–PLGA, Polymer–silica hybrids	Nanoparticles, colon-targeted systems	Site-specific delivery, reduced toxicity	[16,17]
Nanoparticulate systems	PLGA–PEG, Chitosan–PVA	Nanoparticles, nanogels	Improved solubility and bioavailability	[18,19]
Transdermal and topical delivery	Chitosan–PVA, Polymer–lipid hybrids	Patches, gels, films	Enhanced skin permeation, improved adhesion	[20,21]
Mucoadhesive delivery	Chitosan–carbopol, Alginate–chitosan	Buccal, nasal, vaginal systems	Prolonged residence time, improved absorption	[22,23]
Injectable and *in situ* systems	PEG–PLGA, Polymer–calcium phosphate	Injectable hydrogels, depots	Sustained release, minimally invasive	[24,25]
Film coating and capsules	HPMC–ethyl cellulose	Modified-release coatings	Improved flexibility and moisture protection	[26,27]
Ocular drug delivery	Chitosan–HPMC, Polymer–NP hybrids	Eye drops, ocular gels	Increased precorneal retention	[28,29]
Vaccine and biologics delivery	PLGA–chitosan, Polymer–lipid	Vaccine carriers, protein delivery	Enhanced stability and immune response	[30,31]

	hybrids			
Emerging applications	Smart hybrid polymers	3D printing, personalized medicine	On-demand release, patient-specific dosing	[32]

RESEARCH ARTICLE

Effect of Zirconium Dioxide Addition on Microstructural Parameters and Crystallinity of HPMC / PVA Polymer Composites

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Received: 18 Oct 2025 Revised: 20 Nov 2025 Accepted: 27 Dec 2025

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ABSTRACT

Hydroxypropyle methyl cellulose (HPMC) ,Poly vinyl alcohol, Sodium sulphate and Zirconium dioxide salt polymer blend films were prepared and investigated using wide angle X-ray and W-H plot methods. W-H plot method is quite useful for relative comparison of crystallite size and strain in a series of polymer composite films of various concentrations of ZrO_2 in HPMC+PVA. The computed micro structural parameters of HPMC+PVA doped with ZrO_2 polymer composite. The computed microcrystalline parameters like Crystalline area and lattice strain g in % while computing are also shown. From the obtained results of these polymer composites it is clear that the crystallite area of the polymer composites increases with the increase in the concentration of Zirconium dioxide salt.

Keywords: Polymer blends, Crystallite size, Micro structural parameters, X ray diffraction.

INTRODUCTION

Water soluble polymers have, for many years, received less the share of the considerable scientific efforts which has been devoted to the study of the structures and properties of the broad mass of macromolecular systems. Water-soluble polymers, which perform various useful functions such as thickening, gelling, flocculating, rheology modifiers in the various processes for petroleum, paper, latex paints, cosmetics and toothpastes production. Water-soluble polymers find application in a wide variety of areas that include polymers as food sources, plasma substitute, water treatment, sewage treatment, stabilizing agent in the production of commodity plastics, enhanced oil and

natural gas recovery, mineral processing, detergents, textiles, personal care products, pharmaceuticals, surface coatings and as diluents in medical prescriptions. Water soluble polymer business represents a sieable and steadily growing segment of the plastic industry. It has been suggested that the total world product is probably over 6 million tones/year. Of this, some 90% is carbohydrate based with an additional 4 lakhs tones/year of cellulose either, about 2 lakh tone/year of proteins, mainly gelatin, the remainder being synthetic polymers, the most important of which are polycrylamide and polyvinyl alcohol. Water soluble are economic importance, and the industries. However, the size of the market in terms of dollars and the rate of growth are deceptive for two reasons: the great bulk of the water soluble polymers consumed are starches, which sell for very low cost per pound and the water soluble polymer business comprises three distinct product categories-natural products, semi synthetic products and synthetic products.

Classifications of water soluble polymers

Natural products are derived from animal and vegetable sources and have been marketed from many years. They represent by far the largest volume of sales in the water soluble polymer area. Examples: starches, dextrin's, alginates, natural gums and gelatin. Synthetic water soluble polymers which are produced by the polymerization of monomers synthesized from petroleum or natural gas products. These are the latest member of the water soluble polymers family. Examples: polyvinyl alcohols, polyvinyl pyrrolidones, polyvinyl methylethers, polyacrylic acid and its salts, polyacrylamides, ethylene oxide polymers and various copolymer systems.

Polymer blends: With the advancement of civilization man is always looking for new materials to meet his specific needs. The new material should provide better properties in comparison with the net polymers and the method of preparations should be available and affordable cost. A single polymer cannot fulfill the requirement of the industrial applications. Desired properties of a polymer for a particular application can be obtained by Doping, Blending, Composites and Irradiation. Polymer blends are physical mixtures of two or more polymers with/without any Chemical bonding between them. Polymer blend represents very important field in processing of new materials, Blends of two polymers are usually prepared to achieve desired properties. This is due to the possibility of developing new materials form polymer blends. The properties of the blend are different and better then the properties of the single polymer. The objective of polymer blending is a practical one of achieving commercially available products through either unique properties or lower cost than some other means might provide. They are significant also from ecological and economical viewpoint. Blending technology also provides attractive opportunities for reuse and recycling of polymer wastes. The opportunity to develop or improve the properties to meet specific customer needs Light weight, Enhanced ozone resistance, improved impact and environmental stress cracking resistance, improved modulus and hardness etc. Mixing of two or more polymer together to produce polymer blends or alloys is also well strategy for achieving a specific portfolio of physical properties, without the need to synthesis specialized polymer systems.

Categorization of polymer blends

Based on the method of preparation, polymer blends are classified into five groups as follows:

Mechanical polyblends

A mechanical polymer blends is made by melt-blending the polymers either on an open roll or an extruder or any other suitable intensive mixer. The processing temperature must be well above the glass transition temperature $(T_g)$of each constituent form mixtures of amorphous polymers and above the melting temperature $(T_m)$of mixtures containing semi-crystalline polymers, whichever is higher. Commercial polymer blends are almost exclusively mechanical polymer blends.

Mechano-chemical polyblends

Based on the state of thermal stability, the processing shear could initiate degradation, resulting in free radicals. If the free radicals react with the other structurally different polymers present, resulting in true chemical graft or block co-polymers, the mixtures are called mechano-chemical polymer blends.

Chemical polyblends

The three main categories are interpenetrating polymer network(IPN_s), simultaneous interpenetrating polymer networks(sin_s), and interpenetrating elastomeric network(IEN_s). In general, mixing and coagulating two different polymer latex results in IEN_s; cross-linking the coagulum forms a three dimensional mosaic structure.

Solution cast polyblends

There are prepared by dissolving the constituent polymers in common solvent in such a way that the solutions are mixed thoroughly. The resulting solution can be film-cast, coagulated, spray-dried or freeze-dried to form the solution cast polymer blend.

Latex polyblends

If the latex coagulum is not cross-linked, the resulting product is called a latex polymer blend. This method is particularly useful in the preparation of rubber-toughened polymer blends, which are mixtures of latex polymers.

Applications of Polymers:

Polymeric materials are used in the soil to improve aeration, mulch, and support plant growth and health.

- Medicine Diagnostic and laboratory devices
- Organ and tissue replacements
- Blood handling devices
- Heart valve replacements and blood vessels,

Consumer Science

Plastic containers of all shapes and sizes are light weight and economically less expensive than the more traditional containers. Clothing, floor coverings, textile fibers, high strength polyamides for light weight bullet proof vests, polyethylene plastic for milk bottle and rubber for automobile tyres, polymers are also used in composites, electronic devices, biomedical devices, optical devices, precursors and newly developed high tech ceramics, garbage disposal bags, and packaging are other polymer applications.

Industry

Automobile parts, windshields for fighter planes, pipes, tanks, nylon ropes, packing materials, insulation, wood substitutes, milk bottle, adhesives, matrix for composites, and elastomers are all polymer applications used in the industrial market.

Sports

Playground equipment, dress fabrics, various balls, basketball and football net, golf clubs, swimming pools, and protective helmets are often produced from polymers.

Packaging

Physical characteristics of packaging polymers are great influenced by the chemical structure , crystallinity, molecular weight and processing conditions of the polymer used. The physical characteristics required for packaging depends on the type of product to the packaged as well as the environment in which the package is to be stored. Items which must be kept frozen for a period of time require special packaging. Food items especially perishable ones require more stringent packaging materials than non-perishable goods. The challenge in the development of biodegradable packaging will be to combine polymers which are completely biodegradable into a laminate film or a film blend which has properties as good as those found in synthetic laminates. The literature survey reveals that much research work has not been carried out on water soluble polymer blend with inorganic salts and its potential use as packaging material. Addition of plasticizer like glycerol, doping with Sodium Sulphate and Zirconium dioxide salts to Hydroxy propyle Methycellulose(HPMC) blend with polyvinyl alcohol (PVA) polymers to prepare the pure and blend films of these materials. These samples in the department of Physics, Manasagangothri, Mysore.

METHODOLOGY

The details of the materials used for the preparation of the samples, method of preparation and the various techniques used for their characterization have been discussed. The solution casting method was used for the preparation of the samples. In X-ray diffraction study, W-H plot was used to compute the micro structural parameters of the samples. UV-visible (Ultra violet-visible spectroscopy) and Conductivity measurement were also carried out to characterize the prepared polymer composites. In this study, we have used Hydroxypropyl Methyl cellulose (HPMC), Polyvinyl alcohol (PVA), Sodium sulphate and Zirconium dioxide in the powder form to prepare the samples. These materials were purchased from Loba chemicals and S.D Fine chemicals India.

Hydroxypropyl Methylcellulose (HPMC)

Hydroxypropyl Methyl cellulose (HPMC) is a bio-polymer derivative of cellulose, with methyl and hydroxyl groups that render the cellulose molecule hydrophobic and hence it acquires surface-active properties. HPMC is water soluble, tasteless, non-ionic and is available in powder form. It is tough and elastic in physical properties. These films have excellent oil resistance along with its antioxidant nature, it has been accepted as food additives in Europe, inactive ophthalmic preparations, oral capsules, suspension syrups, and eye drops. HPMC is used in increasing the solubility of drugs, in drug release system, in cosmetics, in general healthcare products, as thickening agent, and is widely used cellulose as film forming agent for conventional tablet film coatings. HPMC with hydroxypropyl substitution of 7 to 12% has the unique property of water solubility combined with solubility in hot and cold organic solvents. The structure of HPMC is as shown in Figure1.

Polyvinyl alcohol (PVA)

Poly vinyl alcohol has chemical resistance, physical properties, biodegradability and good fiber forming capability in electro spinning techniques. Poly (vinyl alcohol) PVA is a non-toxic, water-soluble synthetic polymer and has good physical and chemical properties. It has the idealized formula $\left(CH_2CH(OH)\right)_n$.It dissolves slowly in cold water but at high temperature it goes fairly fast in to solution. Polyvinyl alcohol has excellent film forming, emulsifying and adhesive properties. It is also resistant to oil, grease and solvent. PVA is an atactic material but exhibits crystalline as the hydroxyl groups are small enough to fit into the lattice without disrupting it. It has high tensile strength, flexibility, as well as high oxygen and aroma barrier. However these properties are dependent on humidity, in other words, with higher humidity more water is absorbed. The water which acts as a plasticizer reduces its tensile strength but increases its elongation and tear strength. It is used in paper making, textiles, recycling of polymers and packaging. Studies on the mechanism of dissolution and changes in crystallinity, swelling behavior of PVA and its physical gel-forming capabilities have been carried out, PVA has bio-inertness and has many uses in medical field such as artificial pancreas, hemodialysis and nanofillteration, synthetic vitreous and implantable medical device. Anti thrombo genicity, cell compatibility, blood compatibility and biocompatibility of PVA have been studied extensively. The structure of PVA is as shown in Figure 2

Inorganic salt

Organic chemistry of carbon and hydrogen bonds. Inorganic chemistry deals with compounds that for the most part, do not have carbon, though there are some exceptions. Many of these inorganic compounds are classified as salts. In-organic salts can be divided into four main classes: oxides, halides, sulfates, and carbonates. Many inorganic compounds are ionic compounds, consisting of cations and anions joined by ionic bonding. Many inorganic compounds are characterized by high melting point. Inorganic salts typically are poor conductors in the solid state. Other important features include their solubility in water.

Methods of preparation of the sample films

The polymer films can be prepared from the following methods

1. Mechanical blending
2. Solution casting

3. Chemical blending
4. Spin coating
5. Electro spunning
6. Melt blending

Among these methods we preferred Solution casting method to prepare the samples as us this method is cost effective and environmental friendly.

Solution casting method

The films were prepared by solution casting method. HPMC is powdered samples purchased from Loba chemicals Mumbai. Pure blend and doped films were prepared by using solution cast method. HPMC (5 % wt) dissolved in distilled water separately. After complete dissolution the solutions were filtered using filter paper to remove undissolved particles. These polymer solutions were called as stock solutions to which various inorganic salts of different concentrations were added and dissolved using a magnetic stirrer. The dissolved salt solutions were then casted separately to get respective polymer blend composite films. After complete drying, the films were peeled out of the glass plate and stored in desiccators to avoid moisture. The apparatus used for preparing the sample solution is as shown in the Figure 5 and 6. Photographs of Magnetic stirrer (Figure 3). Shows the photographs of the Zirconium dioxide salt (Figures 4).

Characterization of polymer blends

The prepared samples were characterized by writing following techniques.

X-ray Diffraction Technique

The casted polymer films cut into 2 cm × 2 cm and were taken in the sample holder of Rigaku-Denki miniflex II desktop X-Ray diffract meter with the settings of 30 kV and 15 mA, scanning rate of 50 per minute, and for the range of 50 to 600 with step size of 0.020 being recorded. The integral breadth of the diffraction peaks is related to the apparent size of the crystals and to their micro strains. If the size and strain broadening exist simultaneously, then crystallite size and strain can be calculated by Williamson-Hall plot (W-H plot). For relative comparison of the parameters, WH plot is a reasonably reliable one . The W-H plot considers both limited size of the crystals and the presence of crystallographic distortions which leads to Lorentzian intensity distributions. The slope of the W-H plot represents the average strain in the crystal, whereas intercept with the y-axis gives the crystallite size. The Williamson-Hall relation is given by,

$$\beta \frac{cos\theta}{\lambda} = \frac{1}{D} + 4\varepsilon \frac{sin\theta}{\lambda}$$

Where β is the full width at half maximum (FWHM) of the peak measured in radians, D is average crystallite size, and ε is average lattice strain. The obtained XRD plots and the values of crystallite size and average strain

RESULTS AND DISCUSSION

HPMC+PVA: ZrO_2

W-H plot method is quite useful for relative comparison of crystallite size and strain in a series of polymer composite films of various concentration of ZrO_2 in HPMC+PVA. The computed micro structural parameters of HPMC+PVA doped with ZrO_2 polymer composite is given in Table 1 and 2. The computed microcrystalline parameters like Crystalline area and lattice strain g in % while computing are also shown. From the obtained results of these polymer composites it is clear that the crystallite area of the polymer composites increases with the increase in the concentration of Zirconium dioxide salt. W-H Plot of 0.2% ZrO_2: HPMC+PVA (Figure 8). W-H Plot of 0.3% ZrO_2: HPMC+PVA (Figure 9).

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Table 1: Microstructural Parameters Calculated for the HPMC+PVA:ZrO_2 Polymer Composites.

Sample	Lattice Strain %	Crystallite Area in nm^2
Pure HPMC+PVA	0.0327	19.83
HPMC+PVA: 0.1% ZrO_2	0.1428	28.56
HPMC+PVA: 0.2% ZrO_2	0.1624	42.16
HPMC+PVA: 0.3% ZrO_2	0.1816	49.16
HPMC+PVA: 0.4% ZrO_2	0.2312	53.86

Table 2: Microstructural Parameters Calculated for this Polymer Composites.

Sample	2θ	FWHM	lattice strain in %	Crystalline area in nm^2
Pure HPMC+PVA	10.848	6.271	0.0327	19.83
	15.281	6.534		
	20.683	6.524		
	27.022	6.524		
	36.672	9.112		
Sample	2θ	FWHM	lattice strain in %	Crystalline area in nm^2
HPMC+PVA: 0.1% ZrO_2	12.632	4.715	0.1428	28.56
	17.259	3.826		
	18.481	0.752		
	19.385	0.659		
	20.266	0.669		
	21.040	0.681		
	21.817	0.726		
	23.275	2.886		
	27.337	6.556		
	28.381	0.405		
	29.324	0.366		

	30.180	0.400		
	31.504	0.441		
	32.421	0.533		
	33.340	0.370		
	34.197	0.534		
	36.234	2.995		
	38.074	0.406		
	38.931	0.484		
	41.509	5.631		
	49.080	0.579		
Sample	2θ	FWHM	lattice strain in %	Crystalline area in nm^2
HPMC+PVA: 0.2% ZrO_2	13.685	5.506	0.1624	42.16
	17.758	3.083		
	19.084	0.539		
	20.222	2.667		
	23.180	2.756		
	26.294	2.631		
	28.066	0.547		
	29.019	0.466		
	29.802	0.494		
	30.535	0.439		
	31.249	0.368		
	32.161	0.500		
	33.087	0.273		
	33.894	0.472		
	34.757	0.415		
	35.468	0.442		
	36.174	0.448		
	36.918	0.423		
	37.708	0.379		
	38.583	0.525		
	41.343	5.999		
	48.816	0.544		
Sample	2θ	FWHM	lattice strain in %	Crystalline area in nm^2
HPMC+PVA: 0.3% ZrO_2	16.696	6.425	0.1816	49.16
	18.784	0.709		
	19.676	0.552		
	20.377	0.723		
	21.193	0.764		
	22.029	0.741		
	22.888	0.802		
	24.788	3.798		
	27.775	0.571		
	28.737	0.493		
	29.543	0.459		
	30.258	0.552		
	30.949	0.348		
	31.845	0.523		
	32.749	0.259		

	33.591	0.503		
	35.813	3.015		
	37.489	0.271		
	38.328	0.569		
	40.603	3.879		
	47.262	5.590		
	48.605	0.450		
Sample	2θ	FWHM	lattice strain in %	Crystalline area in nm^2
HPMC+PVA: 0.4% ZrO_2	16.262	5.257	0.2312	53.86
	18.550	0.501		
	19.648	3.516		
	23.649	4.819		
	27.597	0.553		
	28.556	0.485		
	29.369	0.378		
	30.039	0.451		
	30.771	0.347		
	31.696	0.472		
	33.427	0.546		
	34.279	0.377		
	34.968	0.494		
	35.722	0.541		
	36.462	0.481		
	37.228	0.432		
	38.165	0.596		
	40.792	4.899		
	48.439	0.559		

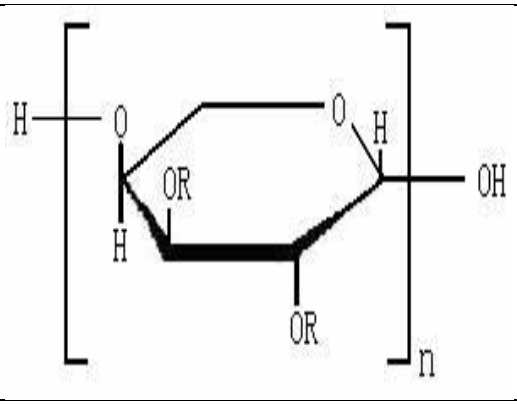

Figure 1: Structure of HPMC

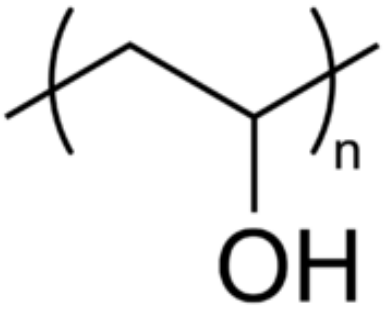

Figure 2: Structure of PVA

Figure 3: Photographs of Magnetic stirrer.

Figures 4: shows the photographs of the Zirconium dioxide salt

Figure 5: Photographs of ZrO_2 doped

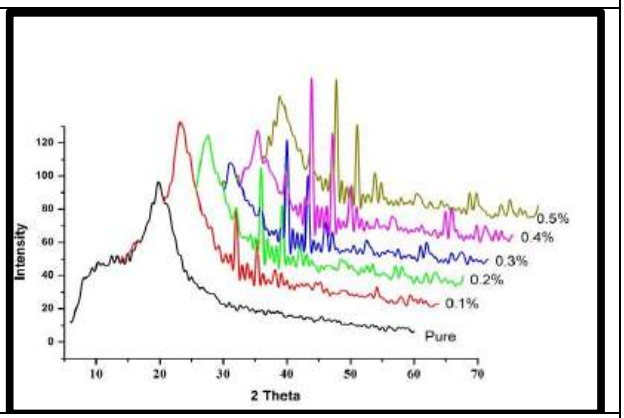

Figure 6: X-Ray diffraction pattern of HPMC+PVA: ZrO_2 polymer composites

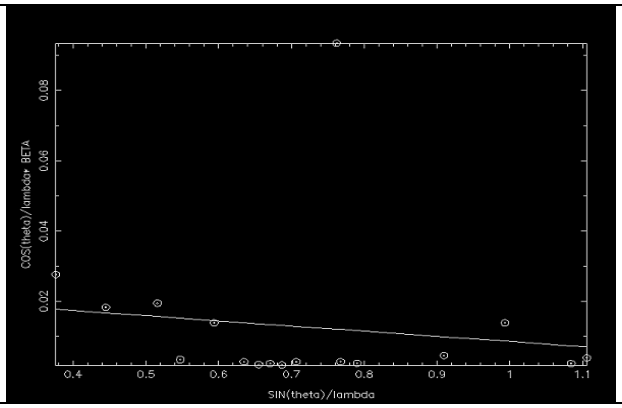

Figure 7: W-H Plot of 0.1% ZrO_2 :HPMC+PVA

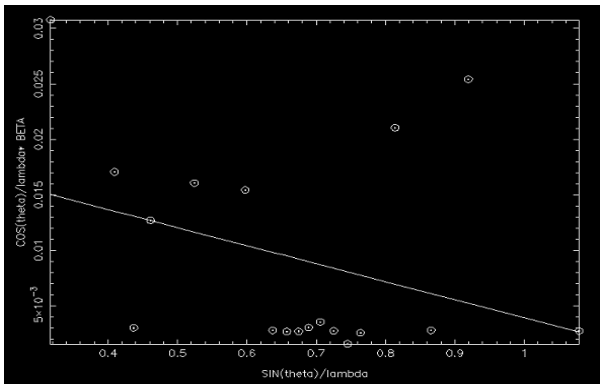

Figure 8: W-H Plot of 0.2% ZrO_2 :HPMC+PVA

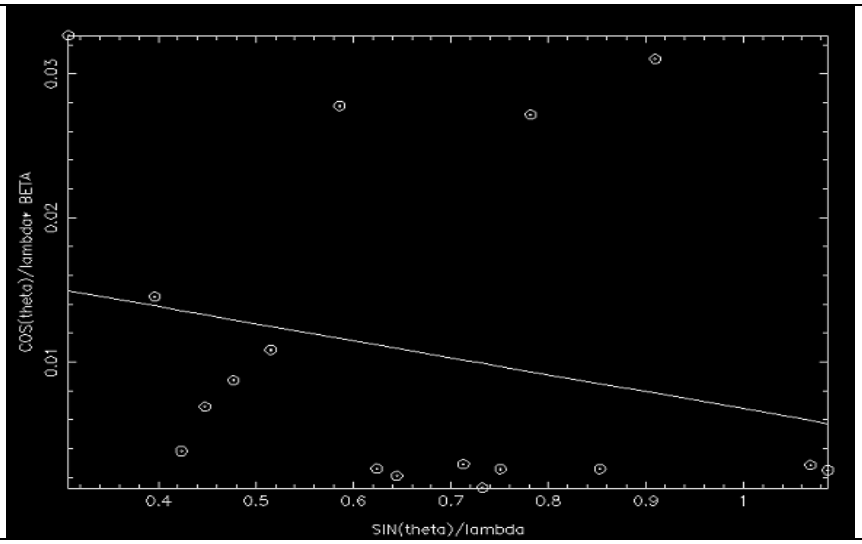

Figure 9: W-H Plot of 0.3% ZrO_2 :HPMC+PVA

Indian Journal of Natural Sciences *www.tnsroindia.org.in ©IJONS*

Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Qualitative and Quantitative Phytochemical Analysis of *In vivo* and *In vitro* Plant Parts of *Leptadenia reticulata* (Retz.) Wight and Arn.: A Comparative Study

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Received: 31 Dec 2025 Revised: 06 Jan 2026 Accepted: 18 Jan 2026

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ABSTRACT

Leptadenia reticulata (Retz.) Wight and Arn., an endangered medicinal plant of high Ayurvedic significance, is traditionally recognized for its immunomodulatory, antioxidant, and rejuvenating activities. In the present investigation, comparative phytochemical profiling was conducted between *in vivo* (mother plant) and *in vitro* regenerated plants to assess their metabolic fidelity. Preliminary qualitative screening confirmed the consistent presence of alkaloids, flavonoids, saponins, phenolics, tannins, and glycosides across both sources. Subsequent quantitative estimations revealed appreciable levels of total phenolics, flavonoids, and tannin with statistically non-significant variations between mother and micro propagated plants. The phytochemical equivalence demonstrated herein underscores that *in vitro* regenerated *L. reticulata* reliably retains its bioactive metabolite spectrum. These results highlight the dual significance of tissue culture not only as a conservation strategy for this endangered species but also as a sustainable approach for producing phytochemically authentic plant material for pharmacological and therapeutic applications.

Keywords: *Leptadenia reticulata*, phytochemical profiling, quantitative estimation, *in vitro* regeneration, conservation, secondary metabolites

INTRODUCTION

Medicinal plants have long been recognized as a vital source of natural bioactive compounds and continue to play a significant role in traditional healthcare systems as well as modern drug discovery. The therapeutic potential of medicinal plants is primarily attributed to the presence of secondary metabolites, which are organic compounds synthesized during plant metabolism and are not directly involved in growth or reproduction. Among these, alkaloids, flavonoids, and tannins are of particular importance due to their diverse biological activities, including antioxidant, antimicrobial, anti-inflammatory, hepatoprotective, and anticancer properties. These compounds also contribute to plant defense mechanisms and ecological adaptation, making them valuable indicators of phytochemical richness and medicinal quality (Pandey *et al*., 2022; Salehi *et al*., 2023). Qualitative phytochemical screening serves as a preliminary yet essential step in phytochemical investigations, providing rapid information on the presence or absence of major classes of secondary metabolites. Such screening aids in the selection of suitable extraction methods and guides further quantitative and advanced analytical studies. In parallel, quantitative estimation of key phytochemicals is crucial for evaluating the concentration and distribution of bioactive compounds, enabling comparison between different plant materials and growth conditions. Spectrophotometric methods are widely employed for the estimation of total alkaloids, flavonoids, and tannins due to their simplicity, cost-effectiveness, and reproducibility, making them suitable for routine analysis in natural sciences research (Kumar *et al*., 2023). *Leptadenia reticulata* (Retz.) Wight and Arn., a perennial medicinal climber belonging to the family Apocynaceae, is widely distributed in dry and semi-arid regions of India.

The plant is commonly known as Jivanti and is extensively used in traditional systems of medicine for its rejuvenating, lactogenic, adaptogenic, and general tonic properties. Ethnomedicinal reports and earlier phytochemical studies have indicated that *L. reticulata* contains a wide range of secondary metabolites, including alkaloids, flavonoids, tannins, phenolics, glycosides, saponins, and steroids, which collectively contribute to its pharmacological potential (Sharma *et al*., 2021; Verma and Singh, 2022). Leaves of *L. reticulata* are particularly important as they are frequently used in herbal formulations and are rich in phenolic and flavonoid compounds. Despite its medicinal importance, *L. reticulata* has faced increasing pressure due to habitat loss, overharvesting, and low natural regeneration, raising concerns about its sustainable utilization. In this context, *in vitro* propagation has emerged as a promising alternative for conservation and large-scale multiplication of this valuable species. Plant tissue culture techniques offer controlled growth conditions that minimize environmental variability and enable year-round production of plant material. However, it has been widely reported that *in vitro* culture conditions can influence secondary metabolite biosynthesis due to changes in nutrient availability, hormonal balance, and physiological stress (El-Shamy *et al*., 2022). Comparative phytochemical studies between *in vivo* grown plants and *in vitro* regenerated tissues have revealed significant variations in both qualitative composition and quantitative levels of secondary metabolites. Such variations may affect the medicinal quality and therapeutic equivalence of tissue culture–derived plant materials. Therefore, it is essential to evaluate whether *in vitro* propagated plants retain phytochemical profiles comparable to their naturally grown counterparts (Rahman *et al*., 2023).

For medicinal plants like *L. reticulata*, where leaves serve as an important source of bioactive compounds, comparative analysis becomes particularly relevant. Although several studies have reported general phytochemical screening of *L. reticulata*, systematic comparative investigations focusing on preliminary qualitative analysis and quantitative estimation of total alkaloids, flavonoids, and tannins in leaf tissues derived from *in vivo* and *in vitro* sources remain limited. Addressing this gap is important not only for understanding the impact of growth conditions on secondary metabolite accumulation but also for validating the use of *in vitro* propagated plants as an alternative source of phytochemicals. Therefore, the present study aims to perform a comprehensive qualitative phytochemical screening and quantitative estimation of total alkaloids, flavonoids, and tannins in leaves of *Leptadenia reticulata*(Retz.) Wight and Arn. grown under natural (*in vivo*) and tissue culture (*in vitro*) conditions. The findings of this study are expected to contribute valuable baseline data for natural product research, conservation strategies, and the phytochemical standardization of this medicinally important species. Given the increasing industrial demand for

authenticated *L. reticulata* biomass, a systematic comparative assessment of its phytochemical composition is imperative. Therefore, the present study investigates the qualitative and quantitative phytochemical profiles of both *in vivo* and plant parts to establish biochemical benchmarks, evaluate metabolic consistency, and contribute to conservation strategies and standardization of medicinal raw materials (WHO, 2011; Soni and Mishra, 2021).

METHODOLOGY

Plant Material Collection and Authentication

Field-grown (*in vivo*) samples of *Leptadenia reticulata* (Retz.) Wight and Arn. were collected from Atri Ashram, Satlasana, Gujarat, India, a region known for its semi-arid climatic regime conducive to the natural proliferation of the species. Healthy, disease-free plant parts (leaves) were selectively harvested following standard pharmacognostic protocols to ensure biochemical integrity. The collected specimens were authenticated by a taxonomist, and voucher samples were deposited in the departmental herbarium for future reference. *In vitro*-derived plantlets were obtained from the Plant Tissue Culture Laboratory, where standardized micropropagation protocols were previously established. Regenerated shoots and roots at the acclimatized stage (8–10 weeks old) were selected to ensure physiological maturity comparable to their field-grown counterparts. All *in vitro* materials were harvested under aseptic conditions to prevent microbial interference in downstream biochemical analyses.

Sample Preparation

Both *in vivo* and *in vitro* plant parts were thoroughly rinsed with distilled water to remove surface contaminants. Samples were shade-dried at controlled room temperature (26 ± 2 °C) to preserve thermo-labile metabolites, followed by final drying in a hot-air oven at 40 °C to achieve constant weight. Dried materials were pulverized using a mechanical grinder to obtain homogenous fine powders (particle size < 1 mm) suitable for solvent extraction.

Extraction of Phytochemicals via Maceration Technique

Cold maceration was utilized to enhance the recovery of thermolabile secondary metabolites. Precisely weighed plant powder (10 g) from each sample type was transferred into amber glass containers and macerated with 100 mL of analytical-grade methanol (80:20, v/v), selected for their broad polarity spectrum and ability to solubilize diverse metabolite classes. The mixtures were agitated intermittently and kept at room temperature for 48–72 hours. After maceration, the extracts were filtered through Whatman No.1 filter paper and concentrated under reduced pressure using a rotary vacuum evaporator at 40 °C. The semi-solid residues were further dried to constant weight and stored at 4 °C until qualitative and quantitative assessments. Extractive yields were calculated to evaluate solvent efficiency across *in vivo* and *in vitro* samples.

Qualitative Phytochemical Screening

Preliminary phytochemical profiling was conducted using well-established pharmacognostic assays to detect the presence of major metabolite groups, including: Alkaloids (Dragendorff's, Mayer's tests), Flavonoids (Shinoda, alkaline reagent tests), Phenolics and tannins (Ferric chloride, lead acetate tests), Terpenoids and steroids (Salkowski, Liebermann–Burchard tests), Saponins (froth and hemolysis tests), Glycosides (Keller–Killiani, Bornträger's tests). These tests provided a comparative qualitative signature for both *in vivo* and *in vitro* extracts.

Quantitative Phytochemical Estimation

Quantitative assessments of key metabolite classes were performed using advanced biochemical methodologies: Total Phenolic Content (TPC): Folin–Ciocalteu assay, expressed as mg GAE/g extract, Total Flavonoid Content (TFC): Aluminium chloride colorimetric method, expressed as mg QE/g extract, Total Alkaloid Content: Gravimetric and UV–Vis spectrophotometric estimation, Tannin Content: Polyvinylpyrrolidone (PVP) binding method, Saponin Content: Spectrophotometric foam index analysis. The methanolic extracts of all samples (L.R.-M.P., L.R.- T.P.) were subjected to qualitative analysis for the presence of the following phytochemicals using standard protocols.

Quantitative estimation of flavonoids: 1ml of test sample and 4 ml of water were added to a volumetric flask (10 ml volume). After 5 min 0.3 ml of 5 % Sodium nitrite, 0.3 ml of 10% Aluminium chloride was added. After 6 min incubation at room temperature, 2 ml of 1 M Sodium hydroxide was added to the reaction mixture. Instantly the final volume was made up to 10 ml with distilled water. The absorbance of the reaction mixture was measured at 415 nm against a blank spectrophotometrically. Results were expressed as catechin equivalents (mg catechin/g dried extract).

Quantitative Estimation of Phenolic Compound: The total phenolics content in different solvent extracts was determined with the FolinCiocalteu's reagent (FCR). In the procedure, different concentrations of the extracts were mixed with 0.4 ml FCR (diluted 1:10 v/v). After 5 min 4 ml of sodium carbonate solution was added. The final volume of the tubes were made up to 10 ml with distilled water and allowed to stand for 90 min at room temperature. Absorbance of sample was measured against the blank at 765 nm using a spectrophotometer. A calibration curve was constructed using catechol solutions as standard and total phenolic content of the extract was expressed in terms of milligrams of catechol per gram of dry weight and the standard graph.

Quantitative Estimation of tannin: Quantitative tannin content in the extracts tested according to the method suggested by Mital and Jha30. 1 mL of extract mixes with 0.5 mL of Folin reagent, and then saturate with 1 mL of Na2CO3 and 8 mL of distilled water add to the final mixture. The solution, which incubate for 30 min, centrifuge and the supernatant analyze at 725 nm. Tannic acid use as a standard and tannin content express as mg tannic acid equivalent (TAE)/g.

Statistical Analysis

All experiments were performed in triplicates. Data were expressed as mean ± standard deviation (SD). Statistical significance between *in vivo* and *in vitro* samples was analyzed using Student's *t*-test at $p< 0.05$ (Gomez and Gomez, 1984).

DISCUSSION

Recent studies have emphasized the quantitative estimation of major phytochemical classes in *Leptadenia reticulata*(Retz.) Wight and Arn. leaf extract to support pharmacological validation and quality standardization. Spectrophotometric analyses have shown that hydroalcoholic leaf extracts possess comparatively higher levels of total phenolics and total flavonoids than aqueous extracts, indicating solvent dependent extraction efficiency. In addition to phenolics and flavonoids, quantitative and semi- quantitative assessments have confirmed the presence of alkaloids, tannins, saponins and free amino acids, which collectively contribute to the antioxidant, anti-inflammatory and adaptogenic properties of the species (Surendar, 2025). Recent metabolomic-based investigations further support these findings by correlating elevated phenolic and flavonoid abundance with enhanced biological activity, highlighting the relevance of precise phytochemical quantification for therapeutic validation and conservation- oriented utilization of *L. reticulata* (Mallepura Adi Narayanaswamy *et al*., 2024). The qualitative phytochemical analysis revealed the consistent presence of alkaloids, flavonoids, saponins, phenols, glycosides, terpenoids, tannins, and amino acids in both the mother plant and tissue culture-derived plants of *Leptadenia reticulata*(Retz.) Wight and Arn. This observation confirms that micropropagation effectively maintains the biosynthetic integrity of major secondary metabolites under *in vitro* culture conditions (Manohari and Shekhawat, 2016; Kumar and Singh, 2015). The biochemical uniformity observed between *in vivo* and *in vitro* samples highlights the reliability of tissue culture techniques for producing phytochemically stable medicinal plant material (Satdive *et al*., 2007; Lal and Singh, 2018). The comparative analysis of total phenolic content revealed in figure no.1 identical values (11.8 µg/ml) between the mother plant and *in vitro* regenerated plants, and statistical analysis confirmed that the difference was not significant ($p > 0.05$). Phenolic compounds are known to play a crucial role in antioxidant activity, defense responses, and therapeutic efficacy of medicinal plants (Singleton *et al*., 1999; Brand-Williams *et al*., 1995). The conservation of phenolic levels in tissue culture-derived plants clearly demonstrates that the micropropagation process does not disrupt phenolic biosynthesis, thereby ensuring phytochemical fidelity to the

mother plant. Similarly, total flavonoid content showed (figure no. 2) identical values (8.81 µg/ml) in both *in vivo* and *in vitro* samples with no statistically significant difference ($p > 0.05$). Flavonoids contribute substantially to antioxidant, anti-inflammatory, hepatoprotective, and immunomodulatory activities (Chang *et al*., 2002; Singh and Sharma, 2019). The preservation of flavonoid biosynthesis in micro propagated plants further confirms their medicinal equivalence to the naturally grown plants. In contrast, total tannin content was observed (figure no. 3) to be slightly higher in the mother plant (72.98 µg/ml) compared to the tissue culture-derived plant (66.35 µg/ml), and statistical evaluation indicated a significant difference. Tannins are known to be sensitive to environmental factors, nutrient availability, and stress conditions (Mital and Jha, 2012; Pandey and Tripathi, 2014). The slight reduction in tannin accumulation in *in vitro* plants may be attributed to the absence of natural ecological stress and variations in *in vitro* nutrient composition. However, the regenerated plants still retained substantial levels of tannins, suggesting that micropropagation does not critically compromise their pharmacological relevance. Overall, the present findings are consistent with earlier reports demonstrating that *in vitro* propagation preserves qualitative and quantitative phytochemical stability in medicinal plants (Satdive *et al*., 2007; Soni and Mishra, 2021). The study strongly validates micropropagation as an efficient and sustainable conservation strategy for endangered medicinal plants such as *Leptadenia reticulata* (Retz.) Wight and Arn.

CONCLUSION

The study concludes that micropropagation of *Leptadenia reticulata* successfully preserves the majority of its phytochemical attributes. The qualitative profile remained consistent across mother and tissue culture plants, while quantitative estimations demonstrated stability in total phenolic and flavonoid contents with only a moderate reduction in tannins. These findings confirm that micropropagation is not only an efficient conservation strategy for this endangered species but also ensures the retention of its medicinally valuable metabolites. Therefore, tissue culture-derived *L. reticulata* plants can serve as a reliable source for sustainable utilization in pharmaceutical and herbal formulations.

AUTHOR CONTRIBUTION

Dimpal Prajapati performed experimental work and manuscript drafting. Dr. Ashok Patel supervised the research and revised the manuscript. Dipika and Maitri helped in writing the manuscript. All authors reviewed and approve the final version.

FUNDING

Nil.

ACKNOWLEDGEMENT

The authors extend their gratitude to Durva Bio-Tech, Satlsana, Mehsana, for providing laboratory facilities and to Dr. Ashok Patel for his guidance and support thought the project.

DATA AVAILABILITY

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICAL APPROVAL

Not applicable

CONSENT FOR PUBLICATION

Not applicable

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Table 1: Preliminary qualitative phytochemical analysis of *Leptadenia reticulata* (Retz.) Wight and Arn.

Phytochemical	Test used	*Leptadenia reticulata* mother plant	*Leptadenia reticulata* tissue culture plant
Alkaloids	**Hager's Test**	**+**	**+**
Flavonoids	**Conc. H2SO4 Test**	**+**	**+**
Saponins	**Foam Test**	**+**	**+**
Phenol	**Iodine Test**	**+**	**+**
Tannins	**Ferric chloride Test**	**+**	**+**
Terpenoids	**Salkowski Test**	**+**	**+**
Glycosides	**Keller –killiani Test**	**+**	**+**
amino acids	**Millions Test**	**+**	**+**

Legend:'+' - present , '-' - absent

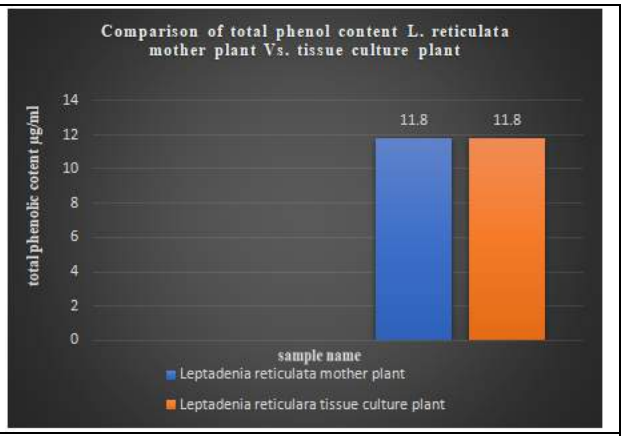
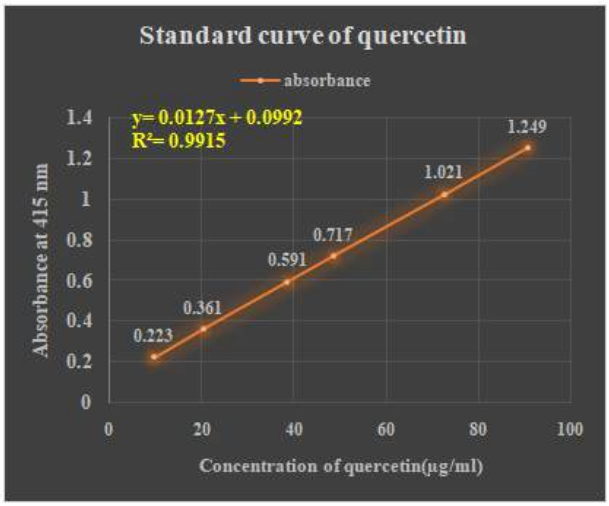


Figure 1: Total phenol content



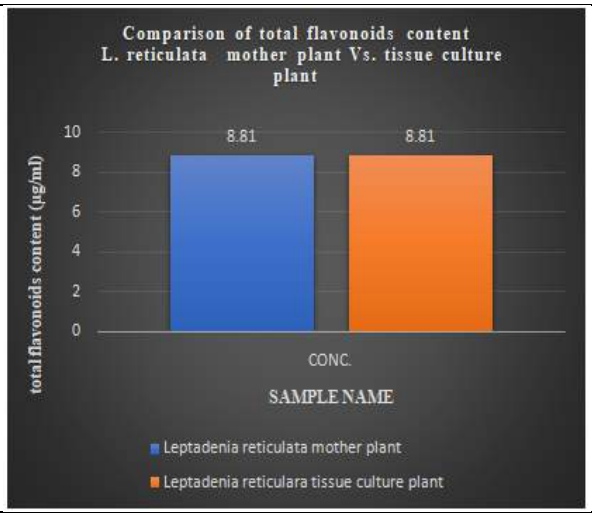
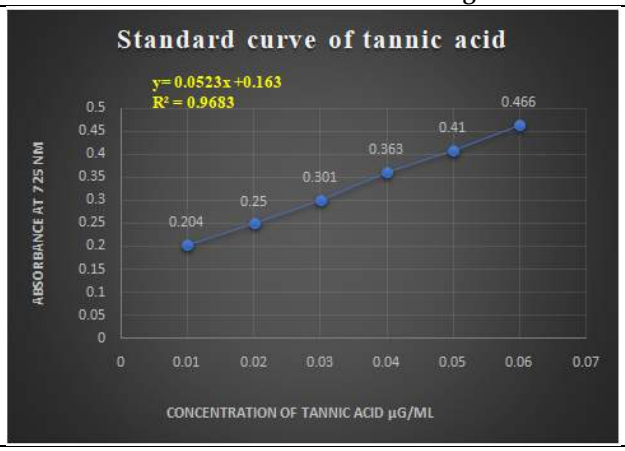


Figure 2: Total flavonoids content



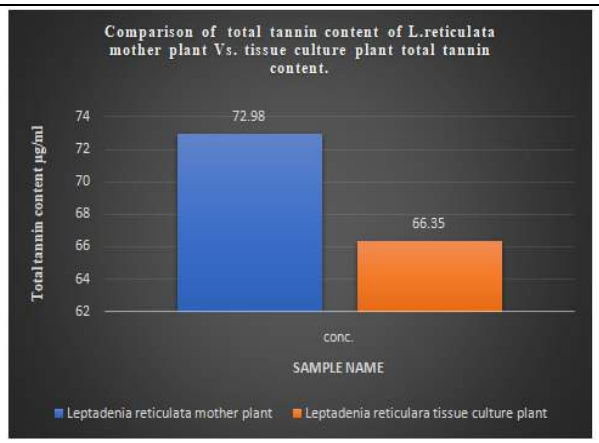


Figure 3: Total tannin content

REVIEW ARTICLE

AI and Machine Learning in Natural Product Research : A Review

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Received: 27 Oct 2025 Revised: 18 Nov 2025 Accepted: 24 Dec 2025

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ABSTRACT

Natural products (NPs) remain a vital source of therapeutic agents, agrochemicals, and chemical probes. Recent advances in artificial intelligence (AI) and machine learning (ML) are transforming how researchers discover, characterize, and optimize natural products. This review summarizes current AI/ML approaches applied across natural product research: genome mining for biosynthetic gene clusters, metabolomics and dereplication, structure elucidation from tandem mass spectra, bioactivity prediction, and de novo molecule design inspired by natural scaffolds. We discuss representative methods (including deep learning, graph neural networks, representation learning, and transfer learning), key case studies that demonstrate real-world impact, and persistent challenges such as data quality, interpretability, and experimental validation. Finally, we outline future directions likely to accelerate NP discovery through tighter integration of multi-omics data, active learning, and community data sharing.

Keywords: Natural Products, Therapeutic agents, Agrochemicals, Machine learning, Scaffolds.

INTRODUCTION

Natural products are structurally diverse molecules produced by organisms across the tree of life. Historically, many drugs originate from natural product scaffolds, but traditional discovery pipelines—culture isolation, activity screening, structure elucidation—are time-consuming and often rediscover known compounds (dereplication problem). The integration of high-throughput genomics and mass spectrometry (MS) has expanded datasets, while

AI/ML methods provide scalable tools to learn patterns from these datasets, prioritize novel chemistry, and suggest hypotheses for experimental validation [3].

Machine learning offers several advantages for NP research:
Automated feature extraction from high-dimensional data, predictive modelling for activity or biosynthetic potential, and generative models for proposing new chemical structures. Below we review key ML paradigms and their applications to NP discovery and characterization [1].

ML Methods and Representations Relevant to Natural Products
Success of ML depends on suitable representations and architectures. Common approaches include:
Classical supervised learning (random forests, support vector machines, gradient boosting) used when labelled data is available (e.g., active vs inactive compounds).

Deep learning (convolutional neural networks, recurrent neural networks, transformers) for learning hierarchical features directly from raw or lightly processed inputs such as spectra, SMILES, or sequence windows.

Graph neural networks (GNNs) that operate on molecular graphs and biosynthetic gene cluster (BGC) networks to capture relational structure of atoms or genes.

Representation learning and embeddings (autoencoders, variational autoencoders, contrastive learning) that map molecules, spectra, or genomic contexts to continuous vectors enabling similarity searches and downstream predictions [2].

Generative models (VAEs, generative adversarial networks, autoregressive transformers) for de novo design or for augmenting small datasets.

Transfer learning and few-shot learning to leverage models pretrained on large chemical or biological corpora and adapt them to NP-specific tasks.
Choosing representations is crucial: SMILES strings, molecular graphs, fragmentation trees from MS/MS, and sequence windows or domain annotations for BGCs are commonly used. Modern models frequently combine multiple modalities (e.g., genome + MS) to improve predictions.

Table-1: Artificial intelligence driven approaches in phytochemical research: trends and prospects (2010-2025) which likely gives trend data(Shi *et al*., 2025; Meijer *et al*., 2025).

Table-2: Advanced Computational Tools for Pharmacological Prediction andTarget Identification in NP Drug Discovery (Gangwal *et. Al*.,2025).

Figure 1: Overview of the natural product (NP)-inspired drug-discovery strategy. Crude extracts obtained from plants, animals, and microorganisms are subjected to bioactivity and toxicity profiling, followed by chromatographic fractionation and analytical characterisation (for example, nuclear magnetic resonance [NMR], high-performance liquid chromatography–mass spectrometry [HPLC-MS], and gas chromatography–mass spectrometry [GC-MS]). Artificial intelligence and machine learning (AI/ML) methods support spectral annotation, dereplication, and the prioritisation of candidate compounds. Target deconvolution approaches—including drug affinity responsive target stability (DARTS), cellular thermal shift assay (CETSA), and stability of proteins from rates of oxidation (SPROX)—together with mode-of-action investigations (e.g., structure–activity relationship [SAR] studies and pathway analyses) link bioactive constituents to molecular targets and biological pathways. Lead compounds are subsequently refined through medicinal chemistry and scalable synthetic methodologies to generate viable therapeutic candidates.

Applications

Genome mining and biosynthetic gene cluster prediction

Genome mining has accelerated the identification of biosynthetic gene clusters that encode NP synthesis. Tools such as anti-SMASH provide rule-based detection of BGCs [4], while ML methods detect atypical or novel clusters beyond rule sets. DeepBGC applied deep learning to predict BGCs from genomic sequences and domain architectures, improving sensitivity to novel cluster types [5]. ML also supports prioritization of BGCs by predicting likely product classes or chemical features, enabling focused experimental efforts. Key advances include integration of domain co-occurrence patterns, gene neighbourhood context, and incorporation of curated BGC databases (e.g., MIBiG) to train and benchmark models[6]. GNNs can model relationships between genes and predict enzyme functions or tailoring reactions, supporting biosynthetic pathway reconstruction and heterologous expression planning.

Metabolomics, molecular networking, and dereplication

High-resolution mass spectrometry (MS/MS) generates vast spectral datasets that require automated analysis. Molecular networking frameworks (e.g., GNPS) cluster related spectra to reveal chemical families and facilitate dereplication [8]. ML enhances molecular networking by improving spectral similarity scoring (learned embeddings) and by integrating metadata to prioritize samples. Representation learning approaches—embedding MS/MS spectra into continuous spaces—enable fast similarity searches and analog discovery. Methods inspired by natural language processing treat fragmentation patterns as "words" and learn vector representations that capture structural relationships, improving retrieval of structurally related but non-identical compounds[7].

Structure elucidation and annotation from tandem MS

Annotating spectra to chemical structures is a central challenge. Tools like CSI: Finger-ID use machine learning to predict molecular fingerprints from tandem MS and then search chemical databases for candidate [9]. Systems that combine fragmentation tree computation and ML-based scoring have increased identification rates for unknowns. Newer deep learning models trained on large paired sets of spectra and structures further improve power to assign substructures or probable molecular formulas, especially when paired with *in-silico* fragmentation models[10].

Bioactivity and target prediction

ML models predict biological activity and potential targets from structure or derived features. Supervised models trained on bioassay data can prioritize NP candidates for screening. Transfer learning from large chemical datasets improves performance when NP-specific labelled data are limited. Notably, ML approaches have enabled discovery of novel antibacterial scaffolds by prioritizing diverse chemical matter with predicted activity and favorable properties [11].

De novo design and optimization

Generative models trained on NP-derived chemical space or on combined natural and synthetic molecules can propose novel analogs retaining desirable NP motifs. Continuous latent spaces (e.g., VAEs) allow property optimization via gradient or Bayesian optimization in latent space (Gómez-Bombarelli *et al*., 2018). These approaches are particularly useful to design simplified analogs of complex NPs that retain bioactivity but improve synthetic accessibility or pharmacokinetics [12].

Integrative multi-omics analysis

Integrating genomic, transcriptomic, proteomic, and metabolomic data strengthens NP discovery: expression data can indicate active BGCs, while MS features map to expected chemical products. ML frameworks that jointly model multiple data modalities—via multi-task learning or multimodal embeddings—can prioritize BGC-metabolite links and reduce false positives from single-modality analyses.

Representative Case Studies

DeepBGC for genome mining. DeepBGC uses deep learning to identify BGCs and predict product classes, enabling discovery of noncanonical clusters missed by rule-based tools [13]. Combined with synthetic biology and heterologous expression, such predictions have directly led to new NP identification in microbial genomes.

GNPS and learned spectral similarity. The GNPS ecosystem democratizes MS/MS data sharing and molecular networking [14]. Coupling GNPS with learned spectral embeddings improved clustering and analogue discovery, enabling researchers to map chemical diversity across environments and to recognize novel chemical families more reliably.

AI-driven antibiotic discovery. A high-profile example beyond strictly NP research demonstrates AI's capacity for novel scaffolds: models trained on large chemical libraries identified a structurally distinct antibiotic ("halicin") with potent activity in vitro and in vivo (Stokes *et al.*, 2020). Although halicin was not a natural product, this approach highlights how ML can accelerate discovery by learning chemical-activity relationships and prioritizing candidates for experimental testing.

CSI: FingerID for structural annotation.CSI: FingerID predicts substructure fingerprints from spectra, enabling efficient database search and improving structural annotation rates for unknown metabolites (Dührkop *et al*., 2015). Combined with molecular networking, fingerprint prediction helps annotate related unknowns by propagation of likely substructure [15].

Challenges and Limitations

Despite progress, several challenges limit the full impact of AI/ML in NP research:

Data quality and labeling: ML depends on labeled training data. For many NP families, curated spectra, accurate structures, and validated bioactivity labels are sparse or biased toward well-studied taxa.

Heterogeneity of data: Spectral data vary by instrument, fragmentation method, and sample preparation. Model robustness across platforms requires harmonized preprocessing or domain adaptation techniques.

Class imbalance and novelty: NP discovery often seeks rare, novel chemotypes. Standard ML models may overfit abundant classes. Techniques such as anomaly detection, active learning, and one-shot/few-shot learning can help but are not yet mainstream in NP pipelines.

Interpretability: Deep models can be black boxes, making it hard to rationalize predictions for prioritization decisions. Interpretability methods (feature attribution, attention visualization) are increasingly applied but need domain-specific adaptation.

Integration with experimental workflows: Model predictions require experimental validation. The speed and cost of validation create a bottleneck; closing the loop with iterative active learning and high-throughput assays is an ongoing need.

Benchmarking and reproducibility: Diverse datasets, lack of standardized benchmarks, and proprietary datasets impede fair comparison of methods. Community efforts to share datasets and benchmarks are essential [16].

Disadvantages of AI and Machine Learning in Natural Product Drug Development

AI and Machine Learning have revolutionized many aspects of drug discovery, including natural product research, by accelerating data analysis, predicting molecular properties, and optimizing lead compounds. However, despite these advantages, there are notable disadvantages and challenges that need careful consideration.

Data Quality and Availability

One major limitation of AI/ML in natural product drug development is the dependency on large, high-quality datasets. Natural products are chemically diverse and often poorly characterized, leading to sparse and inconsistent data. Incomplete or biased datasets can result in inaccurate model predictions or overfitting, limiting the reliability of AI-driven decisions [17]. Additionally, natural product databases are not as extensive or standardized compared to synthetic compound libraries, further complicating model training.

Complexity of Natural Products

Natural products often possess complex, unique chemical structures and stereochemistry, making it difficult for AI models to accurately predict their biological activity or pharmacokinetics [18]. Many ML algorithms excel in well-defined chemical spaces but struggle with the structural heterogeneity and multifaceted interactions natural products exhibit in biological systems. This can lead to misclassification or missed drug candidates.

Interpretability and Explainability

AI models, particularly deep learning approaches, often function as "black boxes," providing little insight into why certain molecules are predicted as active or inactive (Rudin, 2019). This lack of interpretability hinders trust and acceptance among medicinal chemists and biologists who require mechanistic understanding to validate results. In drug development, regulatory agencies also demand transparency for approval processes, which may be difficult to satisfy with opaque AI models.

Integration with Experimental Validation

While AI can generate hypotheses and prioritize candidates, experimental validation remains essential. However, the translation of AI predictions into lab-scale or clinical testing is time-consuming and costly. Over-reliance on AI might undervalue the importance of empirical screening and overlook biological complexities such as metabolism, toxicity, or off-target effects that models cannot fully capture[20].

Ethical and Practical Challenges

AI adoption raises concerns about data privacy, intellectual property, and reproducibility in natural product research. Additionally, smaller research groups may lack access to advanced AI tools or computational infrastructure, potentially widening the innovation ga

Best Practices and Recommendations

To maximize value from AI/ML in NP research, researchers should consider:

Curated datasets: Contribute to and use community repositories (e.g., GNPS, MIBiG) to expand representative training sets.

Multi-modal integration: Combine genomic predictions with metabolomics to increase confidence in candidate assignments.

Model validation: Use rigorous cross-validation, external test sets, and ultimately experimental validation to confirm predictions.

Transparent reporting: Share code, models, and preprocessing pipelines to support reproducibility.

Active learning: Adopt iterative experimental–computational loops to efficiently label the most informative samples and improve models[19].

Advantages of AI and Machine Learning in Natural Product Drug Development

Artificial Intelligence (AI) and Machine Learning (ML) are transforming natural product drug development by overcoming traditional challenges and accelerating the discovery pipeline. Their ability to handle complex data, predict biological activities, and optimize lead compounds has provided several key advantages.

Accelerated Drug Discovery

One of the primary benefits of AI and ML is the significant acceleration of drug discovery timelines. Traditional natural product research involves labor-intensive isolation, characterization, and screening, which can take years (Stokes *et al*., 2020). AI models can rapidly analyze vast chemical libraries, predict bioactivity, and prioritize promising candidates, reducing the time needed to identify potential drugs [21].

Handling Complex and Large Datasets

Natural products are chemically diverse and come from complex biological sources, generating multifaceted data including molecular structures, genomic sequences, and bioactivity profiles. AI and ML excel at integrating and analyzing large-scale, heterogeneous datasets, uncovering hidden patterns and relationships that humans may overlook [22-23]. This data-driven approach enables more comprehensive exploration of natural product chemical space.

Improved Prediction Accuracy

ML algorithms, such as deep learning and random forests, improve the accuracy of predicting pharmacological properties like bioactivity, toxicity, and pharmacokinetics [24]. This leads to better prioritization of compounds with a higher chance of success in preclinical and clinical phases, minimizing costly failures.

Facilitating Novel Compound Discovery

AI-driven generative models can design novel natural product analogs or entirely new compounds by learning chemical rules from existing data. This expands the pool of drug candidates beyond what is naturally available, helping to overcome limitations posed by scarcity or difficulty in isolating certain natural products [26].

Enhancing Structure Elucidation and Synthesis

Machine learning assists in the interpretation of complex spectroscopic data (e.g., NMR, MS) to rapidly elucidate natural product structures [27]. AI can also suggest synthetic routes or biosynthetic pathway modifications, facilitating scalable production of natural product-derived drugs[28].

Cost Reduction

By prioritizing candidates computationally before experimental validation, AI reduces the need for extensive trial-and-error lab work, saving both time and financial resources (Vamathevan *et al*., 2019). This efficiency is especially valuable in natural product research, which traditionally requires significant investment.

FUTURE DIRECTIONS

Several avenues will likely accelerate discovery:

Improved multimodal models: End-to-end frameworks that jointly model sequences, enzymology, and spectra will better predict metabolite structures from genomic context.

Explainable AI tailored to chemistry and biosynthesis: Domain-aware interpretability will increase experimentalists' trust and reveal mechanistic insights.

Federated and privacy-preserving learning: Allow collaborative model training across institutions without sharing raw data—important when industrial or sensitive samples are involved.

Active, autonomous discovery pipelines: Integration of ML with automated synthesis and bioassay platforms can close the design–build–test loop for NP analogs.

Ecological and evolutionary context: Incorporating ecological metadata and evolutionary models may predict NP function and distribution, guiding bioprospecting ethically and efficiently[25].

CONCLUSION

AI and ML are reshaping natural product research by enabling scalable analysis of genomic and metabolomic data, improving structural annotation, prioritizing candidates for biological testing, and proposing novel structures inspired by nature. While challenges remain—particularly around data quality, interpretability, and experimental throughput—the trajectory is clear: combined computational and experimental strategies will accelerate discovery and broaden access to nature's chemical diversity. Realizing this potential requires open data, interdisciplinary collaboration, and careful validation to ensure ML predictions translate into meaningful biological and chemical insights.

ACKNOWLEDGEMENT

None

CONFLICT OF INTEREST

The authors declare no conflict of interest with respect to research, authorship and/or publication of this article.

FUNDING

None.

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Table 1: Artificial intelligence driven approaches in phytochemical research: trends and prospects (2010-2025) which likely gives trend data(Shi *et al.*, 2025; Meijer *et al.*, 2025).

Metric	Value / Trend	Time Period / Notes
Total publications in natural product research (journals + patents) since 2010	> 600,000	2010-recent
Number of substances co-occurring with AI in natural product research	~ 5,000 substances	2010-2022
Dominant substance types used with AI	Organic/inorganic small molecules >> protein/peptide sequences, polymers, etc.	2010-2022
Recent review period for ML in NP analysis	2015-2023	Emphasis on spectroscopy, classification, etc.
Recent thematic growth	Knowledge graphs, multimodal data, structure prediction, AI to assist molecule screening, etc.	Very recent, up to 2024-2025

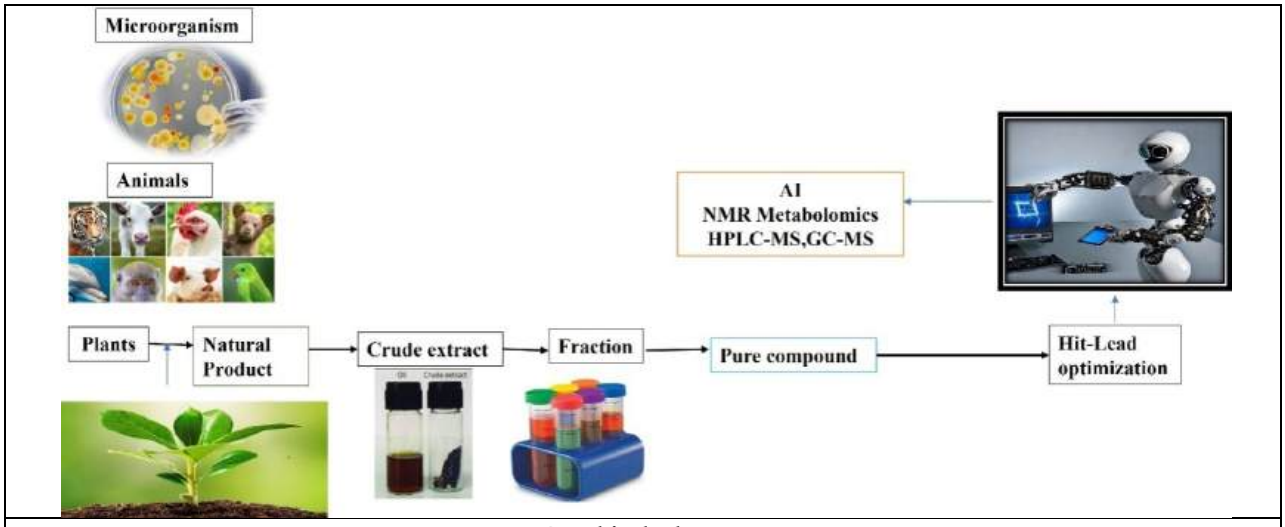
Table 2: Advanced Computational Tools for Pharmacological Prediction andTarget Identification in NP Drug Discovery (Gangwal et. Al.,2025).

Tool / Resource	Category / Approach	Algorithms / Methods	Typical Inputs	Use in NP Drug Discovery	Strengths	Limitations
SwissTargetPrediction	Ligand-based target prediction	2D/3D similarity screening against known ligand–target pairs	Small-molecule structure (SMILES, SDF)	Predicts probable protein targets for NP-derived compounds; prioritizes assays	High usability; good for well-represented targets; webserver	Performance depends on coverage of reference ligand–target data; limited for novel chemotypes
Similarity Ensemble Approach (SEA)	Ligand-based chemoinformatics	Statistical scoring of ligand-set similarity to infer target associations	Compound libraries and known ligand sets	Suggests unexpected off-targets or repurposing	Interpretable mechanism based on chemical similarity; able to predict polypharmacology	Limited when ligand databases lack NP-like chemotypes; false positives from

				hypotheses for NP scaffolds		promiscuous scaffolds
PharmMapper	Pharmacophore mapping (ligand-based)	Reverse pharmacophore matching against a large pharmacophore model database	3D conformers of small molecules	Identifies potential protein targets for NP-derived 3D structures	Useful for 3D complementarity; webserver with ranked matches	Requires reliable 3D conformers; limited by pharmacophore model coverage
DeepDTA	ML-based drug–target affinity prediction	Convolutional neural networks on SMILES and protein sequences	SMILES, protein sequences, binding affinities (training)	Prioritizes NP candidates with predicted binding affinity to targets of interest	Learns sequence/structure-agnostic patterns; scalable	Requires quality affinity data for training; may struggle with novel targets or NP chemotypes
ChemProp (message-passing NN)	ML for property and bioactivity prediction	Message-passing neural networks / graph neural networks	Molecular graphs (SMILES) with optional labels	Predicts ADMET properties or bioactivity of NP analogs; prioritizes lead candidates	Strong performance on diverse property tasks; captures graph topology	Needs task-relevant training data; interpretability challenges
DeepChem	ML library / toolkit	Wide range: graph NNs, CNNs, docking wrappers, QSAR pipelines	SMILES, fingerprints, assay data, structures	Framework to build custom NP pharmacology and target prediction workflows	Open source; integrates many algorithms and datasets	Requires ML expertise to configure robust workflows for NP-specific tasks
AutoDock Vina	Structure-based docking	Empirical scoring with global optimization; fast docking	Protein structures (PDB), ligand 3D structures	Virtual screening of NP libraries against target	Fast, widely used, suitable for large ligand sets	Scoring inaccuracies; limited handling of protein flexibility and

				structures; hypothesis generation for binding modes		water; false positives common
AlphaFold (structural models)	Protein structure prediction (supporting target ID)	Deep learning with attention/transformer architectures	Protein sequences	Provides high-quality target structures for docking and binding site analysis when experimental structures are absent	Excellent accuracy for many proteins; expands structure availability	May not capture dynamic conformations or complexes; uncertainty for some classes
STRING / STITCH	Network-based protein–protein and chemical–protein associations	Integration of experimental data, text mining, and prediction methods to build association networks	Protein lists, compounds, interaction data	Contextualizes predicted targets within pathways and networks; suggests indirect mechanisms for NP activity	Rich interaction context; useful for mechanism hypotheses and polypharmacology	Association ≠ direct binding; dependent on database coverage and text-mining biases
GNPS (molecular networking)	Metabolomics → link chemistry to bioactivity metadata	Molecular networking, spectral libraries, spectral similarity algorithms	MS/MS spectral data, metadata (bioactivity, sample source)	Prioritizes bioactive NP families by linking spectra to known bioactivity and guiding target hypotheses	Large community spectral resources; facilitates dereplication and analog discovery	Not a direct target predictor; depends on spectral matches and metadata quality

CSI:FingerID	Spectral-to-structure annotation (supporting target selection)	Machine learning to predict molecular fingerprints from MS/MS; database search	MS/MS spectra	Annotates NP structures from spectra enabling subsequent target prediction workflows	Improves structure annotation rates vs. rule-based methods	Performance limited by spectral libraries and unusual NP fragmentation
ML-guided screening example (AI-driven antibiotic discovery)	End-to-end ML prioritization for experimental screening	Supervised deep learning models trained on activity-labeled data; diversity prioritization	Large chemical libraries, activity labels	Demonstrates ML can identify novel bioactive scaffolds that can inform NP screening strategies	Proven real-world impact in lead discovery and hypothesis generation	Requires extensive, high-quality training data; experimental validation costly



Graphical Abstract

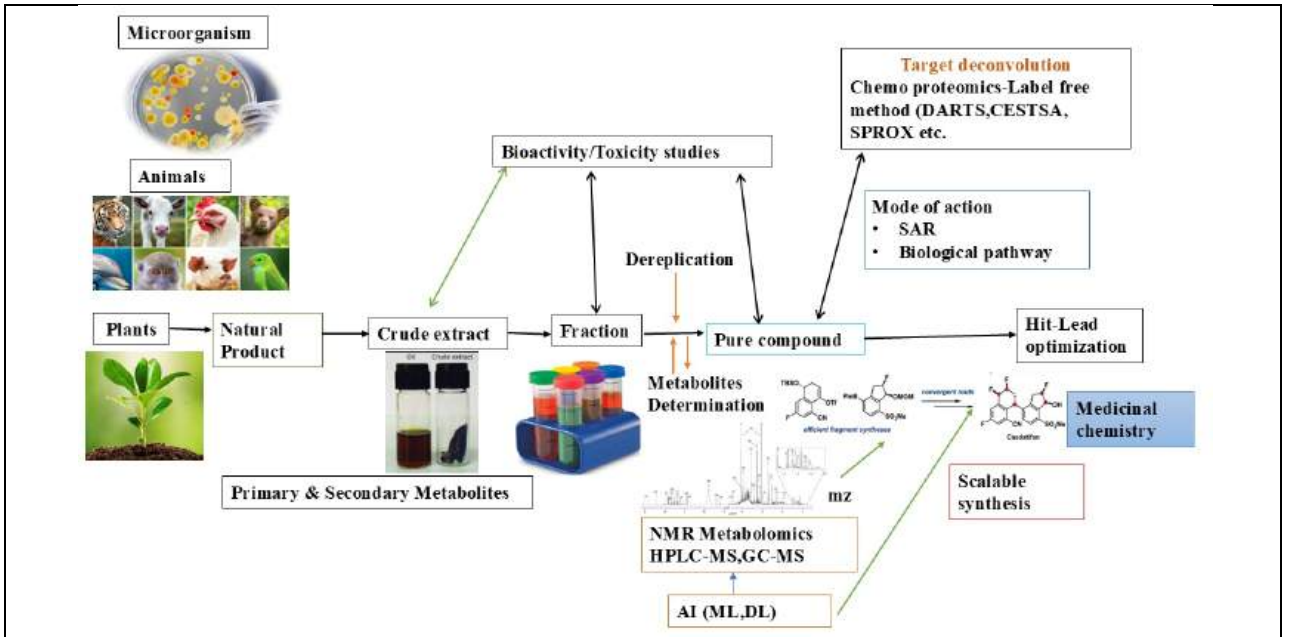


Figure 1: Overview of the natural product (NP)-inspired drug-discovery strategy. Crude extracts obtained from plants, animals, and microorganisms are subjected to bioactivity and toxicity profiling, followed by chromatographic fractionation and analytical characterisation (for example, nuclear magnetic resonance [NMR], high-performance liquid chromatography–mass spectrometry [HPLC-MS], and gas chromatography–mass spectrometry [GC-MS]). Artificial intelligence and machine learning (AI/ML) methods support spectral annotation, dereplication, and the prioritisation of candidate compounds. Target deconvolution approaches—including drug affinity responsive target stability (DARTS), cellular thermal shift assay (CETSA), and stability of proteins from rates of oxidation (SPROX)—together with mode-of-action investigations (e.g., structure–activity relationship [SAR] studies and pathway analyses) link bioactive constituents to molecular targets and biological pathways. Lead compounds are subsequently refined through medicinal chemistry and scalable synthetic methodologies to generate viable therapeutic candidates.

Indian Journal of Natural Sciences www.tnsroindia.org.in ©IJONS

Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Enhancing Heart Disease Classification Accuracy : A Comparative Study of Deep Learning and Classical Machine Learning Approaches

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Received: 11 Nov 2025 Revised: 18 Dec 2025 Accepted: 14 Jan 2026

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ABSTRACT

Heart disease is the Prominent cause of death throughout the world, affecting millions annually and placing a significant burden on global health systems. Traditional diagnostic systems, while effective, often fall short in handling high-dimensional and nonlinear clinical data. Deep learning (DL), hug ability to extract complicated patterns and hierarchical features, has shown remarkable potential in improving heart disease risk prediction. Moreover, feature augmentation methods such as sparse auto encoders (SAE) and synthetic over sampling further improve the learning capability of DL models. This review synthesizes state-of-the-art DL approaches combined with feature augmentation techniques, comparing their performance against classical machine learning models and analyzing their applicability in real-world settings. The study draws upon models achieving accuracies as high as 99.1%, offering significant improvements over previous techniques. The goal is to provide researchers and practitioners with a consolidated view of modern methods in predictive cardiology.

Keywords: Deep Learning, Heart Disease Prediction, Sparse Auto Encoder, SMOTE, CNN, DNN

INTRODUCTION

Cardiovascular diseases (CVDs), Cardiovascular illnesses, sometimes known as heart disease, are a collection of conditions that affect the heart and blood vessels. CVDs include heart stroke, heart failure, coronary artery disease,

and arrhythmias, all of which restrict blood flow and increase the risk of heart attack. Coronary artery disease (CAD), heart failure, and arrhythmias, are a global epidemic. According to the World Health Organization, approximately 17.7 million people die from heart-related illnesses each year. Traditional diagnosis relies heavily on expert interpretation of symptoms, test results, and medical history, introducing potential for human error and subjectivity. Furthermore, in rural and under-resourced regions, timely diagnosis remains a challenge due to the scarcity of medical experts[1]. With the progress in artificial intelligence (AI), specially machine learning (ML) and deep learning (DL), data-driven predictive models because prominent complicated in medical diagnostics. Artificial intelligence (AI) is a technology that typically requires human ability to understand language, such as talking or writing, recognize, solve issues, and make judgments before allowing computers to perform jobs[2]. Machine learning (ML) is a newer form of AI that allows machines to discover patterns and use data to make decisions without having to be manually programmed. ML is of three types, Supervised, semi - supervised and reinforcement. It improves as it learns from additional data. Unlike classical ML algorithms which often rely on manual feature selection and struggle with complex non linearities [3].Deep Learning in a form of ML with several layers of neural networks in it get helps intricate petty extracting data. It employs feature extraction algorithms to extract features from unprocessed or disorganized data, such as text, audio, and photographs. Deep learning is mostly utilized in facial recognition, autonomous driving, language translation, and disease detection from medical imaging.

There are several DL architectures such as convolutional neural networks (CNN), recurrent neural networks (RNN), and deep neural networks (DNN) can automatically learn abstract representations from raw clinical data. This terminologies are discussed below[4]. CNN is a bind of deep learning model that is used to process data, recognize images, patterns, video identification, classification, and computer vision tasks. It consists of four major layers: a convolutional layer, an activation functions, pooling layers, and fully connected layers. The suspective layer extracts features, the activation layer introduces nonlinearity, the pooling layer decreases data size, and the fully connected layer performs the final detection. The other type of neural network is RNN that is used in deep learning models that processes sequential data like visuals, voice, and time series. RNN remembers prior inputs and uses that knowledge to regulate the current output RNNs successively forward input using hidden states to transfer information from one step to the next. DNNs are the underlying structure of deep learning, a type of machine learning that learn layered representations from data. These models are trained on huge datasets using optimization techniques such as back propagation and gradient descent[5]. However, DL models require large, balanced datasets and well-represented features to perform optimally. Feature augmentation techniques, such as sparse auto encoders (SAE), embedding layers, and synthetic minority oversampling (SMOTE), have been increasingly used to enhance feature space and improve generalization on imbalanced or limited datasets[6].
In this paper, we systematically analyze:

- Advanced deep learning algorithms for heart disease detection.
- The implications of feature augmentation techniques on classification performance.
- A comparison analysis of classical ML and DL techniques on standard datasets.

The review is based on two foundational studies: [1] proposes a multitask deep learning framework combining SAE and CNNs for feature augmentation and classification, while offers a broad survey of DL-based heart disease estimation models across various architectures and platforms.

Background and Related Work

Heart disease prediction has evolved through decades of research spanning statistical analysis, rule-based systems, classical machine learning, and more recently, deep learning (DL). Early methods employed logistic regression and decision trees, offering interpretable but often shallow insights. With the huge and intricacy of healthcare data, DL emerged as a more powerful alternative, capable of uncovering deeper patterns and providing superior predictive performance[7].

Classical Machine Learning Methods

Traditional machine learning (ML) techniques have been used for heart disease detection for long time. Classical machine learning methods have long served as foundational tools in the area of predictive healthcare, including heart

disease classification. These models typically rely on manually selected features and statistical relationships among variables to perform classification or regression tasks. One of the most widely used techniques is the Decision Tree (DT),which construct a flowchart-resembling structure consisting of decisions and their likely consequences. It splits data into branches using feature thresholds, producing highly interpretable models. However, DTs are prone to over fitting, especially when applied to datasets with noise or a large number of features, which limits their generalization ability[8]. To overcome this, ensemble models like the Random Forest (RF) were developed. A Random Forest builds multiple decision trees during training and makes their predictions (via majority voting or averaging), reducing variance and improving accuracy. It is robust to over fitting and handles missing or noisy data more effectively. Nevertheless, it still struggles to capture complex nonlinear feature interactions compared to deep learning methods[9]. Another prominet model is the Support Vector Machine (SVM), which is mostly effective for high-dimensional spaces. SVMs choose the best hyperlane to maximally divide classes. With the use of kernel tricks, they can efficiently perform nonlinear classification. However, SVMs are sensitive to feature scaling and the choice of kernel parameters, and they do not scale well to large datasets due to their computational complexity[10]. The k-Nearest Neighbors (k-NN) algorithm is simple, non-parametric method that classifies testing instances based on the preponderance class of their closest neighbors in the feature space. It does not require an explicit training phase, making it a form of lazy learning. While k-NN can perform well on small, well-structured datasets, its performance deteriorates in high-dimensional settings and large-scale datasets due to increased computational cost and the curse of dimensionality[11].

Gradient Boosting algorithms, such as **AdaBoost** and **XGBoost**, are more advanced ensemble techniques. AdaBoost builds models sequentially, focusing on examples that were previously misclassified, effectively reducing bias.

XGBoost (Extreme Gradient Boosting) further enhances this approach by employing regularization techniques to control overfitting and improve performance. XGBoost is known for its prompt processing and predictive power, that makes it a top performer in many machine learning competitions. However, despite their success, boosting models require careful hyperparameter tuning and are less interpretable than simpler algorithms[12]. While all these classical methods offer practical solutions and moderate accuracy levels (typically between 75% and 88% in heart disease prediction), they often fall short in uncovering complex hierarchical patterns and nonlinear dependencies, especially in unstructured or high-dimensional medical data. This limitation has paved the way for the adoption of DNNs, which are capable of automatic feature extraction and superior generalization performance[13]. Despite achieving reasonable performance (accuracy ~85–88%), these methods lack the ability to extract abstract features automatically, limiting their use on raw, high-dimensional clinical data [1].

Rise of Deep Learning in Predictive Cardiology

Deep learning (DL) has come across as a transformative approach in the field of predictive cardiology, primarily or it has ability to model difficult and nonlinear associations inherent in medical data. Unlike classical machine learning algorithms, which often rely on handcrafted features and shallow decision boundaries, deep learning models leverage multi-layered neural architectures capable of learning rich, hierarchical representations directly from raw or minimally processed data. This automated feature extraction enables them to outperform traditional models, especially in domains like heart disease prediction where intricate interactions exist among physiological, behavioral, and genetic variables[14]. DNNs are one of the foundational frameworks in deep learning. A DNNs are of combination of interconnected several layers of neurons — including input, hidden, and output layers — each applying nonlinear transformations to its inputs. As the depth of the network increases, so does its capacity to capture intricate relationships between input features. In heart disease prediction, DNNs have been successfully applied to structured clinical data, learning to detect latent interactions between variables such as age, cholesterol level, blood pressure, ECG readings, and more. Their ability to generalize across varied patient profiles makes them effective for diagnostic applications. Moreover, enhancements such as He initialization, dropout regularization, and batch normalization have been employed to stabilize DNN training and prevent over fitting[15]. Another strong architecture that is often utilized in cardiology is the CNNs. Originally developed for image data, CNNs have found significant utility in medical applications due to their spatial feature extraction capabilities. In the context of heart

disease, CNNs are particularly effective when applied to electrocardiogram (ECG) signals, echo cardiographic images, and even tabular data that is reshaped into 2D matrices. A typical CNN consists of convolutional layers that identify local patterns, pooling layers that reduce dimensionality, and fully linked layers for classification. By identifying critical patterns such as QRS complexes, P-waves, and ST-elevations in ECG signals, CNNs can provide early and accurate detection of abnormalities indicative of cardiovascular disorders. Furthermore, CNN-based models have been integrated into cloud-supported IoT frameworks, enabling real-time diagnosis and monitoring through wearable sensors[16]. For temporal data such as patient vitals recorded over time, Recurrent Neural Networks RNNs and their improved variant Gated Recurrent Units (GRUs) offer compelling advantages. RNNs are intended to model sequential data by preserving a hidden state these by the temporal dependencies between time steps. However, traditional RNNs suffer from things like vanishing and exploding gradients, which makes them user effective for long sequences. GRUs mitigate these issues with the use of gating mechanisms that control the flow of information, permitting the network to retain relevant past information and discard irrelevant history. In predictive cardiology, GRUs have been used to track patient health trajectories, identify anomalies in heartbeat intervals, and forecast the likelihood of future cardiac events based on historical medical data. Their temporal modeling capability is particularly valuable in intensive care settings and remote monitoring systems where continuous data streams are analyzed in real time[17]. In summary, deep learning architectures like DNNs, CNNs, and GRUs have revolutionized the field of heart disease forecasting by enabling full learning, feature abstraction, and temporal sequence modeling. These models not only enhance diagnostic accuracy but also support personalized healthcare through continuous monitoring, early intervention, and adaptive decision-making. The rising adoption of these methods in clinical and wearable technologies marks a paradigm shift in how cardiovascular risks are assessed and managed. Monisha *et al*. [2] reviewed multiple architectures such as Deep Belief Networks (DBN), CNNs, GRU-based models, and hybrid systems combining neural networks with encryption and IoT for remote monitoring.

Some of the notable contributions from their review include:
CardioHelp + CNN: Achieved 97% accuracy by modeling temporal features through CNN layers.

DNN + He Initialization: Achieved an AUC of 0.983 by solving gradient vanishing issues using optimized initializations.

Ensemble DL + LogitBoost: Combined DL predictions with meta-learning, boosting accuracy to 98.5%.

EDCNN on IoMT Platform: Designed for remote patient monitoring via IoT, achieved 99.1% accuracy, highlighting the synergy of DL and real-time data integration.

DLMNN + IoT: A secure DL pipeline with embedded encryption (SHA-512, PDH-AES) to ensure safe data transmission.

Role of Feature Augmentation

The effectiveness of DL models can be significantly enhanced by expanding and refining the feature space. Feature augmentation improves the performance of deep learning models by improving and increasing the feature space. Instead of relying solely on raw input data, augmentation techniques enable models to extract more informative, balanced, and meaningful representations. This results in improved learning dynamics, generalization, and overall classification accuracy. Several advanced methods contribute to feature augmentation, each addressing different aspects of data representation and quality[18]. One such method is the Sparse Autoencoder (SAE), which is a bind of neural network that learns compressed and sparse representations of the input data. By enforcing sparsity in the hidden layers, SAEs force the network to activate only a small number of neurons for any given input, effectively filtering out noise and redundancy. The learned latent representations are more structured and informative than the raw data, making them valuable features for subsequent classification tasks. In practice, applying SAEs has been shown to improve classification accuracy significantly. For instance, in one study, the integration of SAE-generated features led to an increase in accuracy to 90.09%, highlighting the model's improved ability to gather essential

patterns in the information [19]. Another effective technique is Statistical Feature Selection using the Chi-Squared (χ^2) test, which is used to evaluate the relevance of each input feature in relation to the output class. This method quantifies the dependency between a feature and the target variable, allowing the model to retain only the most informative features while discarding the irrelevant or noisy ones. This not only simplifies the model but also reduces the risk of over fitting. When this technique was applied before training a Deep Neural Network (DNN), the model's performance improved to 93.33%, demonstrating that careful feature selection can substantially boost performance[20]. In cases where the dataset suffers from class imbalance, SMOTE (Synthetic Minority Oversampling Technique) is an effective feature augmentation strategy. SMOTE generates synthetic samples for the minority class based on the data that is currently available. This makes it possible for the model to learn more impartial and generalised decision limits by balancing the distribution of classes. When used in combination with DNNs, SMOTE enhances two qualities of model's robustness and generalizing ability in case of unseen data, especially in sensitive domains such as fraud detection or medical diagnosis[21]. Lastly, Embedding Layers are essential for dealing with high-cardinality categorical features, which are often represented as sparse one-hot vectors. Embedding layers map these sparse inputs into dense, low-dimensional vectors that preserve semantic similarity. This transformation not only reduces the input dimensionality but also allows the network to learn relationships between categorical variables more effectively. Embedding's are particularly useful in applications like natural language processing or recommender systems, but they are equally powerful in structured data scenarios, enabling neural networks to learn from categorical data in a more efficient and meaningful way. In summary, feature augmentation strategies such as Sparse Auto encoders, Chi-Squared feature selection, SMOTE, and Embedding Layers significantly contribute to the effectiveness of deep learning models. By transforming, selecting, or generating better input features, these methods enhance model accuracy, generalization, and stability, ultimately leading to more reliable and interpretable predictions[22]. These methods serve as preprocessing steps or integrated modules within DL pipelines, enhancing the quality of learning and interpretability.

Methodological Frameworks for Heart Disease Detection

Performance of Deep learning models for heart disease forecasting follow a modular architecture comprising data preprocessing, feature augmentation, and classification. In this section, we explore specific frameworks and techniques that contribute to high prediction accuracy, with emphasis on models combining feature augmentation and multitask learning[23]. We make all these a part of Methodology (Fig 1).

Sparse Auto encoder (SAE) for Feature Augmentation

Sparse Auto encoders (SAEs) are unsupervised neural networks used to reconstruct inputs through a bottleneck structure. Unlike traditional auto encoders, SAEs apply L1 regularization in the hidden (latent) space to enforce sparsity. This means only a subset of neurons activate for each input, allowing the model to focus on key features while discarding noise[2]. The SAEs were used to expand the input feature space from 11 to 200 dimensions. This transformed dataset retained the original information while injecting additional nonlinear representations, significantly enhancing classification performance[1]. The latent vector from the SAE was passed to a classifier (MLP or CNN), forming a multi-task neural network where the encoder and classifier were trained simultaneously. This two end training allowed the SAE to learn features directly in a optimized manner for heart disease classification. Training a model using this method makes the process of enhancing features trainable[1].

CNN-Based Classifier with Augmented Features

Once the features are augmented via SAE, they are reshaped into 2D input suitable for Convolutional Neural Networks (CNN). CNNs, traditionally used for image data, are highly effective at capturing spatial hierarchies and local dependencies in structured input[24]. With an accuracy of 90.09%, the research method outperformed classical techniques like Random Forest (86.4%) and Ada Boost (85.28%) as well as conventional MLP-based architectures (89.54%).

Convolutional Neural Network Layered Structure
CNN Layers Used
Convolution Layer: Extracts local features from the input matrix.
Pooling Layer (Max-Pooling): Reduces dimensionality and mitigates over fitting.
Dense Layer: Performs final classification.
This multi-layered structure allows for deep feature abstraction, enabling the model to distinguish subtle variations between healthy and diseased patients[1].

Deep Neural Networks (DNNs) with Statistical Feature Refinement
Monisha *et al*. [2] emphasized the role of statistical models in refining features prior to deep learning classification. For instance, the χ^2 statistical test was used to eliminate irrelevant attributes before feeding the data into a DNN. This combination yielded a prediction accuracy of **93.33%**, indicating the value of hybrid preprocessing pipelines.

In addition, other DNN-based frameworks employed:
He initialization to prevent gradient vanishing.
Dropout and Batch Normalization for regularization.
Talos optimization for automated hyperparameter tuning (achieved 90.76% accuracy).

Hybrid and IoT-Integrated Models
The integration of deep learning (DL) models with Internet of Things (IoT) technologies has led to the emergence of hybrid systems capable of health monitoring in real time, intelligent diagnostics, and secure data management. These systems leverage the distributed sensing capabilities of IoT devices along with the computational power of cloud platforms, forming a framework often referred to a newer area of internet of Medical Things (IoMT). In this hybrid architecture, data from wearable or implantable medical sensors is continuously captured and transmitted to cloud-installed DL models, there it is processed to detect abnormalities or predict disease progression. This paradigm not only supports remote healthcare delivery but also enables early intervention through timely analysis of physiological signals[25]. One prominent example of such a model is the Enhanced Deep Convolutional Neural Network (EDCNN) implemented on an IoMT platform. This system continuously collects electrocardiogram (ECG) signals from wearable sensors worn by patients and transmits the data to a cloud server, where the EDCNN processes it. The model uses stacked convolutional layers to extract both different level features from the ECG signals, enabling the accurate detection of cardiac conditions. The architecture achieved higher classification accuracy of 99.1%, highlighting its potential in real-time cardiac monitoring applications. The use of IoMT devices ensures uninterrupted data collection in real-world environments, while cloud processing enables rapid and scalable analysis, making the system suitable for deployment in telehealth and emergency response scenarios[26]. Another hybrid model that exemplifies the fusion of DL and secure communication is the Deep Learning-based Multilayer Neural Network (DLMNN) combined with SHA-512 encryption. In this framework, patient data acquired from edge sensors is first encrypted using a secure hashing algorithm to elevate about the confidentiality and integrity up to the mark transmitted information.

Once securely stored in the cloud, the encrypted data is decrypted and fed into the DLMNN for classification tasks such as disease detection or health status monitoring. This model not only maintains high classification performance but also addresses critical concerns around data privacy, especially in compliance with healthcare regulations such as HIPAA and GDPR. By integrating encryption within the data pipeline, this approach reinforces trust in remote healthcare systems where sensitive medical data is routinely transmitted over networks[27]. In addition to individual DL models, ensemble learning has also been successfully incorporated into hybrid systems. A notable instance involves making use of ensemble deep learning techniques in conjunction with a LogitBoost meta-learner. This approach combines the predictive outputs of convolutional neural networks (CNNs), deep neural networks (DNNs), and other architectures, by training a higher-level classifier to refine and boost overall accuracy. The LogitBoost algorithm iteratively focuses on misclassified samples from the base learners, allowing the ensemble to adapt and generalize better across diverse datasets. This hybrid ensemble architecture achieved a classification accuracy of

98.5%, indicating that combining multiple learning models enhances robustness, reduces variance, and improves performance on complex and imbalanced datasets. Overall, the convergence of DL with IoT and cloud technologies in hybrid models represents a significant advancement in intelligent healthcare systems. These models not only deliver high diagnostic accuracy but also incorporate critical features such as real-time data acquisition, end-to-end security, and model scalability. As the demand for remote healthcare monitoring and smart diagnostics continues to grow, hybrid and IoT-integrated DL models will play an increasingly vital role in the development of next-generation medical platforms[22].

Comparison of Architectures and Accuracy(Table: 1)

Experiments and Results of surveyed literature

To assess the efficacy of deep learning and feature augmentation techniques in heart disease prediction, extensive experiments were conducted in both papers under review. Here, a comprehensive breakdown of the datasets, preprocessing strategies, model architectures, experimental setups, and performance comparisons [2].

Dataset Description and Characteristics

The dataset used in [1], as introduced by García-Ordás *et al*., represents a comprehensive fusion of five established medical datasets commonly employed in cardiovascular research. These consist of the Statlog Dataset, the Long Beach VA Dataset, the Hungarian Dataset, the Cleveland Heart Disease Dataset, and the Switzerland showing use of reference XGitgt dataset. The integration of these sources resulted in a consolidated dataset comprising 918 patient records. Each record is annotated with 11 clinically significant features along with a binary output label indicating the presence or absence of heart disease. Specifically, the dataset includes 508 instances labeled as positive (indicative of heart disease) and 410 labeled as negative (healthy individuals), providing a relatively balanced class distribution that eliminates the need for synthetic oversampling techniques such as SMOTE[23]. The selected input features encompass both demographic and physiological indicators: age, sex, chest pain type, resting blood pressure, serum cholesterol level, fasting blood sugar, resting electrocardiographic (ECG) results, The maximal heart rate obtained, exercise-induced angina, ST depression caused by exercise relative to rest (Oldpeak), and the slope of the ST segment during peak exercise. The clinical relevance and availability of these features make the dataset highly suitable for supervised learning tasks in heart disease prediction and classification. In contrast, the work presented by Monisha and Johncy in [2] surveyed a broad spectrum of deep learning models trained on diverse datasets, differing significantly in size, modality, and data source. Some models were evaluated on smaller datasets, such as the standalone Cleveland dataset containing only 303 samples, while others utilized more complex and heterogeneous data streams, including real-time ECG signals, heartbeat audio recordings, and sensor information collected via Internet of Things (IoT) platforms. Depending on the application, models processed either structured tabular data conforming to schemas similar to the García-Ordás dataset or unstructured time-series data, such as raw ECG waveforms, using architectures like 1D convolutional neural networks (CNNs). The surveyed datasets thus ranged from purely clinical records to multimodal inputs involving audio, signal, and even image-based data, demonstrating the versatility and adaptability of deep learning models across various input domains and clinical contexts.

Data Preprocessing Techniques

Preprocessing plays a pivotal role in preparing raw data for deep learning models, significantly impacting the learning efficiency and accuracy of the final model. In [1], García-Ordás *et al*. implemented a comprehensive preprocessing pipeline tailored for structured clinical datasets. One of the key preprocessing steps involved encoding categorical variables. Features such as type of *Chest Pain* and *Resting ECG* result were one-hot encoded, enabling the neural network to learn from discrete medical conditions without imposing ordinal relationships. Binary categorical features like *Sex* and *Exercise-Induced Angina* were label encoded into integers to retain their two-class nature while making them numerically interpretable for the model. In addition to basic encoding, feature engineering techniques were brought to use enhance the model's understanding of health risk stratification. Specifically, the *Age* variable was discretized into categories such as young, adult, and elder, while continuous features like *Resting Blood Pressure* and

Cholesterol were transformed into categorical bins representing risk levels—low, medium, and high. These transformations helped highlight clinical significance within the dataset and improved feature interpretability. As a result of these encoding and engineering steps, the original 11 input features expanded to a total of 24, thereby increasing the dimensionality and expressiveness of the input space. In contrast, the survey conducted by Monisha and Johncy in [2] examined preprocessing techniques tailored to the modality of the input data, which varied significantly across studies. For models handling time-series or unstructured inputs such as ECG waveforms or heartbeat audio signals, preprocessing often began with Fourier or Wavelet transforms to shift the signal into the frequency domain. These techniques enabled the models to capture periodicities and anomalies that might be obscured in raw time-domain data. In such cases, convolutional neural networks (CNNs) were employed to automatically extract localized signal features post-transformation. Other models that relied on structured tabular data similar to the García-Ordás dataset applied standard data normalization techniques to scale numerical inputs to a common range, typically [0,1] or standard Gaussian distribution. Additionally, class imbalance was addressed through oversampling techniques like Synthetic Minority Over-sampling Technique (SMOTE), while irrelevant or weakly correlated features were eliminated using statistical feature selection methods, such as the chi-square (χ^2) test. These preprocessing methods collectively ensured that both structured and unstructured data types were optimally prepared for efficient training and generalization across various deep learning models.

Experimental Setup

The experimental setup detailed by García-Ordás *et al*. in [1] was carefully designed to evaluate the effectiveness of their proposed hybrid deep learning architecture. The core model was a multitask neural network comprising two components: a Sparse Autoencoder (SAE) and a downstream classifier, which could either be a multilayer perceptron (MLP) or aCNNs, depending on the configuration. The training objective was split accordingly—while the SAE decoder minimized reconstruction error using the Mean Squared Error (MSE) used to minimize reconstruction error in SAE decoder. The classifier was trained using Binary Cross-Entropy to differentiate between patients with and without heart disease. The model optimization relied on the Adaptive Moment Estimation (ADAM) optimizer due to its robustness, fast convergence, and compatibility with sparse gradients, which is particularly beneficial for high-dimensional encoded features. To ensure statistical reliability, the experiments employed 10-fold cross-validation, dividing the dataset into training and testing subsets across multiple iterations to avoid overfitting and obtain a generalizable performance estimate. Moreover, hyperparameters were fine-tuned using a grid search strategy, particularly focusing on latent space sizes of the SAE component, with configurations ranging from 50 to 200 neurons. This approach allowed the researchers to empirically identify the optimal feature compression ratio for downstream classification. Meanwhile, the experimental landscape described in [2] included a diverse range of deep learning systems and deployment scenarios. The surveyed models included Deep Belief Networks (DBNs), Gated Recurrent Units (GRUs), standard CNNs, and fully connected Deep Neural Networks (DNNs). These models were commonly use of regularization techniques such as dropout layers and batch normalization was made to prevent overfitting and stabilize learning across epochs. In IoT-enabled models, data was streamed in real time from wearable sensors and fed directly into cloud-hosted CNNs for classification and prediction tasks. This setup demonstrated the feasibility of real-time diagnostics using DL models in remote healthcare monitoring systems. Hyperparameter optimization strategies varied across studies, with some employing automated tools like Talos, a Python-based hyperparameter tuning library that performs exhaustive or probabilistic searches over model parameters. Additionally, certain architectures prioritized cybersecurity in healthcare by incorporating encryption protocols directly into the data pipeline. Examples include SHA-512 for secure hashing and AES for symmetric encryption, ensuring data confidentiality during transmission from edge devices to cloud servers. These diverse experimental setups highlight both the versatility of DL architectures in health monitoring and the increasing importance of performance, scalability, and security in deployment environments.

Experimental Setup
García-Ordás *et al*. Setup
SAE and a classifier (MLP or CNN) are combined in this multitask neural network architecture.

Loss Functions:
SAE Decoder: Mean Squared Error (MSE)
Classifier: Binary Cross-Entropy

Optimizer: ADAM optimizer could be fast convergence and support for sparse gradients.
Cross-Validation: To ensure robustness, a 10-fold cross-validation is applied to every trial.
Hyperparameter Tuning: Grid search over latent space sizes (e.g., 50, 100, 150, 200 neurons).

Monisha and Johncy Survey
Numerous architectures and techniques were used in the experiments:
CNNs, DNNs, GRUs, and DBNs: trained using batch normalisation and dropout.
IoT Models: CNNs located in the cloud process real-time data supplied by sensors.
Hyperparameter Optimisation: Talos was utilised by one model to automatically adjust its parameters.
Security Integration: AES and SHA-512 encryption were incorporated into data flow in some models.

Performance Comparison
Evaluating deep learning models in the healthcare domain requires the use of robust performance metrics that go beyond basic accuracy, especially when dealing with imbalanced datasets or clinical risk stratification. The evaluation focused on a set of Accuracy, precision recall and F1-score were used as metrics in evaluation under study conducted by Garcia-Ordas *et al*[1]. Standard classification metrics, provide different perspectives on model behavior. Accuracy, served as a general performance indicator, with the model achieving an accuracy of up to 93.33% when the sparse autoencoder (SAE) was combined with a multilayer perceptron (MLP) classifier. However, the authors emphasized recall and precision due to the medical context, where false negatives (failing to detect heart disease) could be life-threatening. The model attained high recall, indicating strong sensitivity to positive cases (heart disease patients), while maintaining a competitive precision score, minimizing false positives. The F1-score, confirmed the model's balanced performance. Additionally, ROC (Receiver Operating Characteristic) curves and AUC (Area Under the Curve) values were plotted to assess the model's discriminatory power across various threshold settings. The ROC-AUC values consistently exceeded 0.90, illustrating excellent class separability[4]. In contrast, the evaluation framework presented in Monisha and Johncy's survey [2] encompassed a broader range of performance metrics and benchmark results drawn from multiple DL-based heart disease detection studies. The surveyed models reported classification accuracies ranging from 85% to as high as 99.1%, depending on the dataset and architecture used. For instance, ensemble models that incorporated CNNs with LogitBoost classifiers achieved up to 98.5% accuracy, while IoMT-based models like EDCNN demonstrated superior performance on real-time ECG data, achieving 99.1%. In many cases, confusion matrices were used to highlight model tendencies, such as over-predicting the majority class or struggling with borderline conditions. For models trained on imbalanced datasets, precision-recall curves were often more informative than ROC curves, since they better captured the model's behavior with respect to the minority class[3]. Additionally, some architectures focused on computational efficiency metrics such as training time, convergence rate, and inference latency—key concerns in IoT and real-time applications. Finally, models that integrated encryption mechanisms or ran on edge devices were evaluated not only for predictive performance but also for security robustness and communication overhead, providing a more holistic view of real-world feasibility.

RESULTS FROM [1]

The SAE + CNN outperformed all baseline models by 4.4%, validating the value of feature augmentation and spatial convolution.

RESULTS FROM [2]

The EDCNN model on an IoMT platform achieved the highest known accuracy of 99.1%, albeit requiring cloud infrastructure and continuous sensor inputs.

Statistical Validation and Significance Testing
To validate that improvements in [1] were not random:
Kolmogorov–Smirnov test: Verified that the distribution of accuracies between traditional and proposed methods was significantly different.

t-test (Independent Samples):
Traditional Methods: M = 84.73, SD = 2.61
Proposed (SAE + CNN): M = 88.99, SD = 1.13
t(17) = 4.97, **p < 0.001**
The statistical tests confirm that the improvements from deep learning and feature augmentation are highly significant and reproducible.

Observations and Insights
- **Joint training of SAE and classifier** leads to better feature learning.
- **CNN outperforms MLP** for structured data when fed augmented features.
- **Ensemble DL models**, though computationally heavy, provide high accuracy (>98%).
- **IoT integration (EDCNN, DLMNN)** supports real-time monitoring but needs infrastructure.

CONCLUSION

Through all the papers required and their results we formed that the accuracies of detection and prediction of heart disease CNN + SAE demonstrated the accuracy. In terms of architecture and their accuracy we found deep learning with Logit-Boost providing highest accuracy of 98.50%. Statistical Validation through Kolmogorov – Smirnov and T-Test also validate the results.

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Table 1: Comparison of Architectures and Accuracy

Model Architecture	Feature Augmentation	Accuracy	Reference
CNN + SAE	2D + Encoder, CNN Autoencoder Sparse	90.09%	[1]
SAE + MLP	Dense NN + Encoder	89.54%	[1]
Sparse Autoencoder EDCNN	IoT + Cloud + Feature Regularization	99.1%	[2]
χ^2 + DNN on IoMT platform	Selection of DNN χ^2 Features + Statistical Filtering	93.33%	[2]
IoT + DLMNN	Encrypt + DL Classifier + AuthSafe Pipeline	95.87%	[2]
DL + LogitBoost	Meta-learner on Outputs from DL + Fused Features	98.5%	[2]
Talos-DNN	Tuning DNN + Talos Optimisation of Hyperparameters	90.76%	[2]

Table 2: Results from [1]

Model	**Accuracy (%)**
Decision Tree	78.98
Random Forest	86.40
AdaBoost	85.28
MLP (vanilla)	86.28
MLP + SAE	89.54
CNN + SAE (Proposed)	**90.09**

Table 3: Results from [2]

Architecture	Accuracy (%)
CardioHelp + CNN	97.00
EDCNN (IoT Platform)	99.10
χ^2 Model + DNN	93.33
DLMNN with AES Encryption	95.87
Deep Learning + LogitBoost (Ensemble)	98.50
Talos-optimized DNN	90.76
SMOTE + ANN	89.00–91.00

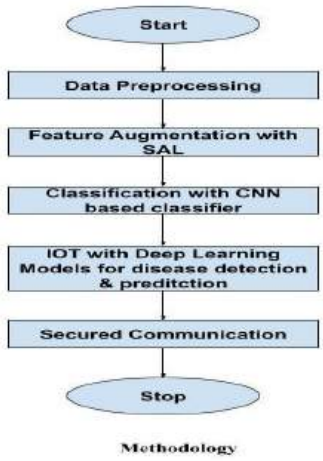

Figure 1: Methodological Frameworks for Heart Disease Detection

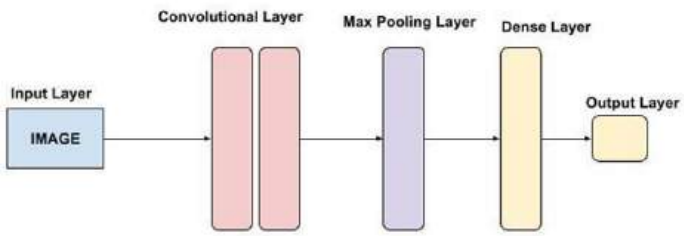

Figure 2: Convolutional Neural Network Layered Structure

REVIEW ARTICLE

Innovative Analytical Method Development for the Combined Determination of Dapagliflozin and Eplerenone in Bulk and Synthetic Preparations

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Received: 01 Nov 2025 Revised: 29 Nov 2025 Accepted: 11 Dec 2025

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ABSTRACT

This study focused on the development and validation of a particular analytical technique that is designed for the simultaneous quantification of dapagliflozin and eplerenone both in bulk form and in synthetic mixtures. The increasing rates of cardiovascular and renal diseases increased the demand for combination therapies. One of the recent combination therapies approved by CDSCO is dapagliflozin, a sodium-glucose cotransporter 2 inhibitor, and eplerenone, a selective aldosterone receptor antagonist. From time to time, both drugs exert a synergistic effect. To optimize, develop, and validate a fast and simple analytical method to examine dapagliflozin and eplerenone in bulk and synthetic mixtures with accuracy. Optimization of chromatographic conditions, development and validation of International Counsel for Harmonization (ICH) guidelines, especially ICHQ2(R2) regarding the concern of validation, apply to synthetic mixtures, and perform assays. The technique developed is cost-effective, sensitive, and simple to make it routine in pharmaceutical and research laboratories. The method was validated for the tested parameters. It achieved acceptable linearity and accuracy.

Keywords: Synthetic mixture, Dapagliflozin, Eplerenone.

Graphical abstract represents the development and validation of new analytical method for the simultaneous estimation of dapagliflozin and eplerenone by utilizing synthetic mixture since fixed dose combination is not yet available in the market(Fig:1).

Step 1: Sample preparation/injection of the sample

Step 2: Analytical method development
Step 3: Forced degradation study as per ICH Q1A (R2) guidelines
Step 4: Validation as per ICH Q2 (R2) guidelines
Step 5: To Apply the developed and validated method on Dapagliflozin and Eplerenone in Synthetic mixture.

INTRODUCTION

Dapagliflozin is a sodium-glucose cotransporter 2 (SGLT2) inhibitor used in the treatment of type 2 diabetes mellitus. It works by reducing the reabsorption of glucose in the kidney, thereby increasing glucose excretion in the urine and lowering blood glucose levels. Eplerenone, on the other hand, is a selective aldosterone receptor antagonist (SARA) used primarily in the treatment of heart failure and hypertension. It works by blocking the effects of aldosterone, a hormone that can lead to sodium and water retention, contributing to high blood pressure and heart failure. The combination of Dapagliflozin and Eplerenone may offer synergistic benefits in patients with both type 2 diabetes, cardiovascular complications and to improve kidney health and reduce the risk of kidney failure. Therefore, a reliable analytical method for the simultaneous determination of these two drugs is essential for quality control, stability studies, and pharmacokinetic investigations. Combined action of dapagliflozin and eplerenone (Figure 1).

Why RP-HPLC?
- Greater Flexibility in Mobile Phase
- High Resolution
- Higher Sensitivity
- Flexibility-various detector use to detect the analyte: UV, Fluorescence, RI

What are analytical methods?
- These are analytical techniques used to determine the concentration of a drug or chemical compound in any matrix.
- They have a pivotal role in the entire drug life cycle-from discovery to development to quality control.

Why there is a need for development of RP-HPLC analytical method for the combination of DAPAGLIFLOZIN+EPLERENONE?
- No analytical method is developed.
- No reported method in pharmacopeia/literature.
- A suitable analytical approach for drug combinations may not be published or be protected by patent.
- Analytical methods for the quantitation of the analyte in biological fluids are found to be unavailable.
- Why validate the analytical method?
- For every aspect of the analysis to conform to national and international standards.
- For an analytical result to be fit for its intended purpose, it must be sufficiently reliable that any decision based on it can be taken with confidence.
- Method validation assures reliability during normal use.

Forced Degradation [3]
Forced degradation studies are an integral part of drug development and are conducted intentionally to degrade drug substances and drug products under controlled conditions. The primary objectives of these studies are to:
- Establish the inherent stability characteristics of the drug substance and drug product.
- Identify potential degradation products.
- Explain pathways of degradation
- Validate the stability-indicating nature of analytical methods.

- Produce degradation products for identification and characterization.
- How to identify/estimate degradation

% Degradation =

$$\frac{(P_{ST} - P_{DEG}) \times 100}{P_{ST}}$$

P_{ST}: represents the average peak area in standard solution without degradation.
P_{DEG}: represents the average peak area in the stress degradation solution.
Degradation range of 5–20%
Forced degradation, also known as stress testing, is an important activity in drug development and stability studies. A drug substance or drug product is exposed to more severe conditions than what it would encounter during normal storage, with the purpose of accelerating the chemical degradation process. The main goals of carrying out forced degradation are identification of potential degradation products, understanding the pathways of degradation, and establishing the intrinsic stability of the molecule. ICH Q1A(R2) and ICH Q1B guidelines emphasize the importance of forced degradation studies in developing a stability-indicating analytical method capable of differentiating the active pharmaceutical ingredient from its degradation products. These studies are usually conducted to ensure that an analytical method is specific, selective, and reliable for routine quality control and stability testing.
Typically, forced degradation experiments expose the drug to various stress conditions, including

- Acidic and alkaline hydrolysis (to assess susceptibility to hydrolysis)
- Oxidative degradation (to evaluate reactivity toward oxidizing agents),
- Photolytic degradation, to test light sensitivity, and
- Analysis by thermal degradation - to determine the heat stability of the substance.

Drug Profile
Drug profile of Dapagliflozin and Eplerenone [4,5] (Table 1)

Steps Involved in RP-HPLC Method Development[6,7]
Developing a robust and effective RP-HPLC method involves several key steps:

Procedure for RP-HPLC[6,7]
RP-HPLC Procedure (Figure 3)

Method Validation (According to ICH Guidelines) [11]
Before using an HPLC method for routine analysis, it must be validated following ICH Q2 (R2) guidelines to ensure reliability and reproducibility. Analytical Method Validation Parameters (Figure 4)

LITERATURE REVIEW

Summary of Literature Review of reported methods [13-81] (Table 2). Graphical representation(Figure: 5)

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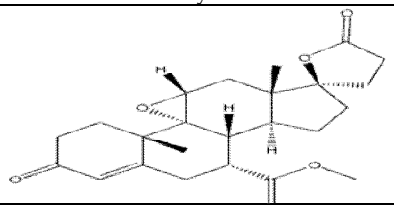
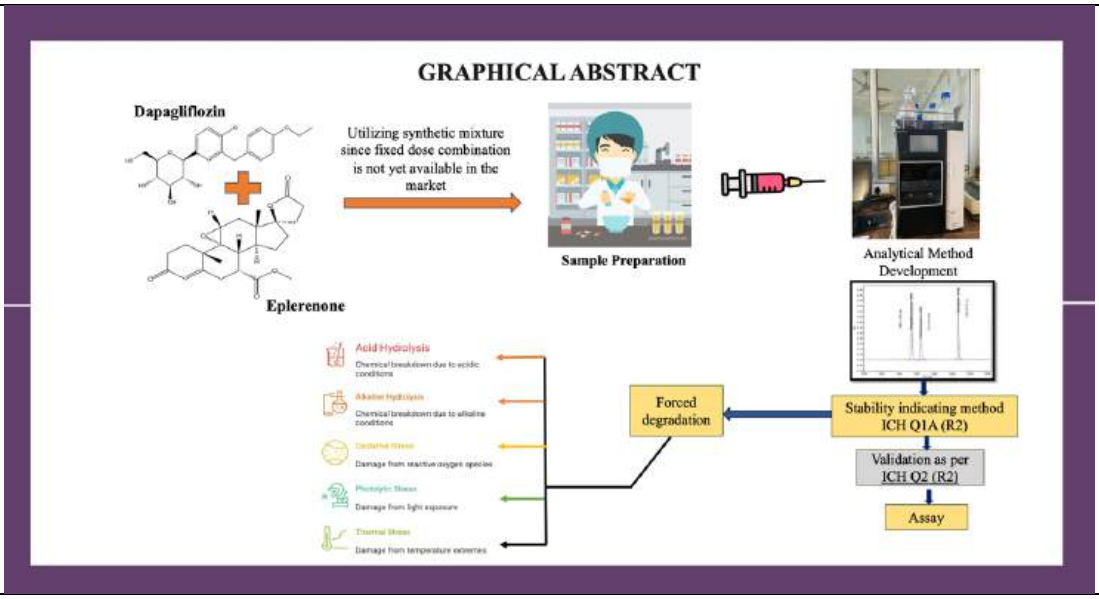
Table 1: Drug profile of Dapagliflozin and Eplerenone [4,5]

Parameters	Dapagliflozin	Eplerenone
IUPAC Name	(2S,3R,4R,5S,6R)-2-(4-chloro-3-(4-ethoxybenzyl) phenyl)-6-(hydroxymethyl) tetrahydro-2H-pyran-3,4,5-triol	Methyl (1R,2S,9R,10R,11S,14R,15S,17R)-2,15-dimethyl-5,5'-dioxospiro [18-oxapentacyclo [8.8.0.01,17.02,7.011,15] octadec-6-ene-14,2'-oxolane]-9-carboxylate
Chemical Structure		
Drug Class	sodium-glucose co-transporter 2 (SGLT2) inhibitor	antihypertensive
Synonyms	Dapagliflozine Dapagliflozina Dapagliflozin 461432-26-8 (2S,3R,4R,5S,6R)-2-(4-chloro-3-(4-ethoxybenzyl) phenyl)-6-(hydroxymethyl) tetrahydro-2H-pyran-3,4,5-triol	Eplerenon eplerenone Inspra 9,11-epoxy-7-(methoxycarbonyl)-3-oxo-17-pregn-4-ene-21,17-carbolactone Molecular Formula
Molecular Formula	$C_{21}H_{25}ClO_6$	$C_{24}H_{30}O_6$
Molecular Weight	408.9 g/mol	414.5 g/mol
Color/ Form	Color-White to light Form-crystalline powder form,	Color-White to off-White Form-crystalline powder
Solubility	Practically insoluble in toluene and n-hexane, slightly soluble in water and in aqueous	Very slightly soluble in water, Soluble in chloroform and dichloromethane

	solvents	
Log P	2.7	1.3
pKa	12.6	16.44
Half Life	12.9 hours	4-6 hour
Melting point	65-70°C (149-158°F)	242°C
Therapeutic Use	With proper diet and exercise dapagliflozin act as a sodium-glucose cotransporter-2 (SGLT2) inhibitor commonly used for managing type 2 diabetes mellitus by preventing the absorption of glucose in the kidneys. Dapagliflozin helps in reducing blood glucose levels by promoting the excretion of excess sugar through urine. However, it is not effective for individuals with type 1 diabetes or those who rely entirely on insulin therapy.	Eplerenone belongs to the general class of medicines called antihypertensives. It is used to treat hypertension (high blood pressure) alone or together with other medicine. This medicine is also used to treat heart disease like congestive heart failure (CHF) and heart attack
	Dapagliflozin and eplerenone combination therapy works through complementary mechanisms to improve kidney health and potentially reduce the risk of kidney failure.	
Storage Condition	At room temperature between 68°F to 77°F (20°C to 25°C)	At room temperature, between 68°F to 77°F (20°C to 25°C)

Table 2: Summary of Literature Review of reported methods [13-81]

Name of method	Dapagliflozin	Eplerenone	Dapagliflozin+ another drug	Eplerenone + another drug	Dapagliflozin + Eplerenone
UV spectroscopy	1	2	3	Not reported	Not reported
HPLC	3	1	9	1	Not reported
RP-HPLC	9	5	17	1	Not reported
HPTLC	1	Not reported	2	1	Not reported
LC-MS	1	Not reported	2	Not reported	Not reported
UPLC	2	2	2	Not reported	Not reported
TLC	Not reported	Not reported	1	Not reported	Not reported
UFLC	Not reported	1	Not reported	Not reported	Not reported
Official Method HPLC	Not reported	2	Not reported	Not reported	Not reported
Total Methods:69					



Graph 1: Graphical abstract

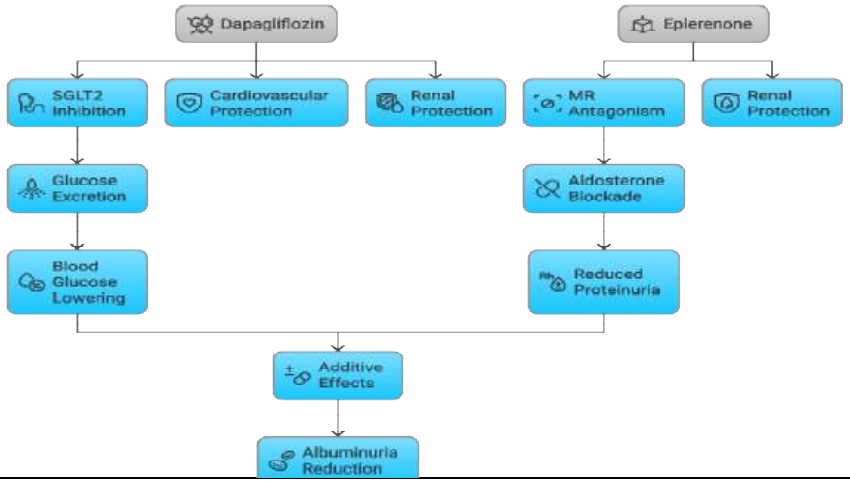


Figure 1: Combined action of dapagliflozin and eplerenone

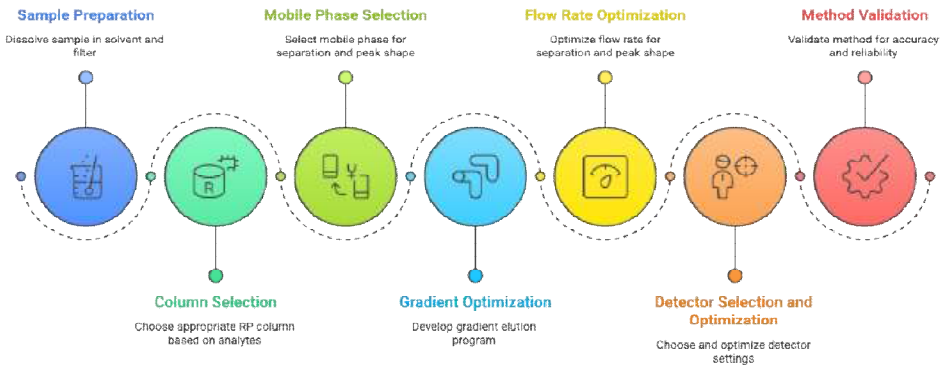


Figure 2: Steps involved in RP-HPLC

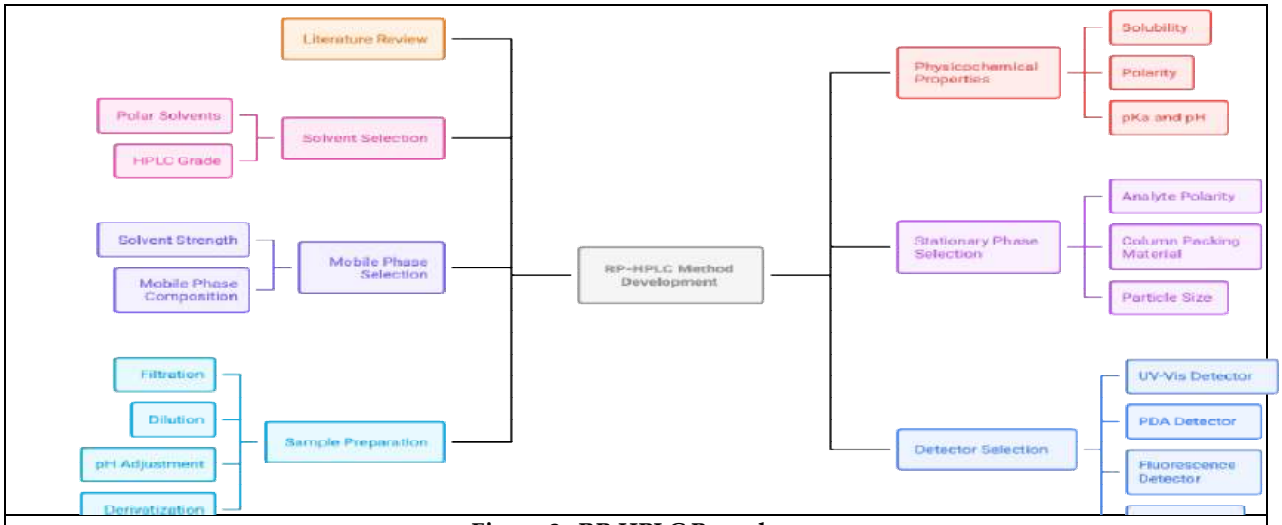


Figure 3: RP-HPLC Procedure

Figure 4: Analytical Method Validation Parameters

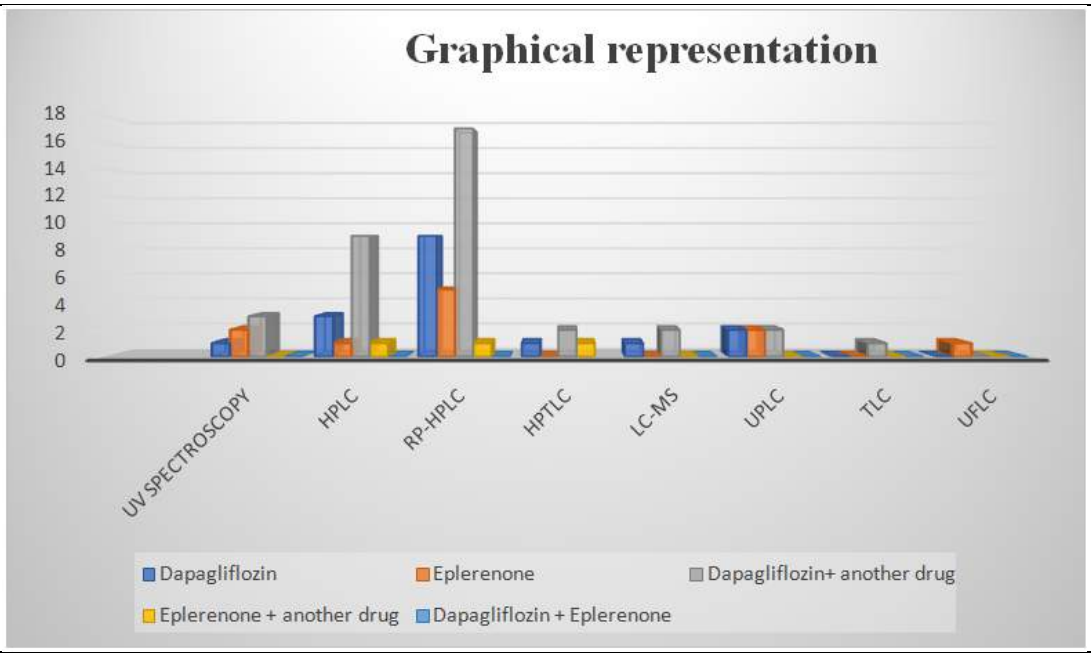


Figure 5: Graphical representation

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Shear and Impact Forces: A Comparative Analysis between Gymnastics and Wrestling

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Received: 28 Nov 2025 Revised: 13 Dec 2025 Accepted: 22 Dec 2025

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ABSTRACT

Sports like gymnastics and wrestling have a different way in which athletes interact with the ground,thus resulting in different loads and injuries. Gymnastics is all about giving the human body air, and it is done very quickly, physically giving large vGRF along with it. It does not only affect bones but also loading patterns and joint stability. Taking the abovementioned battle scenario, wrestling is that the majority consists of throws, and defense actions. however, the joint loads of knee, hip, and shoulder are subjected to high anterior-posterior shearing and rotation. A force plate and motion capture were used in this study to make a comparison between athletes of different disciplines in regard to shear and impact forces. The study was conducted with thirty trained participants which included 15 gymnasts and 15 wrestlers. The peak vertical force, shear force, loading rate, and impulse were finally assessed for sport-specific tasks. Gymnasts presented peak vertical forces, and loading rates that were greater in magnitude than the others, in contrast to this wrestler made shear forces that were significantly bigger. It is clear from the results of the research that sport-specific mechanical environments do have an impact on injury patterns, training strategies, and equipment design through their interaction with the body.

Keywords: gymnastics, wrestling, ground reaction forces, shear forces, impact forces, biomechanics, loading rate.

INTRODUCTION

Most of the time, high-intensity sports athletes are subjected to various external forces that can exceed normal physiological tolerance. These are from rapid movements such as jumping, landing, sprinting, tackling, throwing, or resisting an opponent. If the musculoskeletal system cannot adequately absorb or dissipate these forces, then there is a higher risk of potential acute injuries (e.g., ligament tears, joint sprains) and chronic injuries (e.g., overuse syndromes, cartilage wear, stress-related bone disorders) [1]. The competency of the body in managing these forces depends upon neuromuscular coordination, joint alignment, surface compliance, and technical execution [2]. Vertical impact forces could be one of the most important loading conditions in dynamic sports. They occur mostly during ground contact subsequent to jumps, dismounts, or rapid deceleration. Excessive vertical impacts may conduct high loads into the lower extremities, making them susceptible to ankle sprains, tibial stress fractures, patellofemoral pain, plantar fascia irritation, and early degenerative changes in knee cartilage. The magnitude and rate of the vertical forces determine the stress on joint structures. When forces are applied in a very short period, the body has less time to prepare protective responses such as greater joint flexion or muscular co-contraction [3]. Shear forces are those acting parallel to the supporting surface and result from sliding, pushing, pulling, grappling, and rotational activities. Such loads, particularly those related to twisting or valgus movements, stress the ligaments and soft tissues responsible for stabilization. Strong correlations exist between high shear forces and injuries to the ACL, meniscal tears, shoulder instability, and strain on the hip and lumbar regions. In contrast to vertical impacts, which are mainly gravity-driven, the application of shear forces is frequently a result of a sudden change in the opponent's movement or external contact [4].

Gymnastics consists of different aerial transitions, explosive takeoffs, and high-energy landings. The athletes get very high and rotate with a lot of momentum in the air as the main part of the trick, thus needing absolute control while landing. The vertical ground reaction forces have been measured during gymnastic dismounts and by far most studies report over (10–15 times) an athlete's body weight consistently. Such forces act in a very short time, often less than 100 milliseconds, giving very little opportunity for the active muscular absorption or adjustments in the joint position. The very quick application of the force increases the mechanical stress on the entire lower extremity-feet, ankles, knees, and spine-which is one of the reasons why gymnastics is one of the sports most prone to impact-related injuries [5]. Another arena of biomechanics is wrestling, which is characterized by constant physical contact, weight manipulation, and the application of force on the opponent. Takedowns, sprawls, lifts, and pins produce large horizontal shear loads and torsional forces across the joints. The rapid velocity and force in matches, coupled with the unpredictability of these interactions, are a great demand for neuromuscular control and joint stability. Hence, wrestling is highly linked to the occurrence of knee, shoulder, and cervical spine ligament sprains, as well as joint dislocations and soft-tissue trauma [6].

There is a vast amount of literature on gymnastics and wrestling, but not many studies have compared them through the lens of biomechanics. Previous research has done mostly pointing out the differences in injury occurrence, analyzing movements, or measuring force separately for each sport. Only a few have looked at the basic differences in mechanical environments, especially vertical vs. shear loading patterns [7]. It is essential to know these differences when the training strategies are developed for each specific sport, when the performance surfaces such as mats and landing platforms are optimized, and when the injury-prevention programs that target the specific needs of each discipline are designed. Thus, the main objective of this research is to determine the values of peak vertical forces, shear forces, loading rates, and vertical impulses in the case of both trained gymnasts and wrestlers. By doing so, the research will reveal the differences in force profiles and the shared biomechanical characteristics of the two sports, with a direct impact on athlete's training, performance, and safety in the long run.

MATERIALS AND METHODS

Participants

The examination involved thirty active male athletes, out of which 15 were artistic gymnasts and the other 15 were freestyle wrestlers. All the athletes were training and competing at the time of collecting the data. The average training age of the gymnasts was 8.4 ± 2.3 years, while that of the wrestlers was 7.9 ± 2.0 years, which reflects that both groups had considerable time of being exposed to sport-specific training loads. Before the start of the experiment, the participants were screened for eligibility, and the inclusion criteria were a minimum of five years of structured sport participation, the ability to safely perform high-intensity technical tasks, and no musculoskeletal injury six months prior to testing. Athletes with histories of major orthopaedic surgeries, chronic lower-limb injuries, or neurological conditions were not allowed to take part in the study. The athletes' written informed consent was obtained before their participation. Standardized instructions and safety guidelines were provided to ensure compliance and minimize risk during the testing procedures.

Protocols

In order to make a valid comparison between various sports, the athletes did the movements that represent the typical high-load conditions in their disciplines. In the case of gymnasts, these were the two vertical impact–dominant tasks they performed: (1) drop landings off a standardized height of 1.5 meters and (2) forward salto landings executed using competition-level technique. These actions were picked because during the execution, always generate great vertical ground reaction forces. Wrestlers, however, were subjected to two shear-dominant actions: (1) single-leg takedowns, which involve forward excessive driving force and contact with the opponent, and (2) defensive sprawls, which require quick hip extension and upper-body stabilization against horizontal load. Five successful repetitions of each assigned task were performed by each athlete, with a one to two-minute rest interval in between attempts to prevent fatigue. Prior to testing, a warm-up involving dynamic stretching and sport-specific drills was done to ensure readiness and decrease the risk of injury. The athletes were told to use their training or competition intensity, but to keep the correct form throughout the movements.

Instrumentation

Data gathering took place in a controlled indoor biomechanics laboratory that had measurement equipment perfectly in sync. Ground reaction forces were measured by a tri-axial force plate with a sampling rate of 1000 Hz, which made it possible to detect with great accuracy the rapid changes in vertical and horizontal forces during high-impact and shear-intensive tasks. To obtain three-dimensional joint kinematics, reflective markers were put on anatomical landmarks, and a 12-camera motion capture system working at 200 Hz was utilized. Thus, the accurate alignment of movement phases and force measurements was assured. Moreover, a high-speed video camera that recorded at 500 frames per second was used in correspondence to visually confirm critical events like initial contact, peak force time, and each task's end. The alliance of force plate, motion capture, and high-speed imaging made a comprehensive and a dependable dataset that supported the detailed biomechanical analysis of the movements in both gymnastics and wrestling.

Data Processing and Statistical Analysis

The raw data related to force and motion were exported and processed in MATLAB. Filtering of force signals was done through a sophisticated and complex zero-lag Butterworth low-pass filter of the 4th order with a frequency of 50 Hz as a cutoff so that noise was reduced but the true signal was preserved. Peak vertical ground reaction force, peak shear force, loading rate, and vertical impulse were the four primary variables extracted from each trial. The peak forces were determined as the highest values found within the vertical or horizontal force-time graphs, while loading rate was measured as the slope between the first contact and the peak force. Vertical impulse was derived from the vertical force used in the numerical integration. The values averaged from the five successful trials were taken for each athlete to create a representative measure.

Statistical methods were employed, and SPSS software was utilized for this purpose. The Shapiro–Wilk test was conducted to certify the normal distribution of all variables. As the normality assumptions held, independent t-tests were performed to compare the gymnastics and wrestling groups. Moreover, Cohen's d effect size was computed to characterize the magnitude of the differences which was further classified as small (0.2), medium (0.5), or large (0.8 or above). The significance of the statistics was determined to be $p < 0.05$ for all the comparisons. A comparative analysis showing the differences between gymnasts and wrestlers can be seen in Table 1, Figure 1 shows the Mean Value of Peak Vertical Force (N),Figure 2 shows the Mean Value of Peak Shear Force (N), and Figure 3 shows the Mean Value of Vertical Impulse (Ns).

RESULTS AND DISCUSSION

RESULTS

The outcomes of these comparisons are briefly outline below.

Ground reaction force characteristics of gymnasts and wrestlers were compared and the differences were very clear, and the differences were very clear and statistically significant. Gymnasts exhibited peak vertical forces of ground reaction substantially higher than that of wrestlers who averaged 3200 ± 450 N against 2100 ± 400 N with a significant p-value of (<0.001) and a large effect size (d = 2.62), thus indicating that gymnastics movements do not only load the athletes' bodies, but the vertical loads are much larger. However, wrestlers were found to have significantly higher peak shear forces (850 ± 150 N) as compared to gymnasts (600 ± 120 N) which was also a strong level of significance (<0.001) and a large effect size (d = 1.86), thus reflecting the shear-dominant nature of the wrestling actions. The loading rate values were also a point of differentiation between the sports; gymnasts reported very high loading rates ($1.8 \times 10^5 \pm 0.4$ N/s) as compared to the lowest rates in wrestlers ($0.9 \times 10^5 \pm 0.3$ N/s), thus the rapid force application during gymnastics landings was highlighted. Vertical impulse values were also higher in gymnasts (52.0 ± 7.5 Ns) than in wrestlers (38.5 ± 6.8 Ns), with a significant p-value (0.002) and a large effect size (1.67), indicating that gymnasts are subjected to greater total force over the time of landing phases. These results together suggest a clear marking of force profiles between gymnastics and wrestling; the former being the case of intense vertical impact loading, while the later being the case of high horizontal shear loading.

DISCUSSION

The study findings reveal basic biomechanical differences between gymnastics and wrestling that are mainly due to the nature of the technical and physical requirements of each sport. In the case of gymnasts, vertical ground reaction forces and loading rates were always significantly higher, thus confirming that gymnastics is an impact sport that involves high-velocity landings, aerial transitions, and very limited time for force absorption. The vertical loads that are so high cause stress on the lower body and spine, resulting in injuries like stress fractures, ankle sprains, and so on being more common. The steep loading rates in gymnasts mean that there are rapid deceleration forces that the musculoskeletal system has to bear within very short periods of time. Such conditions not only require but also demand great lower limb strength and perfect landing techniques to prevent high joint compressive forces or misalignments.

In contrast, wrestlers experienced shear forces that were specifically higher and showed how demanding grappling, takedowns, and changing directions, as well as opponents' forces, were. The vertical impacts in wrestling are not substantial, but the players do have to bear very strong anterior–posterior and mediolateral forces that they either must resist or generate to keep their balance, stability, and control. The high shear forces can account for the frequent occurrence of ACL injuries, meniscal tears, shoulder instability, and lower-back strain among wrestlers to some extent. The situation in wrestling is made more difficult by its spontaneous and often opponent-controlled nature, in which a particular moment of a live engagement could suddenly change the direction and amount of the forces. The athletes in each discipline will have specific loading environments that biomechanical load patterns highlight the

necessity for sport-specific injury prevention strategies [8]. The contrasting force profiles between gymnastics and wrestling not only point out the necessary conditioning but also the specific technical training interventions. The characteristics of gymnastics movements are such that it is more than ever essential to develop through eccentric strength mainly in the quadriceps, hamstrings, and calves for shock absorption during landings. One through which proper skill development leads to vertical force tolerance safely is the progressive height-based landing from the height of the chosen vertical force [9]. Proper joint alignment during landing may also be beneficial in minimizing the risk of injury due to excessive loading rates. On the other hand, wrestlers' interventions should aim to develop neuromuscular control, joint stability, and horizontal as well as torsional forces' resistance. Strengthening conditions can consist of drills struggling against shear-force, training for balance disturbance, exercises for core stability, and conditioning for rotational strength. Given that wrestling is extremely reactive and competition-oriented, simultaneously training in proprioceptive and balance exercises must be set up as a means of improving reflexive joint protective capabilities under the less predictable conditions of loading [10].

The results from the sports studies also point out the importance of correct surface and equipment design for both the disciplines. In the case of gymnastics, the landing mats should be designed in such a way as to manage force from vertical impact entirely and yet let the gymnast hold the technicality, precisions and even have a rebound when that is desired [11]. Mostly, hard grounds raise the risk of injuries by increasing the peak vertical forces, while very soft grounds may negatively affect the balance and make the internal joint loading higher. Hence, the need for a compromise between shock absorption and the responsiveness of performance to be offered. In wrestling, mats play an entirely different role. Mats must primarily prevent sliding so that shear load is not created; however, they should be soft enough so that during contact-based movements, horizontal and torsional forces can be easily absorbed. The proper thickness of the mat and the use of the same material over the entire area help to lower the stress on the knee, hip, and shoulder joints during takedowns, sprawls, and other movements that require defense. Maintenance and evaluation of the surface very regularly should be done and, besides, they are very important for the safety of athletes during repeated high-level intensity movements [12].

Even though this study can produce significant knowledge about the differences in biomechanics between gymnastics and wrestling, some drawbacks must be acknowledged. To begin with, all the examinations were conducted in a laboratory that was controlled, not considering the variability and unpredictability that come with the actual competition conditions. Forces during a performance, particularly in wrestling, can vary significantly due to the difference between the opponents, fatigue, and psychological factors being [13][14]. Furthermore, the population was made up solely of male national athletes, which means that the applicability of the results is limited to female athletes and younger groups. The movements that were tested were made uniform so that there would be no inconsistency, but this might have caused the natural variation in the technique to be [15] blocked. Future research will focus on incorporating in-competition monitoring, larger and more varied samples, wearable sensor technology, and longitudinal tracking to understand the development of cumulative loading exposure over time better.

CONCLUSION

The analysis of the biomechanical disparities between gymnastics and wrestling reveals the basic differences in their aspects' impact on the human body. Very high vertical impact forces and quick loading rates characterize gymnastics, mostly due to the combination of aerial skills and the high speed of landings. Thus, the lower limbs and spine experience a huge amount of stress that is directly connected to the high number of impact-related injuries suffered by gymnasts. On the contrary, the nature of wrestling invokes higher shear and torsional stresses through the dynamic contact, movements caused by the opponent, and quick changes in direction. These force patterns can be the reason for ligament strain, joint instability, and other soft-tissue injuries that are common among wrestlers. The findings of this comparative analysis serve to elucidate the mechanical conditions of both sports and to spotlight the necessity for sport-specific injury prevention approaches. Knowledge of such loading patterns informs targeted

training programs, athlete screening protocols, and appropriate surface and equipment designs matched to the demands of each sport.

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Table 1: Comparative analysis between gymnasts and wrestlers

Metric	Gymnasts	Wrestlers	P Value	Effect Size (d)
Peak Vertical Force (N)	3200 ± 450	2100 ± 400	<0.001	2.62
Peak Shear Force (N)	600 ± 120	850 ± 150	<0.001	1.86
Loading Rate (N/s)	$1.8 \times 10^5 \pm 0.4$	$0.9 \times 10^5 \pm 0.3$	<0.001	2.11
Vertical Impulse (Ns)	52.0 ± 7.5	38.5 ± 6.8	0.002	1.67

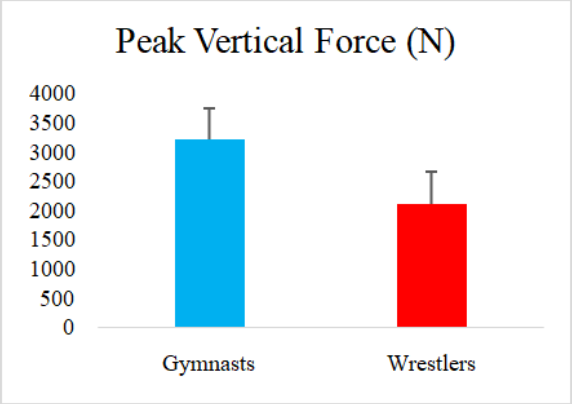

Figure 1: Mean Value of Peak Vertical Force (N)

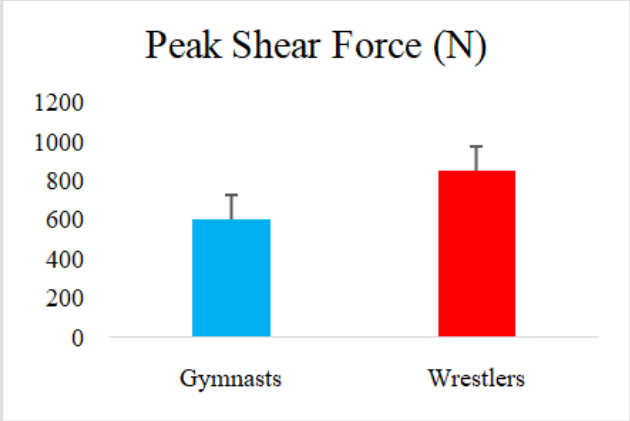

Figure 2: Mean Value of Peak Shear Force (N)

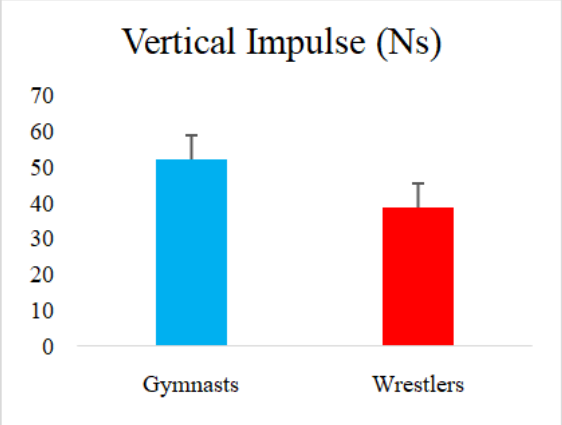

Figure 3 : Mean Value of Vertical Impulse (Ns)

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Physiochemical Parameters, Proximate Composition, Microbiological Quality and Antioxidant Properties of Margarine Produced from oil Extract of Coconut and Papaya

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Received: 30 Jul 2025 Revised: 19 Sep 2025 Accepted: 06 Dec 2025

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ABSTRACT

The present research work was carried out to study the formulation of the margarine extract the microbiological analysis of the margarine sample to determine the microorganisms loaded in the margarine extract through total heterotrophic bacterial count and coliform count and fungal enumeration of the sample. Proximate and physiochemical analysis of margarine formulated from coconut and papaya to identify the nutritional supplement of the compound of the extract. Phytochemical assay to evaluate that compounds present in the sample. The antimicrobial activity of the margarine extraction that was tested by pathogen organisms from margarine extract showed the inhibition of growth in pathogen organisms. Antioxidant activity also shown the radial antioxidant ability. The margarine extract can be used as a natural additive to enrich table spread margarine without affecting its properties while improving its oxidation stability. Anti- inflammatory shown the healing property to able to treat with margarine and so one can develop drugs for the treatment of inflammatory-related disease and its has the good healing properties to treat the injurious substances.

Keywords: Heterotrophic Bacterial Count, Coliform Count, Phytochemical, Margarine.

INTRODUCTION

Traditional medicine is especially common in underdeveloped countries because of its historical and cultural significance. For the treatment of a wide range of illnesses, they employ natural medicines and plant extracts. The World Health Organization's recognition of the extensive use of traditional medicine demonstrates its continued importance in global healthcare. One of the main benefits of conventional medicine is the application of plant extracts and their active components (Davis, 1994). Coconut oil, extensively used in both culinary and industrial realms, is distinguished by its high medium-chain fatty acid content, ranging from 46% to 48% (Marina *et al*., 2009). Coconuts offer nutraceutical advantages. Coconut juice demonstrates estrogenic effects and possesses antibacterial, antiviral, antidote, antioxidant, and antithrombotic properties (Esquenazi *et al*., 2002). These attributes make coconut- derived dietary supplements valuable for averting nutrient deficiencies and promoting overall health. Papaya is also known for its digestive benefits and is rich in manganese, offering advantages in preventing osteoporosis and bone fractures. The intake of papaya seed oil with a notable oleic acid composition has been associated with improved plasma lipid status. Oleic acid, found in the oil, has demonstrated potential in reducing cholesterol and plasma triacylglycerol levels without affecting plasma Low-Density Lipoprotein (LDL) cholesterol concentration. (Yao; Xu, 2021). Margarine, initially developed by French chemist Hippolyte Mege Mouries in the 1860s, originally relied on animal-derived fats, notably bovine fat. By the early 20th century, this progression culminated in the exclusive use of 100% vegetable oil, sourced from options like coconut, palm, melon, papaya and other sources. This transformation mirrored evolving consumer preferences and economic considerations within the margarine industry (Chrysan, 2005). As per the Codex International standard established in 2001, margarine is defined as a water-in- oil emulsion primarily composed of edible oils and fats. This standard outlines that margarine should consist of a minimum of 80% fats and a maximum of 16% water. It is a common practice to blend two or more different oils in margarine production, providing a customized approach to meet specific preferences and requirements (Codex, 2001).The formulation of margarine endetails blending water, additives like salt, and emulsifiers to maintain its quality. Emulsifiers serve three pivotal functions in the margarine production process, as elucidated (Hamilton, 1994). Firstly, they aid in establishing a stable emulsion, ensuring the harmonious integration of water droplets within the vegetable oil. Secondly, emulsifiers modify the crystalline structure of the vegetable oil, contributing to the desired texture of the end product. Lastly, they play a crucial role in preventing the coalescence of water droplets and minimizing splattering during the heating of margarine. The global production and consumption of margarine are experiencing an upward trend due to its lower saturated fat content compared to butter and its cholesterol-free attributes. The combination of coconut and papaya oils in margarine production offers opportunities to optimize resource utilization and product value, these oils present a promising alternative for margarine production, potentially enhancing its health benefits. This study aims to assess the microbiological quality and determine the physicochemical and proximate composition of the resulting margarine (Akubuenyi; Odey, 2022). Margarine finds application as a fat spread, in cooking, and in the production of bakery items (Reyes-Hernandez *et al*., 2007 and Lee *et al.,* 2008)**.** The current study serves as an initial screening phase focused to isolate and identify specific antibacterial compounds that exhibit plant-derived broad-spectrum antimicrobials and is a pioneering work on the antioxidant, anti-inflammatory and phytochemical analysis on the nature of margarine sourced from coconut and papaya extracts.

MATERIALS AND METHODS

Sample collection

The sample of fresh coconut and papaya sample were collected from local market. Coconut sample are coconut and flower and entire papaya sample were taken for extraction and analytical standard.

Extraction of margarine: (Sayed *et al*., 2009)

Margarine was produced from 100% coconut and papaya extract using the method described by Sayed *et al*., 2009. A basic recipe that include 81.7% oil blend, 0.3% emulsifier, 0.8% salt,0.9% skim milk powder, 0.2% flavour, 0.01%

antioxidant and 0.003% colour was used for margarine production. Emulsifier, antioxidant, flavor and colour was dissolved in the heated oil phase. Salt and skim milk powder were dissolved in water phase. The water phase was added gradually to the oil phase while agitating it to form a nice emulsion. For the solidification of margarine, the emulsion was stirred for 10 minutes and then cooled in ice bath containing 10% sodium chloride (NaCl). The emulsion was then mixed and solidified at a temperature of 110^0 C. the margarine sample stored in a refrigerator at 4^0C.

Microbiological Analysis

Preparation of peptone salt saline

Microorganism were isolated by serial dilution technique. 10µg of sample was suspended in 90ml of Peptone Salt Saline and mixed for 2minutes.

Determination of total heterotrophic bacterial count

Serial dilution (10^{-1} -10^{-5}) was prepared from margarine oil samples. 0. l ml was transferred from each selected dilution (10^{-2},10^{-3} and 10^{-4}) into sterile petri dishes in triplicates. The molten sterilized agar (Nutrient agar) were poured into the plates, swirled for even distribution of the inoculum within the agar medium and allowed to solidify and then incubated at 37°C for 24 hours. Thereafter, plates with colony growth were counted and expressed in colony forming unit per millimeter (CFU/ml).

Enumeration of total coliform count

Total coliform count of the samples was determined using the spread plate method on MacConkey agar medium. 0.1ml of the diluent from the samples was aseptically transferred into sterile petri dishes containing already sterilized MacConkey agar, and were swirled for even distribution. They were incubated at ambient temperature for 3-4 days. Plates with colony growth were counted and expressed in colony forming unit per millimeter (CFU/ml).

Determination of total fungal count

Total fungal count was examined using the spread plate method on Sabouraud dextrose agar (SDA). Exactly 0.1ml of the diluent from the samples was aseptically transferred into sterile petri dishes containing already sterilized SDA, and was swirled for even distribution. They were incubated at ambient temperature for 3-4 days. Plates with colony growth were counted and expressed in colony forming units per millimeter (CFU/ml).

Determination of Proximate Composition (Standard AOAC method)

The sample was analyzed for the various nutrient's constituent such as analysis of ash, sugars, carbohydrates, calcium, total solids, carbohydrates, calcium, acidity, crude lipid, crude protein, crude fibre, moisture, pH, energy and vitamin B_{12} by the methods of the Association of official Analytical Chemists.

Physicochemical Parameters (Standard IS method)

Physicochemical properties of oils are determine the acidity, Calcium and colour to know the quality, purity and identification of the margarine extract.

Antimicrobial Activity: (Kirby and Bauer 1950)

The disk diffusion method of Kirby and Bauer has been standardized and is a viable alternative to broth dilution methods for laboratories without the resources to utilize the newer automated methods for broth microdilution testing.

Antibacterial activity

The inoculum was standardized at 1 x 10^6 CFU/ml comparing with turbidity standard (0.5 MacFarland tube).A supply of cotton wool swabs on wooden applicator sticks was prepared. They were sterilized in tins, culture tubes, or on paper, either in the autoclave or by dry heat. The Assay was performed by agar disc diffusion method. For Bacteria: Muller Hinton Agar (MHA) and Blood agar medium is poured in to the petriplate. After the medium was

solidified, the inoculums were spread on the MHA plates with sterile swab moistened with the bacterial suspension of *Staphylococcus aureus, Bacillus pumilus, Escherichia coli, Salmonella sp* with a standard of Ampicillin (20µl/disc). Sterile samples (Disc form) and 20µl of Standard antibiotic (Ampicillin) disc as positive control were placed in MHA plates. The plates were incubated at 37ºC for 24 hrs. The antimicrobial activity was determined by measuring the diameter of zone of inhibition.

Antifungal activity (Seetharaman *et al.*,2021)

Stock cultures were maintained at 4°C on Sabouraud Dextrose agar Slant. Active cultures for experiments were prepared by transferring the stock cultures into the test tubes containing Sabouraud Dextrose broth, that were incubated at 48hrs at room temperature. The assay was performed by agar disc diffusion method. Antifungal activity of the extracts was determined by disc diffusion method on Sabouraud Dextrose agar (SDA) medium. Sabouraud Dextrose agar (SDA) medium is poured in to the petriplate. After the medium was solidified, the inoculums were spread on the solid plates with sterile swab moistened with the fungal suspension of *Candida sp*, *Aspergillus niger* with a standard of Amphoterin B (20µl/disc). Samples were placed over the plate. Amphotericin-B is taken as positive control. The plates were incubated at 37ºC for 24 hrs. Then antifungal activity was determined by measuring the diameter of zone of inhibition.

Antioxidant activity: (Naznin Ara and Hasan Nur 2009)

Antioxidant activity assay is based on the reduction of 1, 1-diphenyl-2-picrylhydrazyl (DPPH). Due to the presence of an odd electron it gives a strong absorption maximum at 517nm.As the electron becomes paired off in the presence of a hydrogen donor, i.e., free radical scavenging antioxidant, the absorption strength is decreased, and the resulting decolourization istoichiometric with respect to the number of electrons captured, the ability of the extract to scavenge DPPH radical was determined by the method described by Naznin Ara and Hasan Nur (2009).

Anti-Inflammatory assay: (Shinde *et al.*,1999)

Fresh blood was collected from the healthy volunteers. The collected blood w as mixed with equal volume of sterilised Alsever solution which act as an anticoagulant The sample was then centrifuged at 3000 rpm for 5 min and packed cells were washed with isosaline (0.85%, pH 7.2) and a suspension was made with isosaline (10% v/v). This was taken as HRBC suspension. The assay mixture contained 1.0 ml of phosphate buffer (0.15 M, pH 7.4), 2.0 ml of hyposaline (0.36%), 0.5 ml HRBC suspension and 1.0 ml of various concentrations of sample (200, 400, 600, 800 and 1000 µg/ml). For control solution, instead of hyposaline, 2.0 ml of double distilled water was added. The mixtures were incubated at 37°C for 30 min and centrifuged at 3000 rpm.

Qualitative Phytochemical analysis: (Seetharaman *et al.*, 2022)

Coconut and papaya plant extracts were analysed for the presence of the following phyto constituents such as tannins, saponin, flavonoids, alkaloids, quinones, glycosides, terpenoids, anthocyanine and Betacyanine, phenols, cumarins, starch, acids, cyanins, cardiac glycosides, proteins and carbohydrates using modified and standard protocol.

RESULTS AND DISCUSSION

Bacterial and fungal count of margarine produced from papaya and coconut oils:

The enumeration of the total heterotrophic bacterial counts of the samples showed that the self- made margarine had no bacterial load. The result of the total coliform count also revealed of no coliform contamination. The total fungal count also followed the same trend in fig.1,2,3.

Evalution of proximate and physiochemical composition

The results of the proximate analysis as contained in Table 1 revealed that the energy content was determined as 161.6, protein content 1.2, Lipid (fat) content 2.04, carbohydrate content 65.9, moisture content 12% and so on. The

result of the physicochemical analysis of the produced margarine revealed that it as shown colour 2 hazen, total soluble solid 100.5%,total titratable acidity4.11g/100g,viscocity 85g/100g , calcium 3.45mg/l, pH 7.09.in Table 2.

Antimicrobial activity

Antibacterial activity

Six microorganisms were tested for the antimicrobial activity of the margarine extraction were done and showed varying degree of inhibition activity. Gram negative organisms such as *E.coli* (15mm), *Salmonella* (10mm), and *Bacillus pumilus* (13mm) showed a moderate inhibitory activity, whereas the gram positive microorganisms showed a maximum inhibitory activity with *Staphylococcus aureus* (19mm) in table 3.

Antifungal activity

The antifungal activity was minimal in *Aspergillus niger* (4mm) and *Candida sp* (6mm) shown minimal inhibitory activity against the extract of margarine. Results indicated that the Gram positive microorganisms were shown the maximum inhibition than Gram negative organisms and the poor zone of inhibition was observed for the fungal strains in table 4.

Antioxidant activity (517nm)

Antioxidant potential of margarine extract from the plant sources were measured by DPPH radial scavenging method with different concentration (1000 µl, 500 µl, 250 µl, 150 µl) showed increased activity in extract concentration. The margarine extract showed 93% antioxidant at1000µl concentration, 90% antioxidant at 500µl concentration, 86% antioxidant at 250µl concentration and 48% antioxidant at 150µl concentration. Results were expressed as percentage inhibition of DPPH in table 5.

Anti-inflammatory activity (560nm)

Anti-inflammatory activity of margarine extract of the plant sources was measured by Human Red - Blood Cells (HRBC) methods with different concentration (1000µl, 500µl, 250µl, 125µl) showed the increases activity of the activity. The margarine extract showed 83.72% of anti-inflammatory at 1000µl concentration, 81.17% of anti-inflammatory at 500 µl, 77.05% of anti-inflammatory at 250µl, 38.84% of anti-inflammatory at 125µl. Results were expressed as percentages of anti-inflammatory activity in table 6.

Phytochemical analysis

The margarine extract of the plant source was analysed for the phytochemical screening. The presence of acids, alkaloids, anthrocyanine and betacyanine, carbohydrates, cardiac glycosides, flavonoids, quinones, saponins, tannins and Terpenoids and absence of coumarins, glycosides, phenols, proteins and starch have beenreported and the results were tabulated. Among them, alkaloids, carbohydrates, flavonoids and glycosides are of high amount, and proteins, phenols, starch are absent in table 7. The present study suggests that the physiochemical parameter, proximate composition, microbiological quality and antioxidant properties of margarine produced from oil extract of coconut and papaya. Odey, 2022 stated the potential of margarine production from blends of melon, coconut and palmkernel oil, and the microbiological qualities and physiochemical composition such as moisture (15.0±0.5), ash (35.0±0.5), crude (17.50±0.25), lipid (22.50±0.03), protein (1.218±0.01), and carbohydrate (7.78±0.01). The physicochemical analysis of the melon, coconut and palm kernel oil showed the low acid value of 1.159. The enumeration of total heterotrophic bacterial count revealed a low microbial count 2.6×10^{-3} CFU/g, total coliform count was 2.5×10^{-2} CFU/g and total fungal count 2.4×10^{-2} CFU/g from this study showed that the melon coconut and palm kernel oil extract have greater potential as industrial raw material beyond been consumed directly or indirectly as ingredient in food. The current investigation indicates that upon microbiological assessment, no bacteria suspected of causing infection were detected, and there were no isolated fungi present. This suggest that the microbial environment being examined displayed no signs of bacterial or fungal presence, possibly indicating a sterile or well-controlled environment. The edibility of margarine in s being safe for human food consumption is brought through the above finding of antimicrobial activity. Therefore margarine extracted from organic source can be an ideal food

for daily Recommended Dietary Allowance. Physiochemical and proximate composition of ash content in the sample was measured at 27%.

Ashing serves as a valuable methods for the analyzing the mineral composition of papaya and coconut extraction. According to the Recommended Dietary Allowance (RDA), adults are advised to consume a fat content of 10%, while infants require a slightly higher intake at 15%. However, a lipid (fat) content of 20% is beneficial in diets as it aids in the absorption of fat-soluble vitamins. With a calcium content of 3.45mg/l, these oils contribute to the building and maintenance of strong bones. The crude fiber content of 16.6% supports the maintenance of internal distention necessary for normal peristaltic movement of the intestinal tract. Additionally, the carbohydrate content of 75g suggests that coconut and papaya oil provide a low source of energy. An increase in the acid value often corresponds to the development of unpleasant flavors and aromas. As per the Codex standard, the maximum acceptable acid level in cooking oil or oil intended for consumption is 4mg KOH/g. The outcomes of this study suggest that margarine made from papaya and coconut oil could be considered suitable for consumption, indicating that the acidity levels are within acceptable bounds. Abbas, 2019 reported that the efficacy of goat margarine was examined against four distinct bacteria, revealing varied results in terms of inhibition zones. *Salmonella typhimurium* exhibited the highest zone of inhibition, while *Escherichia coli* showed the lowest. However, it's noteworthy that certain individuals have allergies to casein, a milk protein, which can trigger severe allergic reactions, including anaphylaxis. The current study investigated the antimicrobial activity, revealing potent effects against pathogenic strains of both Gram-positive and Gram-negative microorganisms. Among the bacteria tested, *Staphylococcus aureus* exhibited the highest susceptibility, while *Salmonella sp.* showed the lowest the lowest. Conversely, when compared to bacterial strains, the fungal strains displayed minimal zones of inhibition, with *Aspergillus niger* and *Candida sp*. exhibiting the least inhibition zones.

The study suggests that coconut and papaya margarine extracts possess natural antioxidant stability. Date kernel oil extracts, both cold and heat-treated, showed a moderate capacity (approximately 93%) for reducing free radicals in terms of anti-DPPH effect. Additionally, the study explores the anti-inflammatory activity of margarine extracts from coconut and papaya, indicating their potential healing abilities against harmful substances. Preliminary phytochemical analysis revealed the presence of various compounds such as alkaloids, anthocyanins, betacyanine, cardiac glycosides, tannins, terpenoids, and flavonoids in the margarine extracts from coconut and papaya. The study investigated using date kernel oil as a natural additive to enhance table margarine without changing its properties, while also boosting its oxidative stability. Date kernel oil contains potent antioxidants like phenolics, flavonoids, and carotenoids. Incorporating this oil into margarine enriched its antioxidant content without affecting its properties. Additionally, it improved the margarine's oxidative stability, as evidenced by a reduction in the DPPH radical. The study suggests that coconut and papaya margarine extracts possess natural antioxidant stability. Date kernel oil extracts, both cold and heat-treated, showed a moderate capacity (approximately 93%) for reducing free radicals in terms of anti-DPPH effect. Additionally, the study explores the anti-inflammatory activity of margarine extracts from coconut and papaya, indicating their potential healing abilities against harmful substances. Preliminary phytochemical analysis revealed the presence of various compounds such as alkaloids, anthocyanins, betacyanins, cardiac glycosides, tannins, terpenoids, and flavonoids in the margarine extracts from coconut and papaya.

ACKNOWLEDGEMENT

The authors are thankful to the Management and the Principal, Valliammal College for Women, Anna Nagar East, Chennai, Sasaam biologicals Pvt. ltd. for the facilities provided and continuous support.

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Table 1: Proximate composition of

S.no	Proximate parameters	Unit	Results
01.	Energy	Cal/100g	161.6
02.	Protein	g/100g	1.2
03.	Fat	%	2.04
04.	Carbohydrates	g/100g	65.9
05.	Iron	mg/100g	0.004
06.	VitaminB	g/100g	0.05
07.	Color	-	Darkbrown
08.	Totalsugar	mg/l	32.58
09.	Calcium	mg/l	0.34
10.	Fiber	mg/l	15.6
11.	Moisture	%	12
12.	Ash	mg/l	20

Table 2: Physiochemical composition of margarine produced from papaya and coconut produced from papaya and coconut

S.no	Physiochemical parameters	Unit	Results	Acceptable Limit
01.	Color	Hazen	2	Max-3
02.	Total dissoluble solids	mg/l	100.5	Max-2000

03.	Total titratable acidity	g/100g	4.11	-
04.	Viscosity	g/100g	5.85	-
05.	pH	25^0C	7.09	6.5-8.5
06.	Calcium	mg/l	3.45	Max75

Table 3: Antibacterial activity of margarine extract

Tested Microorganism	Zone of inhibition (mm) of margarine extract			
	250µg/ml	500µg/ml	1000µg/ml	Control(Ampicillin)20µg/ml
Salmonella sp	2	4	10	15
Bacillus pumilus	10	12	13	18
Escherichia coli	13	13	15	15
Staphylococcus aureus	14	18	19	22

Table 4: Antifungal activity of margarine extract

Tested Microorganism	Zone of inhibition (mm)of margarine extract			
	250µg/ml	500µg/ml	1000µg/ml	Control(AmphoterinB)20µg/ml
Aspergillus niger	2	3	4	10
Candida sp	3	3	6	4

Table.5: Antioxidant activity

Sample	Concentration	Control absorbance	Sample absorbance	Antioxidant activity(%)
Margarine	125	1.094	0.251	38.84
	250	1.094	0.669	77.05
	500	1.094	0.206	81.17
	1000	1.094	0.178	83.72

Table.6. Anti-inflammatory activity

Sample	Concentration	Control absorbance	Sample absorbance	Anti-inflammatory activity(%)
Margarine	125	1.919	0.961	49.86
	250	1.919	0.735	61.69
	500	1.919	0.712	62.89
	1000	1.919	0.498	74.04

Table7.Qualitative analysis on phytochemical analysis of margarine extract

	Qualitative study on phytochemical analysis of margarine extract	
S.NO	Test performed	Result
01.	Acids	Positive
02.	Alkaloids	Positive
03.	Anthocyaninand Betacyanine	Positive
04.	Carbohydrates	Positive
05.	Cardiac glycosides	Positive
06.	Coumarins	Negative
07.	Flavonoids	Positive
08.	Glycosides	Negative
09.	Phenols	Negative
10.	Proteins	Negative

11.	Quinones	Positive
12.	Saponins	Positive
13.	Starch	Negative
14.	Tannins	Positive
15.	Terpenoids	Positive

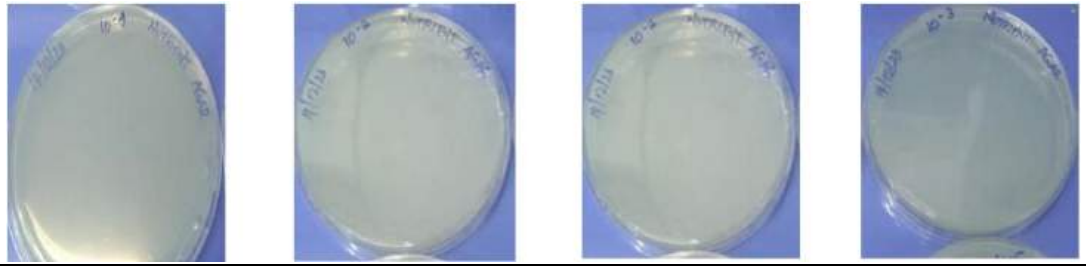

Fig.1. Total heterotrophic bacterial count

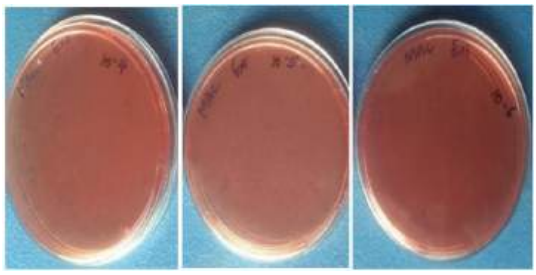

Fig 2. MacConkey agar plate

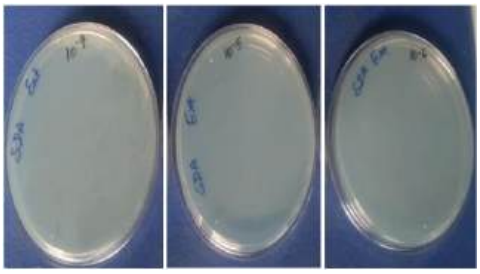

Fig 3.Sabouraud dextrose agar plate

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

A Study on Cybersecurity Awareness and Practices among College Students

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Received: 12 May 2024 Revised: 16 Oct 2025 Accepted: 06 Dec 2025

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ABSTRACT

In an era marked by pervasive digital connection, being aware of cybersecurity practices and raising college students' knowledge of them is crucial. With an emphasis on proactive cybersecurity measures and security hygiene, this research sought to evaluate college students' understanding of cybersecurity and current practices in this area. 470 college students from Coimbatore's top five universities participated in a survey that was administered using a stratified random sample approach. The study aimed to determine the degree to which college students follow security hygiene guidelines and participate in proactive cybersecurity initiatives. The survey provided important insights into the demographic makeup of the respondents. The results of this study offer insightful information about college students' current cybersecurity practices and awareness, which can guide the creation of focused interventions meant to improve cybersecurity education and promote a cybersecurity culture in young people.The results of this study provide insightful information about college students' current cybersecurity practices and awareness, which can guide the creation of focused interventions suggests to enhance cybersecurity education and promote a cybersecurity civilization in young people.

Keywords: Cybersecurity, Awareness, Practices, College Students, Cyber Threats.

INTRODUCTION

In recent years, almost everyone uses the Internet in every part of their everyday lives. The prevalence of cyber threats has grown to be a serious problem in the constantly evolving landscape of technology and digital communication. Students are more susceptible to cyberattacks as more college campuses make use of digital platforms for instruction, communication, and information exchange. With an emphasis on understanding the predominant behaviours and awareness levels among students, the project "A Study on Cybersecurity Practices and Awareness Among College Students" aims to explore the cybersecurity environment within the college demography. We have chosen college students as our target demographic for the following reasons: College students utilize technology and the Internet for two main purposes: socializing and education. And also, their security-aware actions will have a profound and long-lasting effect on society. In addition to the reality that college students utilize technology and the Internet primarily for socializing and education, we have chosen college students as our target demographic. Along with using several other services like video calls, virtual healthcare and education, and business and banking establishment, people can also engage with friends and family online. Beyond all of these benefits, there are drawbacks as well. For example, cyberattacks, which are a worldwide problem these days, might compromise system security and jeopardize the world economy. To safeguard sensitive data against well-publicized security breaches, an effective cybersecurity plan is therefore crucial. In addition, as the number of cyberattacks rises, businesses and institutions particularly those handling data pertaining to health, finances, or national security need to implement robust cybersecurity procedures and safeguards to safeguard their confidential and private clientele.

REVIEW OF LITERATURE

The preference for information security awareness training is growing beyond the scope of information technology college curriculum, as cyber risks continue to expand at an exponential rate. (Slusky, L., and Partow-Navid, P.,2012). There prevails an unsatisfactory situation towards the security issues like password use, malware, social engineering, phishing, and internet scams etc, (Muniandy, L., Muniandy, B., and Samsudin, Z. 2017). In these days students are ready to have a basic knowledge on cybersecurity, but they might not be aware of how to safeguard their information (Alqahtani, M. A. 2022). Furthermore, it seems that the majority of universities lack an ongoing cybersecurity awareness program that would increase students' understanding of how to defend oneself against online attacks (Garba, A., Sirat, M. B., Hajar, S., and Dauda, I. B. 2020). Also, by practicing highly effective internet connectivity practices, these data and security breaches can be mitigated. (Baraković, S., and Baraković Husić, J. (2023).

Statement of Problem

College students are currently living in an era of frequently encountered digital connectivity and rapid technological innovation, which puts them at danger from growing cybercrimes. Due to their increased dependence on digital platforms for social, academic, and personal activities, this group is more vulnerable to identity theft and phishing attempts, among other cybersecurity risks. The apparent lack of understanding among college students about security issues and tactics currently is the challenge at hand. This lack of understanding increases students' privacy and security at critical risk, increased the possibility of monetary losses, data breaches, and misused personal information. In this digital era, issues pertaining to cybersecurity has become increasing critical, especially among college students. Though college students are increasingly dependent on digital platforms for their academic pursuit, there still exist a gap in understanding cybersecurity awareness and practices among college students. Hence this study addresses the gap by investigating the following questions

1. What are the prevailing cybersecurity practices adopted by college students?
2. What is their level of awareness on common cyberthreats
3. What are the cybersecurity practices adopted in protecting personal and academic information?

OBJECTIVES

- To know the existing cybersecurity practices among college students.
- To understand the level of awareness on cybersecurity threats.

METHODOLOGY

This study employs Descriptive research design to explore the cybersecurity practices and awareness among students of selected five colleges in Coimbatore City. PSG College of Arts and Science, PSGR Krishnammal College for Women and Kongunadu Arts and Science College, Krishna Arts and Science College and Government Arts College, Coimbatore were selected for the study based on NIRF Rankings 2023. Stratified Random Sampling Technique is adopted and 100 respondents from each college was collected. Out of 500 respondents selected for the study, 470 responses were included in the study remaining unfilled and incomplete responses were rejected. Statistical tools such as simple percentage analysis and factor analysis was applied to derive the results.

SURVEY RESULTS, ANALYSIS AND DISCUSSIONS

A sample of 470 college students from top five colleges in Coimbatore was surveyed adopting stratified random sampling technique. Among 470 respondents 257 (54.7%) of the respondents are female, 150 (31.9%) of the respondents fall under the age group of 18 – 19 years and 259 (59.1%) of the respondents belongs to arts stream. , 274 (58.2%) of the respondents have a neutral rate of awareness level towards cybersecurity threats, 339 (72.1%) of the respondents have not experienced a cybersecurity incident, 183 (38.9%) of respondents occasionally update their software and operating system as safety measures, 131 (27.8%) of the respondents use pin as authentication mechanism, 161 (34.2%) of the respondents stay informed about cybersecurity threats by receiving updates from their colleges and universities and 285 (60.7%) of the respondents are very much concerned about the security in their digital information at present and in future.

Factor Analysis

Factor Analysis is applied to reduce the complexity of data. When there are more variables on a phenomenon under study, then identifying one, two or few variables that influence the phenomenon under study is involved. There the variables are to be reduced to few factors (Latent Variables) which can be taken as constructs (factors) that influence the phenomenon under study. In this study, factor analysis has been applied to find the underlying dimension (factors) that exists in the 9 variables relating to existing cybersecurity practices. Therefore, factor analysis is applied to find the existing cybersecurity practices among college students. Using SPSS software, these factors can be obtained. Tables 1.(a) and 1.(b) explain the steps to get the factors. Table 1.(a) states the KMO and Bartlett's Test. KMO – Bartlett measure of sampling adequacy is an index used to test the appropriateness of the factor analysis. The KMO is 0.779, and the Chi-square statistics is significant (<0.05). This means the factor analysis is appropriate for this data. Table 1.(b) discuss the Extraction Communalities. Extraction communalities are estimates of the variance in each variable accounted for by the components. The communalities in Table 1.(c) are all high except 2 variables, which indicates that majority of the extracted components represent the variables as well. Table 1.(c) represents total variance for the selected data. The percentage of total variance contributed by the components is given in 1.(d). The percentage of total variance contributed by the first components is 44.900%, by the second component is 12.688. Thus, there are two components for the given set of variables. Table 1.(d) reveals the rotated component matrix. The rotated component matrix gives the variables belonging to each component. The maximum of each row (ignoring –ve sign) indicates that the respective variable belongs to the respective component. Table 1.(e) exhibits the factors extracted from factor analysis. Based on the rotated component matrix two factors and its underlying items are summarised. Table 1.(e) explores the factors extracted from factor analysis related to cybersecurity practices among college students. Thus, among 9 variablesselected for this study, using principal component analysis, the factors have been reducedto two-factor model, and each factor has been given a name, which is associated with thecorresponding

variables based on the values obtained from the rotated component matrixtable. 'Proactive Cybersecurity Practices' are the most important cybersecurity practices followed by the college students . The second cybersecurity practices followed by the college students is 'Security Hygiene Measures'. In conclusion, 'Proactive Cybersecurity Practices' and 'Security Hygiene Measures' and the Cybersecurity practices followed by the college students.

CONCLUSION

The study on cybersecurity practices and knowledge among Coimbatore college students offers important new information on how prepared this group is for cyberattacks right now. The study aims to evaluate current cybersecurity measures and knowledge levels regarding cyber dangers using a thorough survey that included 470 college students from the top five universities in the region. The findings show that college students have varying levels of cybersecurity knowledge and behaviors. There is still a sizable disparity in the implementation of proactive cybersecurity measures, even though a sizable number of respondents showed a basic grasp of cybersecurity concerns.The significance of improving proactive cybersecurity practices and security hygiene procedures among college students is highlighted by key findings. Even though cyber risks are common, a significant proportion of participants could not possess the necessary tools to safeguard themselves from possible assaults. The introduction of comprehensive cybersecurity education programs catered to college students' requirements is one of the recommendations arising from this study. It is also reported that most students are aware of possible consequences. These courses ought to emphasize teaching useful cybersecurity skills, encouraging ethical online conduct, and increasing public knowledge of new and emerging cyberthreats. The outcomes of this research highlight the value of giving cybersecurity education top priority and encouraging college students to adopt a proactive cybersecurity mentality. Through the implementation of focused actions and the resolution of identified gaps, we can reduce the potential dangers connected with cyber-attacks and foster a more secure digital future for all.

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Table 1.(a): KMO and Bartlett's Test

Kaiser-Meyer-Olkin Measure of Sampling Adequacy.		**.779**
Bartlett's Test of SpheriUrban	Approx. Chi-Square	438.212
	df	36
	Sig.	**0.000**

Table 1.(b): Extraction Communalities

	Initial	Extraction
Regular updation of device software to the latest versions	1.000	.658
Strong and unique passwords for online accounts	1.000	.613
Cautious in sharing personal information online	1.000	.607
Use of two-factor authentication (2FA) for online accounts	1.000	.609
Frequent use security features in devices, such as fingerprint or facial recognition	1.000	.661
Maintaining backup of important files and data	1.000	.535
Familiarity of cybersecurity tools	1.000	.683
Reporting of suspicious activities to responsible authority	1.000	.451
Basic knowledge on cybersecurity best practices	1.000	.367

Table 1(c): Total Variance Explained

Component	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	4.041	44.900	44.900	4.041	44.900	44.900	2.687	29.853	29.853
2	1.142	12.688	57.588	1.142	12.688	57.588	2.496	27.734	57.588
3	.884	9.826	67.413						
4	.835	9.281	76.695						
5	.625	6.948	83.642						
6	.480	5.333	88.976						
7	.397	4.407	93.383						
8	.358	3.978	97.361						
9	.238	2.639	100.000						

Table 1.(d): Rotated Component Matrix

	Component	
	1	2
Regular updation of device software to the latest versions	.106	**.804**
Strong and unique passwords for online accounts	.539	**.568**
Cautious in sharing personal information online	**.770**	.116
Use of two-factor authentication (2FA) for online accounts	**.756**	.194
Frequent use security features in devices, such as fingerprint or facial recognition	**.798**	.154
Maintaining backup of important files and data	**.582**	.443
Familiarity of cybersecurity tools	.125	**.817**
Reporting of suspicious activities to responsible authority	.245	**.625**
Basic knowledge on cybersecurity best practices	.412	.444

Table 1(e): Factors Extracted from Factor Analysis

S.No	Variable Included	Factor Name
F1	Cautious in sharing personal information online	Proactive Cybersecurity Practices
	Use of two-factor authentication (2FA) for online accounts	
	Frequent use security features in devices, such as fingerprint or facial recognition	
	Maintaining backup of important files and data	
F2	Regular updation of device software to the latest versions	Security Hygiene Measures
	Strong and unique passwords for online accounts	
	Familiarity of cybersecurity tools	
	Reporting of suspicious activities to responsible authority	

RESEARCH ARTICLE

Transactions on Affective Computing: A Bibliometric Analysis

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Received: 12 Aug 2025 Revised: 15 Nov 2025 Accepted: 11 Dec 2025

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ABSTRACT

IEEE Transactions on Affective Computing (TAC) is a prestigious international journal, indexed in Scopus, dedicated to publishing research on the design of systems capable of recognising, interpreting, and simulating human emotions and related affective phenomena. This paper provides a thorough overview of the works published in TAC from 2010 to 2024. The main aim of this research is to chiefly determine the publication trend of TAC (IEEE Transactions on Affective Computing) and their citation framework. This paper presents the findings of a bibliometric study of 1032 papers published in TAC between 2010 and 2024. An insightful examination of the TAC publications is performed to ascertain the bibliometric parameters like the citation framework of the journal (a summary of the citation structure is provided), co-citation analysis, annual distribution of publications, yearly citations, yearly trend of significant terms, co-authorship networks, geographic analysis of the sources, country-specific historical and quantitative analysis, along with the most cited papers.

Keywords: Citation analysis, Authorship pattern, Bibliometric studies, Publication trends, Computer

INTRODUCTION

The computer science and application community are expanding tremendously through the contribution of high-quality research and novel discoveries. The accuracy of these research works is validated and regulated by the established journals. The IEEE Transactions on Affective Computing is an international, interdisciplinary journal focused to publishing research findings on the development of systems capable of recognising, interpreting, and simulating human emotions and associated affective phenomena (Muhuri *et al*., 2018). The journal disseminates original research on the principles and theories elucidating the influence of affective factors on human-technology

interaction. It emphasises the role of affective sensing and simulation techniques in enhancing our comprehension of human affective processes, and the design, implementation, and evaluation of systems (List of IEEE Publications - Wikipedia, n.d.). The research papers in this journal can be generally classified into several subject areas like Computing and Processing, Robotics and Control Systems and Signal Processing and Analysis. According to the 2023 Journal Citation Report published in June 2024,the journal met the following matrices:Journal Impact Factor (JIF): 9.6; 5-Year Impact Factor: 11; and #1 position in the field of cybernetics and computer science (IEEE Transactions on Affective Computing, n.d.). Pritchard (1969) defined bibliometrics as "the application of mathematical and statistical methods to books and other media." It involves analysing a compilation of articles that includes bibliographic details such as authors, co-authors, publication dates, Publication Country, subject keywords, and citations (Kumar, 2014). The recent bibliometric application is particularly significant as publication and citation metrics are increasingly utilised as performance indicators for assessing the quality of research conducted by individuals or groups of researchers affiliated with the same or various institutions. In the present paper, the researchers applied bibliometric techniques to the articles published in TAC during the last years (2010 – 2024) to find out the citation framework of the journal, co-citation analysis, annual distribution of publications, yearly citations, yearly trend of significant terms, co-authorship networks, geographic analysis of the sources, country-specific historical and quantitative analysis along with the most cited papers. With the help of these parameters, the researchers tried to find out the present trend of the subject concerned in the journal (Udo-Anyanwu, 2018).

LITERATURE REVIEW

The literature review is typically considered a significant indicator for assessing the growth pattern of the discipline and the extent of scientific research achievements and contributions. Wang *et al*. examines trends in IEEE Transactions on Affective Computing research through statistical literature analyses and citation frequency over time (Wang *et al*., 2021). Preeti and Kumar, in their literature review seek to examine bibliometric studies on research data management and delineate main findings and topics (Sajovic and Boh Podgornik, 2022).The structure and development of a variety of research topics, including visualisation education research, have been extensively studied with science mapping (Wang *et al*., 2021). The world community is eagerly awaiting advancements in AI technology, with much of the current research centred on the potential applications of AI in education (Kavitha *et al*., 2024).Citation analysis, productivity analysis, and collaborative analysis are three common methodologies employed in bibliometric literature (Variant Anna *et al*., n.d.). Computer science, as a field of data processing, excels in data manipulation and information delivery to support decision-making (Supriyadi, 2022). Research on the utilisation and analysis of human-computer interaction (HCI) technologies in healthcare has markedly intensified, illustrating the substantial potential of HCI to enhance medical services, improve patient experiences, and advance health management (Zhao *et al*., 2024). The field of artificial intelligence (AI) in radiology is progressing rapidly. Artificial intelligence has been integrated into breast imaging in practical settings, and various studies have been conducted in this field(Singh and Healy, 2024). Anandhalli and Bhalappa, in their study in 2021 investigates the research output performance of Cloud Computing Technology published in the Scopus database from 2007 to 2019 (Bhalappa and Dr, 2021). Ashrafuddin and Singh. offers a scientometric and keyword-centric examination of research conducted in the field of computer science (CS) within the SAARC area during the past 25 years (Uddin and Singh, 2014). Virtual reality (VR), as an emerging technology in computing, has been extensively utilized in the medical sector and possesses significant developmental potential and application value. Li *et al*. analyse the worldwide and domestic outputs of the principal initiatives using diverse scientometric indicators and methodologies (Li *et al*., 2022). Huangaims to perform a retrospective bibliometric analysis of works concerning rehabilitation medicine that utilize virtual reality technology (J. Guan and He, 2005). An evaluation of the Journal of King Saud University-Computer and Information Sciences (JKSU-CIS) from 2004 to 2014 has been carried out using a scientometric approach (Huang *et al*., 2016). Roshani, Saeed, *et al*. carried out a study where the goal is to model and analyse the relation between research funding and citation-based performance in science to predict the diffusion of new scientific results in society (Hussain, 2017). Farshid, Abedi, and Jafari conducted a study with the objective is to determine the characteristics of scientific products in the field of small-data that are indexed in the Web of Science database and to explain its

application based on the identification of the terms of scientific products connected to this subject in a manner that is distinct from the scientific fields (Roshani *et al*., 2021). Boudry *et al*. carried out research to report on the trends in scientific production and publication, as well as to identify the journals, countries, international collaborations, and important MeSH terms that are involved in artificial intelligence research and its application to ophthalmology (Boudry *et al*., 2022). Luo, DeWitt and Alias present a scientometric review of academic articles to examine the intellectual environment and evolutionary traits of TC research globally from 2001 to 2020 (Luo *et al*., 2022)(Farshid *et al*., 2022). In present paper, the researchers try to adopt best possible methodology for finding the growth parameters of articles published in TAC during 2010 to 2024.

OBJECTIVE OF THE STUDY

There remains a deficiency of written literature regarding the contributions of IEEE Transactions on Affective Computing globally. This analysis addresses the gap by examining computer science articles from 2010 to 2024. The aim of the current research is to identify the prevailing research trends in computer science from 2010 to 2024. The study aims to uncover newly developing research fields in the field of computer science.

a. To find out the total annual output of scholarly publications in the journal (Year-wise).
b. To identify the most cited contributions of the journal.
c. To ascertain the institutional affiliation of the writers.
d. To ascertain the geographical distribution of the articles.
e. To analyse the authorship pattern including their country of origin, affiliating universities, co-authors etc.
f. To analyse the citation pattern including total citation, average annual citation, total SCOPUS citations, total Google citations etc.

RESEARCH METHODOLOGY

This section outlines the complete process and methodology utilised in doing the bibliometric analysis, encompassing the research questions, the methods and software applied, the data sources, and the dataset development. Procedure of the study based (Table 1). The yearly research output of Transactions on Affective Computing form 2010 - 2024 is shown in Table 2 and Figure 1. For the years 2010–2024, this info graphic compiles data from a single publication. There are 1,032 papers in total, with a growth rate of 20.38 percent every year. With 2,694 writers and an international collaboration rate of 34.59%, each publication averages 4.31 co-authors. Just one person writes all of the 22 documents. There are 8,296 keywords in all, including those used by authors and algorithms. The papers reference 56,503 sources, with each paper averaging 50.47 citations. With an average age of 4.79 years, these documents are from very recent, extensive research. Main Information on Affective Computing (Table 2). Main information on affective computing (Fig. 1). Figure 2 illustrates a flawed bibliometric study of IEEE Transactions on affective Computing, indicating a recent rise in interest in this field, likely attributable to developments in artificial intelligence, human-computer interaction, and applications of emotional computing. The post2020 surge corresponds with the growing global research on AI-facilitated emotional intelligence and affective systems. It is possible that a change in publication strategy or a stabilising phase Transactions on Affective Computing is behind the fall in 2024.

This trend in publishing in Transactions on Affective Computing is a reflection of the rising profile and relevance of affective computing in cutting-edge artificial intelligence studies. In the first few years, the trend shows a slow but consistent increase, and then it starts to really take off about 2020. In 2022 and 2023, there was a noticeable increase, reaching its highest point in 2023 when the number of publications peaked. In 2024, production dropped slightly from the levels seen before 2020, although it was still far higher than before. Table 3 and Figure 3 and 4 demonstrate the Total Publication, Average Citation and Total Citation counts for succeeds published in IEEE Transactions on Affective Computing from 2010 to 2024. The examination reveals substantial rise in publications in IEEE Transactions on Affective Computing from 2020 to 2023. The total number of publications increased from 59 in 2020 to a maximum

of 244 in 2023. Nonetheless, there was a reduction to 161 publications in 2024. Nevertheless, citation metrics indicate a contrasting trend, as the average citations per manuscript have declined consistently from 211 in 2010 to merely 4 in 2024. This signifies a considerable increase in publication volume, accompanied by a decrease in citation impact per piece, especially post2020. The reduction in average citations may result from publication saturation or diminished novelty in current research.

The interval from 2022 to 2024 exhibits accelerated publication increase accompanied by diminished citation impact, indicating a potential necessity for improving the quality of contributions. The increase in publications is inversely correlated with the average citations per paper. The average citations have steadily declined from a peak of 225 in 2012 to only 4 in 2024. This drop indicates that although the quantity of published articles has risen, the influence of each publication has substantially decreased. The examination of Table 3 and Figure 3 to 4 reveals a distinct trend of rising articles in the IEEE Transactions on Affective Computing from 2010 to 2024. The number of articles stayed generally constant from 2010 to 2019, with minor variations between 12 and 45 publications annually. A significant increase commenced in 2020, rising from 59 publications to a zenith of 244 in 2023, subsequently declining to 161 in 2024. The abrupt increase in publications from 2020 onwards may be ascribed to the heightened interest in affective computing, developments in artificial intelligence, or enhanced accessibility to publishing. The diminished citation impact suggests that recent works may either lack originality or necessitate additional effort to garner citations. The substantial publication total in 2023 (244 papers) coupled with an average of only 17 citations suggests a possible oversaturation or a prioritisation of quantity over quality. Table 4 and Figure 5 enumeration the most prominent writers of IEEE Transactions on Affective Computing according to overall and fractional article contributions. LI Y's fractional contribution of 5.33, despite co-authoring 29 publications, is significant. LI X (22 papers, 3.52 fractionalisation) and BUSSO C (19 articles, 7.54 fractionalisation) are comparable, with BUSSO C displaying a more considerable contribution. ZHANG X, WANG S, and ZHAO G have important outputs; however, their relative contributions indicate collaboration.

The variation between total and fractionalised publications highlights the impact of authors on research. Some researchers work independently, while others participate in collaborative efforts. Chinese surnames signify significant contributions from Chinese institutions, highlighting the region's pivotal role in emotional computing research. The authors are expected to improve emotion recognition, multimodal artificial intelligence, and human-computer interaction. Table 5 and Figure 6 exhibit the leading affiliations in IEEE Transactions on Affective Computing based on publication count. University of Science and Technology of China (72) and South China University of Technology (68) rank behind Tsinghua University, which has 84 publications. China has made major advancements in the field of emotional computing research, as demonstrated by this position of strength. Lanzhou University (56) and Sun Yat-Sen University (50) further reinforce China's dominance in this domain. In addition to China, the University of Oulu in Finland and Nanyang Technological University in Singapore are notable contributors. The University of New South Wales (34) and Xi'an Jiaotong University (30) possess a notable presence. The presence of Chinese institutions signifies significant governmental and academic investments in artificial intelligence and human-computer interaction research. Contributions from Europe (University of Oulu) and Australia (UNSW) signify a growing worldwide interest in emotional computing. The works that are most frequently cited in IEEE Transactions on Affective Computing are listed in Table 6, which is arranged according to the overall number of citations as well as the number of citations on Google Scholar. It is remarkable that Koelstra *et al*. (2012) has received 3,619 total citations and 5,101 citations on Google Scholar, which is suggestive of the foundational impact it is having on affective computing research during the preceding few years.

Mollahosseini *et al*. (2019) (1,312 citations) and Calvo *et al*. (2010) (1,311 citations) are two additional publications that have received an extensive number of citations. Both of these individuals have made significant advancements in the field of emotion recognition and affective computing. The most significant normalised citation score (20.36) is displayed by Li S (2022), which indicates that they have had a substantial influence in recent times. The works of Eyben (2016) and Soleymani (2012) are of considerable importance, demonstrating consistent citation rates over time. The ranking encompasses both foundational early publications and contemporary impactful studies, illustrating a

fair progression of the discipline. Google Scholar citations typically surpass total citations, indicating extensive academic and industrial impact outside IEEE-indexed publications. The analysis of Table 7 and Figure 7 illustrates the distribution of articles, Single Country Publications (SCP), and Multiple Country Publications (MCP) in IEEE Transactions on Affective Computing according to the countries in which they were published. With 281 articles, including 204 SCPs and 77 MCPs, China is in the lead by a wide margin to its competitors. Based on this dominance, it appears that China is quite active in the field of emotional computing research, and it has a great propensity for cooperation between national organisations.

Nevertheless, it also keeps a decent level of international collaboration, as demonstrated by the fact that it has 77 MCPs working together. Following closely behind with 114 articles, 96 SCPs, and 18 MCPs is the United States of America. Due to the relatively low number of MCPs, it may be deduced that the majority of research conducted in the United States is conducted within the country, with just a little amount of collaboration taking place with other countries. By supplying 55 articles, the United Kingdom demonstrates a balanced approach, with 32 SCPs and 23 MCPs among its contributions. This suggests that there is a combination of national and international relationships that is working well. There are between 31 and 33 articles contributed by Germany, Australia, and France respectively; nevertheless, Germany and Australia have a significantly higher number of MCPs compared to SCPs, which indicates that they have collaborated more than France and Australia. While India, Italy, and Japan each contribute a smaller number of articles overall, India demonstrates a minor tendency towards international partnerships, as evidenced by the addition of eight MCPs. In general, the data reveals that although China is the country that contributes the most to this study field, countries such as the United Kingdom, Germany, and Australia are more collaborative in character. Growing the number of international collaborations could further improve the quality of research and the influence it has on a global scale in this field.

As shown in Table 8 and Figures 8 to 9, the distribution of production and citations in the IEEE Transactions on Affective Computing is broken down by nation. In all categories, China is in the lead, with a total of 1,395 documents and 9,181 citations, which accounts for around forty percent of the total citations. The United States of America and the United Kingdom come in second and third, respectively, with 4,654 and 6,395 citations, despite the fact that the United States has a greater number of papers (734) than the United Kingdom does (310). Despite the fact that their document numbers are far lower, Australia, Germany, and Canada have also made significant contributions, each of which has received more than one thousand citations. Even though they have a lesser number of citations, European countries such as Germany, France, and the Netherlands collectively provide a large share of the research. It is interesting to note that nations such as India and Italy have a lower number of documents, yet their citation counts are quite low. This highlights the possibility that there are constraints placed on the influence of research. Figure 9 is a chart that depicts China's complete domination, followed by the United States of America and the United Kingdom. Based on this distribution, it appears that the output and influence of research are substantially concentrated among a select group of highly influential countries. Figure 10 presents a Sankey diagram depicting the correlation among authors, their respective countries (AU_CO), and their affiliations (AU_UN) in IEEE Transactions on Affective Computing. The left side displays countries, with China as the predominant contributor, succeeded by India, the USA, the UK, Germany, and others.

The core section is comprised of authors, the majority of whom have family names that are commonly used in Chinese, such as Li, Zhang, Wang, and Zhao. A number of universities, the majority of which are Chinese, are displayed on the right side of the page. These universities include the University of Science and Technology of China, Tsinghua University, and Lanzhou University. Throughout the picture, substantial scientific contributions from China are highlighted, with the majority of these contributions coming from authors affiliated with top Chinese universities. The presence of thicker lines indicates a higher frequency of partnership or an increased number of publications. China's pre-eminence in this scientific sector is shown by the fact that contributions from countries other than China are deemed to be insignificant. Additionally, the picture does an excellent job of illustrating notable contributions to the subject matter as well as global research trends. In Figure 11, which is an illustration of the network, a network visualisation of co-authorship ties within IEEE Transactions on Affective Computing is shown.

This representation of the network is displayed. Authors are illustrated as nodes, and the widths of these nodes are proportional to the number of articles they have produced or the amount of influence they have exerted. For the purpose of symbolising the various research clusters or groups that are cooperating with one another, different colours are utilised. Notable people such as Carlos Busso, Bjorn W. Schuller, Maja Pantic, Shangfei Wang, Guoying Zhao, and Yong-Jin Liu are examples of highly significant researchers. In the field of research, these persons are considered to be instances of extremely significant researchers. The visualisation reveals the existence of powerful collaboration networks, particularly among Chinese writers (some examples include Guoying Zhao and Shangfei Wang) and European researchers (some examples include Maja Pantic). When the lines are thicker, it indicates that the co-authorship links are more solid, which suggests that they are regularly collaborated on. Clusters that are smaller and more isolated, on the other hand, are indicative of researchers or research areas that are not as prominent as others. Within the framework, there is a significant emphasis placed on regional linkages, with the most prominent experts in the subject being those from China and Europe.

This visualisation does a fantastic job of identifying key contributors as well as the interrelationships that exist between those contributors themselves. In addition to this, it brings to light a number of widely recognised research organisations and collaborative networks operating within the realm of emotional computing. Table 9 demonstrates that Affective Computing (138 occurrences, 235 link strength) and Emotion Recognition (119 occurrences, 175 link strength) are predominant themes in Transactions on Affective Computing. Techniques such as EEG (46, 99), Deep Learning (44, 75), and Machine Learning (42, 74) are significantly pertinent. The significance of Speech Emotion Recognition and Facial Expression Recognition underscores a robust emphasis on multimodal emotion recognition. Noteworthy emerging methodologies include Transfer Learning and Multi-task Learning. Moreover, fundamental concepts such as Arousal and Valence underscore the significance of psychological and physiological dimensions in the understanding of emotions. Figure 12 depicts keyword visualisation in Transactions on Affective Computing, revealing clusters of total 136 items are come with the filter of minimum 5 keywords of each article occurrence interrelated concepts. Cluster 1-56, cluster 2-51, cluster 3- 20, cluster 4-7 and Cluster 5-2 items all are denoted by different colours. The green cluster emphasises Affective Computing, Machine Learning, and Emotion Recognition, along with other topics such as Stress, Virtual Reality, and Wearable Sensors. The red cluster highlights Deep Learning, Speech Emotion Recognition, Transfer Learning, and EEG. The blue cluster encompasses Psychology, Affect Sensing and Analysis, and Human Emotion Modelling. The yellow region emphasises Arousal, Valence, and Music Emotion Recognition. The visualisation illustrates interdisciplinary linkages, emphasising the necessity of integrating diverse methodologies for effective emotion identification.

CONCLUSION

This study analyses fifteen years of publications from the IEEE Transactions on Affective Computing, as indexed by Scopus, to identify publishing trends, citation patterns, and significant important works. The research utilises several bibliometric and statistical methods to delineate the progression of the journal's publications and its influence in the domain of affective computing. The IEEE Transactions on Affective Computing has established itself as a distinguished journal in the domains of emotion recognition, sentiment analysis, and related fields. Over the years, the publication has consistently acquired high-quality research, positioning itself as an essential resource for scholars and practitioners in affective computing. A comprehensive analysis of the publication framework and citation history reveals fascinating trends. Notably, the year 2023 witnessed the highest volume of publications in the journal's history, with an unparalleled total of 244 papers issued. The surge in papers signifies a growing interest and recognition of emotional computing, as well as the journal's importance as a platform for disseminating research findings. From a citation standpoint, the most significant year was 2012, when the journal achieved a total of 225.39 citations, the highest ever documented. The increased citation count demonstrates the journal's substantial influence on directing research paths and providing essential papers that continue to be cited in subsequent publications. A vital aspect of the analysis involves comparing citation metrics from Scopus and Google Scholar to identify markedly relevant articles. The research conducted by Koelstra *et al*. (2012) is one of the most cited works, garnering 3,619

citations on Scopus and 5,101 citations on Google Scholar. The notable difference in citation counts between the two platforms highlights the paper's broader impact outside traditional academic indexing systems. This bibliometric study indicates that the IEEE Transactions on Affective Computing has experienced significant growth and has had a large impact on the academic community.

The increasing number of publications and heightened citation metrics signify a thriving research field that continually attracts substantial attention. Furthermore, the analysis of highly cited papers provides insights into the foundational research that has shaped the field of emotional computing. This paper presents a comprehensive analysis of the publishing and citation trends of the IEEE Transactions on Affective Computing over the past fifteen years. The findings underscore the journal's importance as an essential resource for academics and demonstrate the lasting impact of foundational works in the domain of emotional computing. This bibliometric assessment provides a historical overview and serves as a crucial reference for forthcoming research endeavours in the field. The IEEE Transactions on Affective Computing has become a prestigious journal in the field of emotion identification, sentiment analysis, and other disciplines. The magazine has continually garnered high-quality research, establishing itself as a cornerstone for academics and practitioners in the field of affective computing. An in-depth examination of the publication framework and citation record uncovers intriguing patterns. In 2023, the journal achieved its highest publishing count in history, with a record 244 papers released. The increase in publications indicates a rising interest and acknowledgement of emotional computing, along with the journal's significance as a venue for sharing research outcomes. From a citation perspective, the most notable year was 2012, when the journal garnered a total of 225.39 citations, the highest recorded to date.

The elevated citation count illustrates the journal's significant impact in guiding research trajectories and offering fundamental studies that are often cited in later works. A crucial element of the analysis is comparing citation metrics from Scopus and Google Scholar to discern notably significant works. The study by Koelstra *et al*. (2012) is one of the most frequently cited publications, receiving 3,619 citations on Scopus and 5,101 citations on Google Scholar. The significant disparity in citation counts between the two platforms underscores the paper's wider influence beyond conventional academic indexing systems. This bibliometric investigation reveals that the IEEE Transactions on Affective Computing has undergone substantial expansion and exerted considerable influence within the scholarly community. The growing volume of papers and elevated citation metrics indicate a flourishing study domain that consistently garners significant interest. The examination of highly cited papers offers insights into the foundational research that has influenced the domain of emotional computing. This report provides a thorough analysis of the publishing and citation trends of the IEEE Transactions on Affective Computing over the last fifteen years. The findings emphasise the journal's significance as a vital resource for scholars and illustrate the enduring influence of seminal papers in the field of emotional computing. This bibliometric evaluation offers a historical perspective and acts as a significant reference for future research initiatives in the discipline

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Table 1: Procedure of the study based

Assembling	Identification
	Domain: Transactions on Affective Computing (1949-3045) **Research objective:** Develop a bibliometric review of TAC **Research questions:** 1. What is the current standing of TAC in the science community? 2. Who are the most productive authors, institutions and countries? 3. Which are the most cited articles of TAC and citation structure? 4. Which are the most frequent keywords and topics in TAC?
	Acquisition
	Search mechanism: Scopus data collection **Search period:** 2010 to 2024. The search was performed on March 2025 **Search Keywords:** SOURCE-ID (19700177034) AND PUBYEAR > 2009 AND PUBYEAR < 2025 AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (PUBSTAGE, "final")) **Total number of publications:** n= 1032.
Arranging	Purification
	Filters: Show final publication year **Exclusions:** 2025 (As the research was conducted on March, 2025, so it justifies the exclusion) **Filtered document type:** Article and Review **Additional results:** **Final number of publications: n=1023** **Computer software:** Excel, R, R studio and VOS viewer
Assessing	Evaluation
	Performance analysis: Bibliometric indicators including the number of publication and citations etc. **Graphical mapping:** Co-citation, bibliographic coupling, co-occurrence of keywords. **Agenda proposal methods:** Analyse the results of TAC and identify the current trends, and areas for future research.
	Reporting
	Reporting conventions: Numbers, explanations, tables, figures.

Table 2: Main Information on Affective Computing

Description	Results
Timespan	2010:2024
Sources (Journals, Books, etc)	1
Documents	1,032
Annual Growth Rate %	20.38
Document Average Age	4.79
Average citations per doc	50.47
References	56,503
Keywords Plus (ID)	5,198
Author's Keywords (DE)	3,098
Authors	2,694
Authors of single-authored docs	22
Single-authored docs	22
Co-Authors per Doc	4.31
International co-authorships %	34.59
article	1,032

Table 3: Average Citations Per Year in IEEE Transactions on Affective Computing

Year	Total Publication	Average Citation	Total Citation
2010	12	211	2536
2011	17	124	2108
2012	38	225	8565
2013	37	80	2974
2014	32	116	3696
2015	33	81	2665
2016	31	103	3197
2017	41	63	2564
2018	45	80	3584
2019	39	92	3595
2020	59	51	3020
2021	80	38	3066
2022	163	35	5716
2023	244	17	4209
2024	161	4	588

Table 4: Most Relevant Authors in TAC

Authors	Articles
Li Y	29
Li X	22
Busso C	19
Zhao G	19
Wang S	18
Zhang X	17
Wang Y	16
Zhang D	16
Zhang Y	16
Zheng W	16

Table 5: Most Relevant Affiliations in TAC

Affiliation	Articles
Tsinghua University	84
University Of Science and Technology of China	72
South China University of Technology	68
Lanzhou University	56
Sun Yat-Sen University	50
University Of Oulu	40
Nanyang Technological University	35
Southeast University	35
University Of New South Wales	34
Xi'an Jiaotong University	30

Table 6: Most Global Citations and Google Scholar Citations of Documents in TAC

Paper	Total Citations	TC per Year	Normalized TC	Google Citations
KOELSTRA S, 2012	3619	258.50	16.06	5101
MOLLAHOSSEINI A, 2019	1312	187.43	14.23	2193
CALVO RA, 2010	1311	81.94	6.20	2118
EYBEN F, 2016	1249	124.90	12.11	1965
SOLEYMANI M, 2012	1246	89.00	5.53	1820
SONG T, 2020	927	154.50	18.11	1259
JENKE R, 2014	807	67.25	6.99	1085
LI S, 2022	714	178.50	20.36	2043
ZHENG W-L, 2019	662	94.57	7.18	929
MAVADATI SM, 2013	618	47.54	7.69	924

Table 7: Country Distribution articles, SCP and MCP in TAC

Country	Articles	SCP	MCP
China	281	204	77
Usa	114	96	18
United Kingdom	55	32	23
Germany	33	14	19
Australia	31	14	17
France	31	25	6
Netherlands	28	13	15
India	26	18	8
Italy	23	12	11
Japan	23	20	3

Table 8: Country production with total citation in TAC

Country	Total Documents	Total Citation
CHINA	1395	9181
USA	734	4654
UK	310	6395
GERMANY	181	1244
FRANCE	167	590
NETHERLANDS	167	487
AUSTRALIA	152	2192
ITALY	147	788
INDIA	103	697
CANADA	100	901

Table 9: Keyword Distribution in TAC

Keyword	Occurrences	Total Link Strength
affective computing	138	235
Emotion recognition	119	175
eeg	46	99
deep learning	44	75
sentiment analysis	44	48
machine learning	42	74
facial expression recognition	41	35

Emotion recognition	39	46
speech emotion recognition	31	30
facial expression	27	35
natural language processing	24	34
transfer learning	23	38
facial expressions	23	29
physiological signals	21	51
affect sensing and analysis	19	30
virtual reality	19	30
multi-task learning	18	33
arousal	15	38
valence	13	35
stress	13	28
convolutional neural networks	13	23
classification	13	21
affect	13	17
psychology	13	17
emotions	13	11
feature selection	12	22
multimodal fusion	12	17
convolutional neural networks	12	14
emotional corpora	11	21
computer vision	11	20
electroencephalogram (eeg)	11	14
feature extraction	10	22
attention	10	16
graph neural network	10	16
physiological measures	10	16
domain adaptation	10	15

Fig. 1: Main information on affective computing.

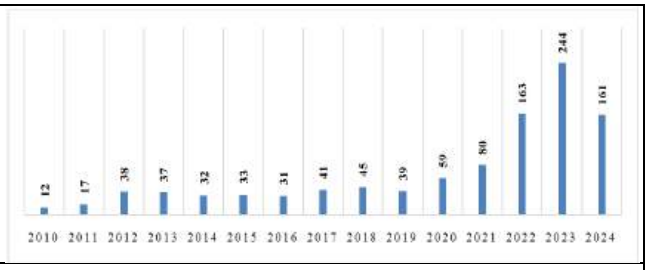

Fig. 2: Annual Scientific Production.

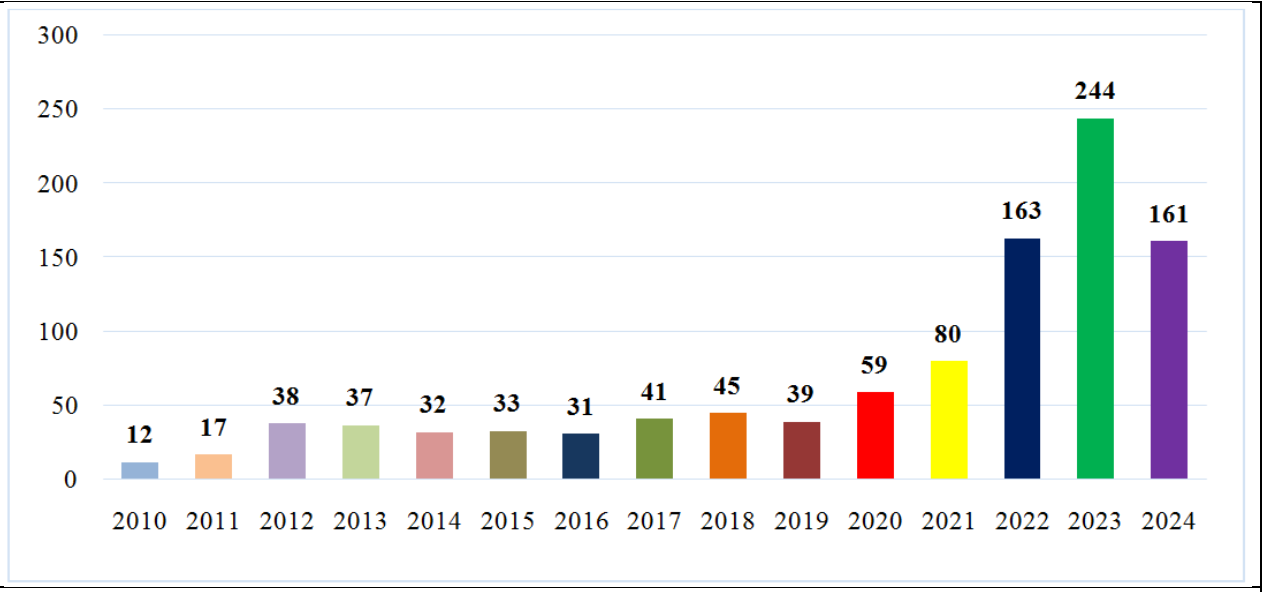

Fig. 3: Total Publication Per Year in TAC.

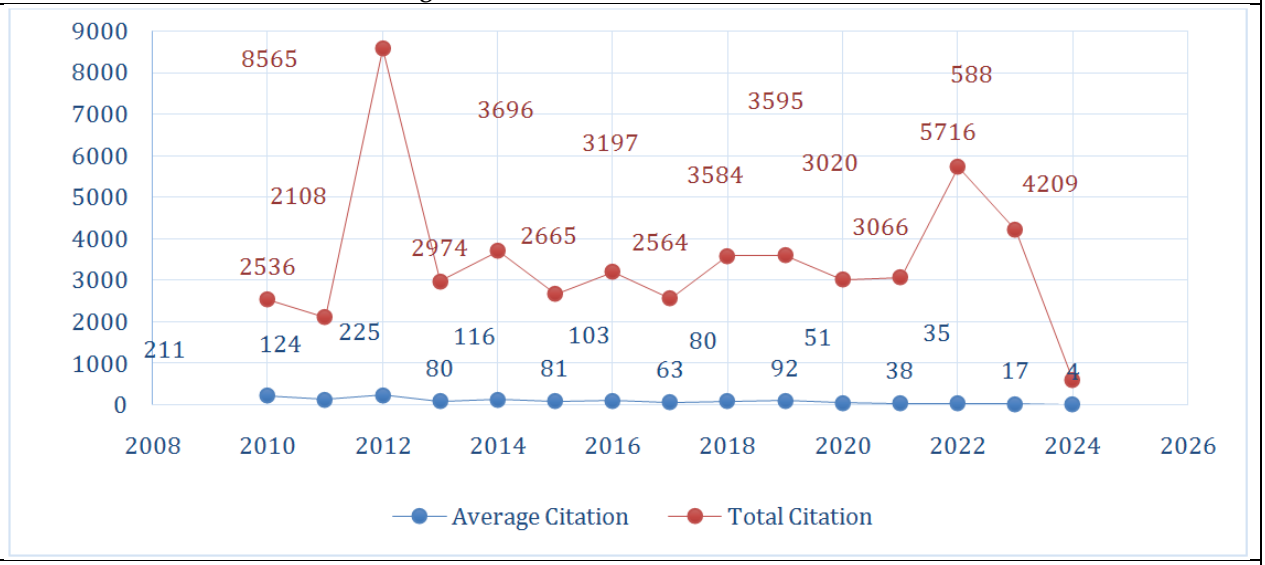

Fig. 4: Total Citations and Average Citations in in TAC.

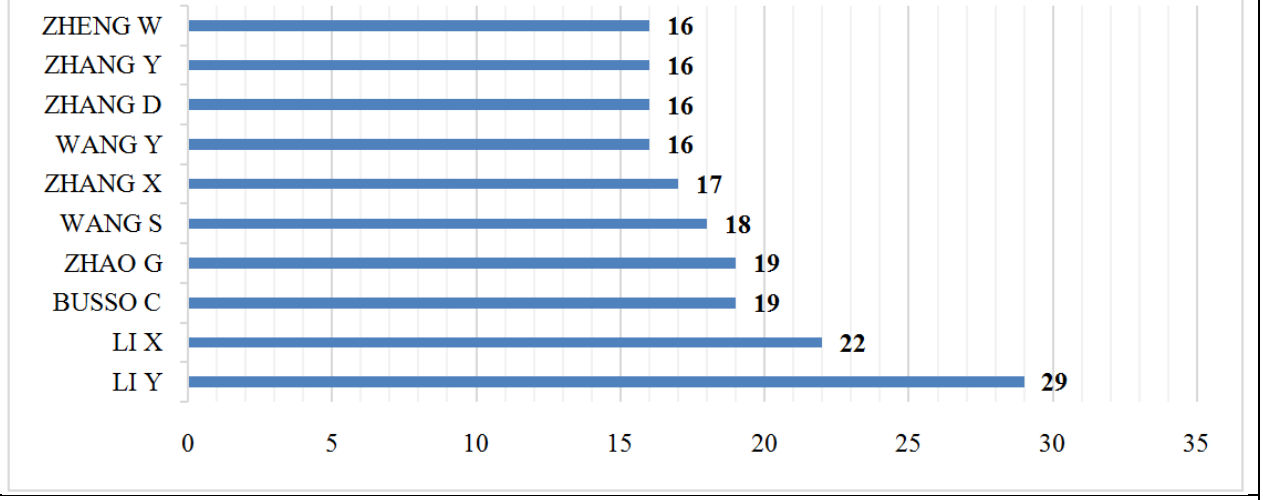

Fig. 5: Most Relevant Authors in TAC

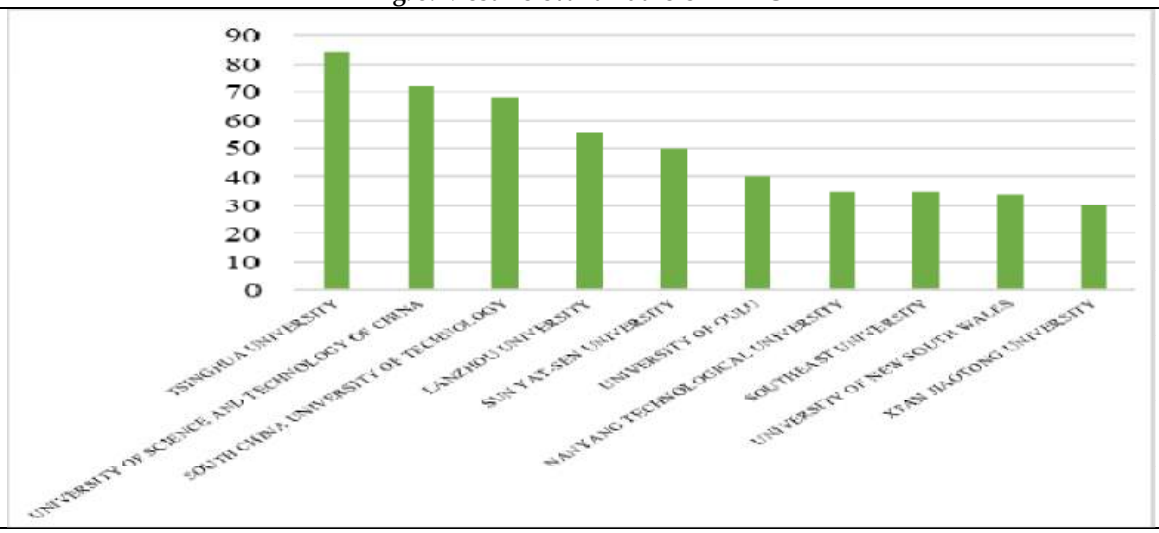

Fig. 6: Most Relevant Affiliations in TAC

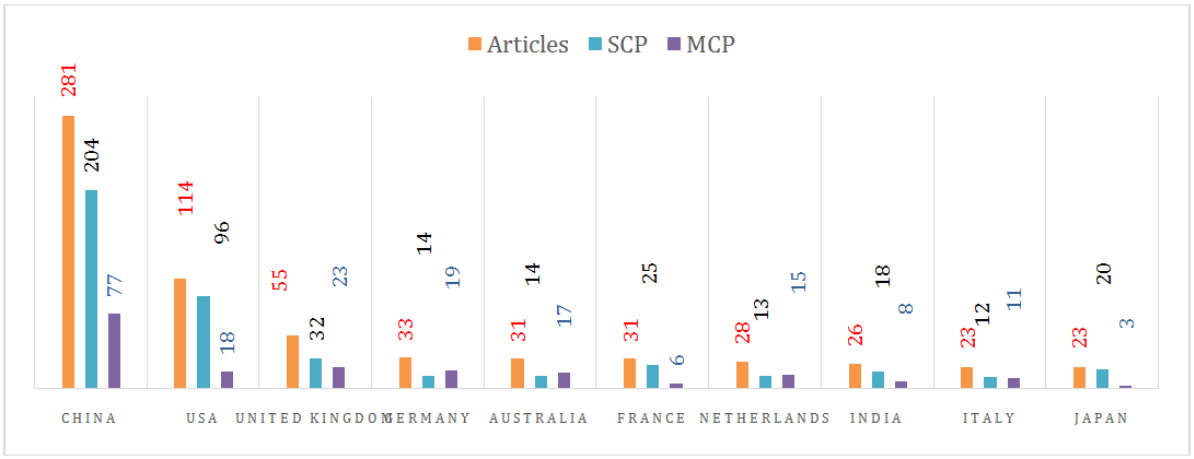

Fig. 7: Country Distribution articles, SCP andMCP in TAC

Fig. 8: Most Cited Countries in TAC

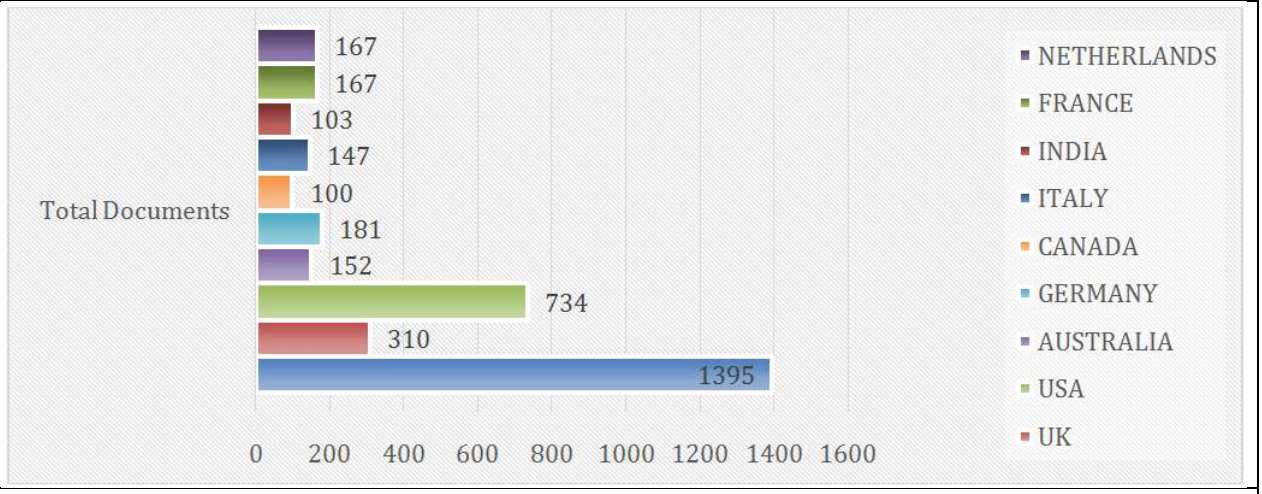

Fig. 9: Most Production Countries in TAC

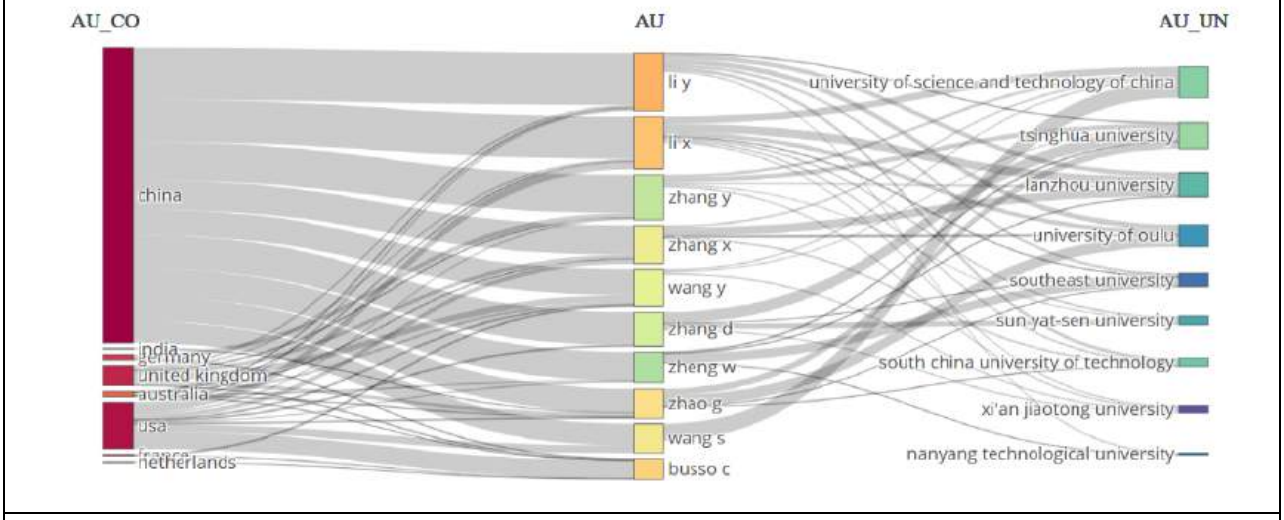

Fig. 10: Co-Relation with authors, Counties and Affiliation in TAC

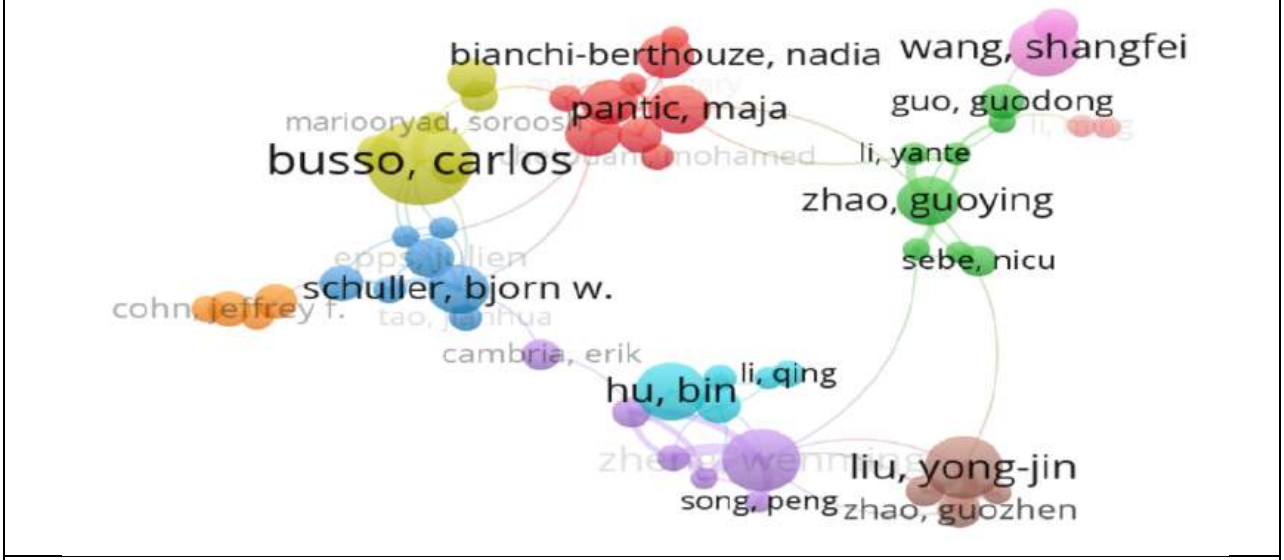

Fig. 11: Co-Relation with Network Visualization in TAC

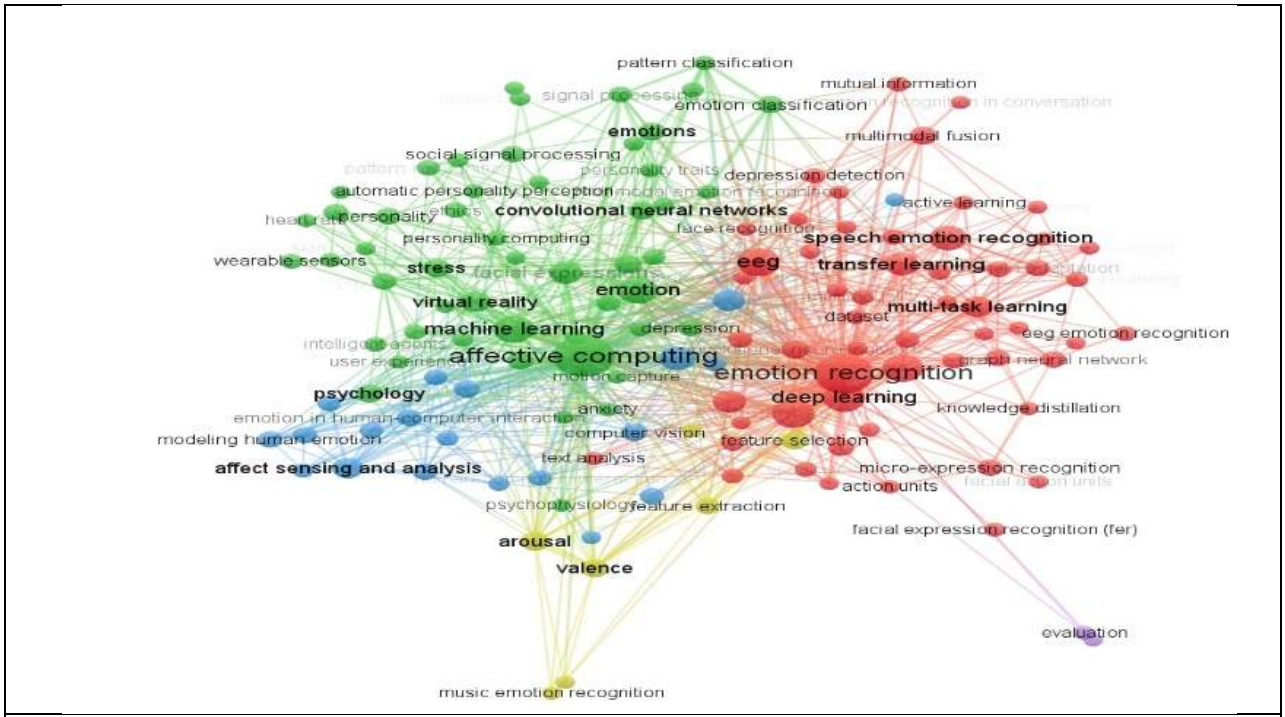

Fig. 12: Keywords Visualization in Transactions in TAC

RESEARCH ARTICLE

Effectiveness of a Midwifery - Led Intervention on Staff Nurses' Knowledge and Attitude Regarding Supportive Maternity Care at a Selected Hospital in Nadiad City

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Received: 01 Nov 2025 Revised: 30 Nov 2025 Accepted: 11 Dec 2025

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ABSTRACT

Midwifery-led care plays a vital role in ensuring respectful and supportive maternity services that uphold women's dignity, safety, and satisfaction during childbirth. Despite global efforts by the WHO and professional bodies to promote respectful maternity care, many healthcare settings continue to face gaps in knowledge and attitude among staff nurses, which can lead to compromised maternal experiences and outcomes. In Nadiad City, limited evidence exists regarding the awareness and application of supportive maternity care principles among nursing staff. Therefore, this study was undertaken to assess the effectiveness of a midwifery-led intervention on supportive maternity care in terms of knowledge and attitude among staff nurses at selected hospitals in Nadiad City. A pre-experimental one-group pre-test post-test design was adopted for the study. Thirty staff nurses working in the obstetrics and gynecology departments of selected hospitals in Nadiad City were chosen using a non-probability convenient sampling technique. Data were collected using a structured knowledge questionnaire and a 5-point Likert attitude scale before and after administering a nurse-led intervention through a PowerPoint presentation. The intervention focused on universal rights of women and newborns, categories of disrespect and abuse, and supportive maternity care practices. Data were analyzed using descriptive statistics (frequency, percentage, mean, and standard deviation) and inferential statistics (paired t-test, chi-square, and correlation). Findings revealed a marked improvement in both knowledge and attitude following the intervention. In the pre-test, 53.3% of participants had poor

knowledge and 63.3% showed an unfavourable attitude toward supportive maternity care. Post-intervention, 73.3% demonstrated good knowledge and 100% developed a favourable attitude. The mean post-test knowledge and attitude scores were significantly higher than pre-test scores ($p < 0.05$), indicating the effectiveness of the midwifery-led educational intervention. A positive correlation was also observed between knowledge and attitude scores, suggesting that improved understanding leads to better perceptions and practices related to maternity care. The study concluded that the midwifery-led intervention was effective in enhancing staff nurses' knowledge and attitude toward supportive maternity care. Regular educational sessions and continuous professional development programs should be implemented to promote respectful, safe, and patient-centered maternity services, thereby improving the overall quality of maternal healthcare in hospital settings.

Keywords: Midwifery-Led Intervention, Supportive Maternity Care, Knowledge, Attitude, Staff Nurses, Nadiad City.

INTRODUCTION

Pregnancy and childbirth are among the most profound experiences in a woman's life, requiring not only clinical safety but also emotional and psychological support. The concept of Supportive Maternity Care (SMC) or Respectful Maternity Care (RMC) advocates for the protection of women's rights to dignity, privacy, informed choice, and emotional well-being during childbirth. Despite policy emphasis, studies across developing nations, including India, report frequent instances of verbal abuse, neglect, and lack of empathy toward women in labor. Such disrespectful maternity practices violate women's rights and discourage them from seeking institutional deliveries, increasing the risk of maternal morbidity and mortality. Midwives and nurses play a pivotal role in improving maternity care experiences. However, inadequate knowledge and negative attitudes among staff nurses often lead to poor implementation of supportive maternity care principles. Therefore, empowering nurses through midwifery-led education can bring transformative change in maternal health outcomes.

Need of the Study

In India, the need to strengthen RMC is underscored by alarmingly high rates of mistreatment during facility-based childbirth. A systematic review estimated a pooled prevalence of over 70%, with some studies reporting rates as high as 98% [1]. While the WHO and the White Ribbon Alliance have provided frameworks for ensuring dignity and respect in maternity care, implementation remains inconsistent across states. Much of the available evidence is geographically concentrated—especially in Uttar Pradesh—thus failing to capture the socio- cultural diversity of the country. Disrespect and abuse in maternity settings manifest through inadequate information sharing, lack of informed consent, compromised autonomy, and overt physical or verbal mistreatment. Such experiences are associated with adverse outcomes including postpartum haemorrhage, obstetric injuries, and psychological sequelae such as post-traumatic stress disorder. Moreover, these experiences contribute to women's reluctance to seek facility-based care, increasing reliance on unskilled birth attendants and elevating the risk of maternal and neonatal mortality [2]. A recent study conducted at a tertiary care hospital in Bhopal explored the extent to which RMC is practiced and perceived by women during labour and childbirth [3]. By examining patient satisfaction and provider-patient interactions, the study revealed critical insights into communication patterns, emotional support, and the overall quality of maternity care. Such research is vital for identifying gaps in policy execution, enhancing healthcare provider training, and ensuring that every woman experiences a safe and dignified birth.

OBJECTIVES OF THE STUDY

To assess the knowledge regarding supportive maternity care before and after the administration of midwifery led intervention on staff nurses at selected hospital Nadiad city.

- To assess attitude regarding supportive maternity care before and after administration of midwifery led intervention on staff nurses at selected hospital Nadiad city.
- To evaluate effectiveness of intervention on staff nurses at selected hospital Nadiad city.
- To correlate post-test knowledge and attitude score on staff nurses at selected hospital Nadiad city.
- To find association between pretest knowledge and attitude score midwifery led intervention on staff nurse at selected hospital Nadiad city with their selected demographic variables.

Hypothesis

H1: There will be a significant difference in the pre-test and post-test scores of knowledge and attitude regarding supportive maternity care among staff nurses after the midwifery led intervention.

H2: There will be a significant association between the pre-test knowledge and attitude scores with their selected demographic variables of staff nurses.

METHODOLOGY

Research Approach: The approach adopted for this study is Quantitative research approach is used in this study.
Research Design: The research design selected for the study is pre and post test design.

Variables

Independent variable: Nurse led intervention on supportive maternity care
Dependent variable: Knowledge and attitude of the staff nurse regarding the supportive maternity care

Research Setting: study was conducted in selected hospitals in OBD department at Nadiad city at Kheda district.

Target population

- In this study the target population consisted all the staff nurse of OBG department/ward in selected hospital.
- All the staff nurse of OBG department / ward

Sampling Technique: The non probable Convenient sampling technique is used for present study.
Sample Size: Sample size for this study 30 staff nurses of OBG department / wardat Nadiad.
Method of Sampling: Convenient sampling technique was used.
Tools for data collection: structure knowledge questionnaire and attitude scale was used for data collection from the study participants.

Ethical consideration

The present study received ethical approval from the Institutional Ethical Committee of Maganbhai Adenwala Mahagujarat University, Nadiad, under reference number MAM Uni/IECHR/2025/06. The committee consisted of 11 members from diverse professional backgrounds. Prior to data collection, formal written permission was obtained from the institute, hospitals, and each individual participant. Informed consent was secured after explaining the purpose and procedures of the study. To ensure confidentiality and protect participants' identities, all personal information was kept strictly confidential and used solely for research purposes. No names or identifying information were disclosed in any part of the study. During data entry and analysis, coded identifiers were used in place of names to maintain anonymity and data privacy throughout the research process.

RESULT

Frequency and percentage of demographic characteristics of Staff nurses (n=30) (Table No.1)
In terms of age, the majority of staff nurses 12 (40.0%) were in the age group of 36–40 years, followed by 7 (23.3%) each in the 26–30 years and 31–35 years groups, and 4 (13.3%) in the 20–25 years group.

Regarding education status, most staff nurses were GNM qualified 13 (43.3%), followed by ANM 11 (36.7%), and B.Sc. Nursing 6 (20.0%).

In terms of total working experience, the highest number of staff nurses had 5–10 years of experience 13 (43.3%), followed by 3–5 years 8 (26.7%), 1–3 years 6 (20.0%), and less than 1
year 3 (10.0%).

Regarding experience in conducting labor, most of the staff nurses had 2–5 years of experience 18 (60.0%), followed by less than 1 year 7 (23.3%), 5–10 years 4 (13.3%), and only
1 (3.3%) had more than 10 years of experience.

Distributions of Knowledge and attitude Regarding Supportive Maternity Care Before and After the Administration of Midwifery-Led Intervention Among Staff Nurses at a Selected Hospital, Nadiad City" (n=30) (Table: 2)

Findings of Knowledge
In the pretest, majority of the staff nurses 16 (53.3%) had poor knowledge, followed by 10 (33.4%) with average knowledge, and only 4 (13.3%) had good knowledge. In the post test, most of the staff nurses 22 (73.3%) had good knowledge, while 5 (16.7%) had average knowledge, and only 3 (10%) remained with poor knowledge.

Interpretation: The data clearly shows a significant improvement in the knowledge level of staff nurses after receiving the midwifery-led intervention. The number of staff nurses with good knowledge increased substantially from 13.3% to 73.3%, while those with poor knowledge decreased from 53.3% to 10%. This indicates that the midwifery-led intervention was effective in enhancing knowledge regarding supportive maternity care among the staff nurses.

Findings of Attitude
In the pretest, a majority of staff nurses 19 (63.3%) had an unfavourable attitude, 11 (36.7%) had a moderate attitude, and none had a favourable attitude. In the post test, all staff nurses 30 (100%) demonstrated a favourable attitude, and none remained in the moderate or unfavourable categories.

Interpretation
The findings clearly show a remarkable shift in attitude among staff nurses following the midwifery-led intervention. Before the intervention, none of the staff nurses showed a favourable attitude, while after the intervention, 100% developed a favourable attitude. This suggests that the midwifery-led intervention was highly effective in improving the attitude of staff nurses regarding supportive maternity care.

Graph
Graph 1: Pretest-post test knowledge and Attitude mean % Enhancement score
Table: Pretest-Posttest Knowledge and Attitude Comparison Among Staff Nurses Regarding Supportive Maternity Care" (n=30)
Table 3 Shows the comparison of pretest and post test scores for knowledge and attitude using paired t-tests. There was a significant increase in the mean knowledge score from 7.73 (SD = 2.80) to 11.93 (SD = 2.29), with a mean

difference of 4.20 and a statistically significant t-value of 8.57 ($p = 0.000$). Similarly, the mean attitude score improved from 23.57 (SD = 2.76) to 42.60 (SD = 2.39), with a substantial mean difference of 19.03 and a t-value of 34.35 ($p = 0.000$), indicating a highly significant improvement. The results confirm the effectiveness of the intervention in enhancing both knowledge and attitude. Both knowledge and attitude showed statistically significant improvements after the midwifery-led intervention. This demonstrates the effectiveness of the intervention in enhancing staff nurses' understanding and positive outlook toward providing supportive maternity care.

Association

The association between the pretest level of attitude and selected demographic variables among staff nurses, using the Chi-square test. The findings indicate that the majority of staff nurses (40%) were in the age group of 36–40 years, followed by 23.3% each in the 26–30 and 31– 35year age groups. Regarding education, most staff nurses were GNM qualified (43.3%), followed by ANMs (36.7%) and B.Sc. Nursing graduates (20%). In terms of total working experience, 43.3% had 5–10 years of experience, while 26.7% had 3–5 years. Most nurses (60%) had 2–5 years of labor room experience. However, the Chi-square values and corresponding p-values for all variables (age, education status, total working experience, and labor room experience) were statistically non-significant ($p > 0.05$), indicating that there was no significant association between the pretest level of attitude and the selected demographic variables.

DISCUSSION

The study revealed a significant improvement in both knowledge and attitude following the midwifery-led intervention. These findings align with similar studies conducted by Kaur *et al*. (2023) and Kumar *et al*. (2021), who reported that educational interventions effectively enhanced nurses' understanding and implementation of respectful maternity care practices. The results underscore the importance of structured, context-specific training in developing supportive maternity environments. The strong correlation between knowledge and attitude suggests that knowledge empowerment directly influences positive behavioral change among nursing professionals. The study's implications extend to policy and practice, suggesting that integrating respectful maternity care modules into continuous nursing education can strengthen patient-centered care and reduce maternal anxiety, fear, and mistrust in healthcare institutions.

CONCLUSION

The midwifery-led educational intervention was effective in significantly improving the knowledge and attitude of staff nurses toward supportive maternity care. Empowering nurses through ongoing training and supervision can promote a culture of respect, empathy, and patient-centeredness in maternity units.

RECOMMENDATION

1. Incorporate respectful maternity care (RMC) modules in hospital orientation and in-service programs
2. Conduct periodic refresher workshops for staff nurses on RMC practices.
3. Implement policy-level changes ensuring accountability and monitoring of RMC standards.
4. Encourage replication of similar studies in different regions to generalize findings.

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Table No.1 Frequency and percentage of demographic characteristics of Staff nurses (n=30)

Demographic Variables	Category	Frequency	Percentage
Age in Years	20-25Year	4	13.3%
	26-30Year	7	23.3%
	31-35Year	7	23.3%
	36-40Year	12	40.0%
Education Status	ANM	11	36.7%
	GNM	13	43.3%
	B.Sc. Nursing	6	20.0%
Total Working Experience	<1Year	3	10.0%
	1-3Years	6	20.0%

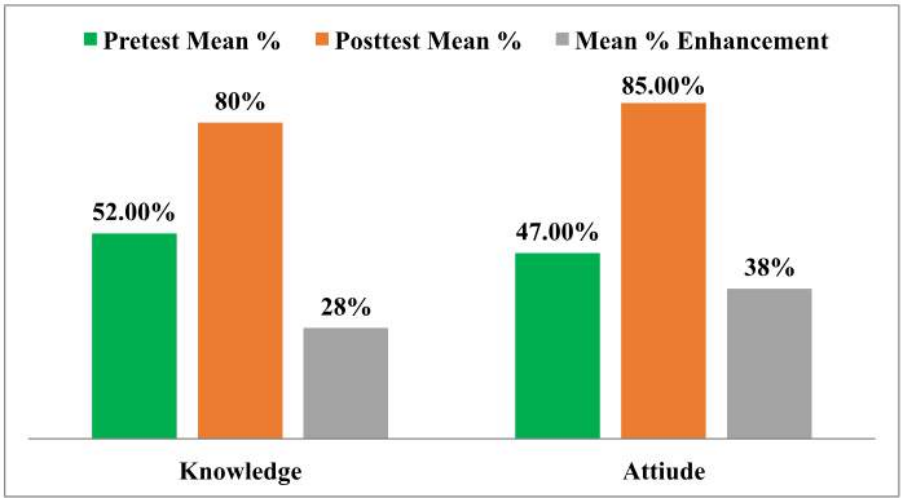
	3-5Years	8	26.7%
	5-10Years	13	43.3%
Experience in Labor Conducting	<1Year	7	23.3%
	2-5Years	18	60.0%
	5-10Years	4	13.3%
	>10Years	1	3.3%

Table 2: Distributions of Knowledge and attitude Regarding Supportive Maternity Care Before and After the Administration of Midwifery-Led Intervention Among Staff Nurses at a Selected Hospital, Nadiad City" (n=30)

Level of Knowledge	**Pretest Knowledge**		**Posttest Knowledge**	
	Frequency	**Percent**	**Frequency**	**Percent**
Poor Knowledge	16	53.3%	3	10%
Average Knowledge	10	33.4%	5	16.7%
Good Knowledge	4	13.3%	22	73.3%
Level of Attitude	**Pretest Attitude**		**Post test Attitude**	
	Frequency	**Percent**	**Frequency**	**Percent**
Unfavourable Attitude	19	63.3%	0	0%
Moderate Attitude	11	36.7%	0	0%
Favourable Attitude	0	0%	30	100%
Total	**30**	**100%**	**30**	**100%**

Table 3: Pretest-Posttest Knowledge and Attitude Comparison Among Staff Nurses Regarding Supportive Maternity Care" (n=30)

Pretest-Posttest Knowledge and Attitude Comparison	**Mean**	**SD**	**Mean Difference**	**Paired t-test score**	**P-Value**	**95% Confidence Interval of the Difference**	
						Lower	Upper
Pretest Knowledge	7.73	2.80			0.000		
Posttest Knowledge	11.93	2.29	**4.20**	**8.57***	S df 29	5.20	3.20
Pretest Attitude	23.57	2.76	**19.03**	**34.35***	0.000 S	20.17	**17.90**
					df 29		



Graph 1: Pretest-post test knowledge and Attitude mean % Enhancement score

REVIEW ARTICLE

A Review on Gels in Drug Delivery : Development, Properties, Classification and Novel Applications in Biomedical and Topical Formulation

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Received: 25 Oct 2025 Revised: 20 Nov 2025 Accepted: 11 Dec 2025

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ABSTRACT

Gels are dynamic semi-solid structures having significant pharmacological and biological applications due to their unique structural and functional properties. By forming a three-dimensional cross-linked network, gels which can be formed of natural or synthetic polymers immobilize liquid media. This leads to better patient compliance, targeted drug administration, and less systemic adverse effects. This study focuses on the development, classification, and properties of gels, with particular attention to topical formulations that enhance drug absorption, prevent hepatic first-pass metabolism, and lessen gastrointestinal irritation. Screening aspects such drug content, extrudability, spreadability, viscosity, and skin irritation studies are discussed in detail. Recent advancements in gel based drug delivery, such as in situ gelling systems and smart gels that respond to pH, temperature, and external stimuli, are being studied for possible uses in minimally invasive and sustained release therapies. Innovative methods that

demonstrate enhanced stability and bioavailability include liposomal gels, phytosomal gels, and microemulsion based organogels. In the future, patient-specific, biodegradable, and intelligent gel systems for regenerative therapies and tailored medicine will be incorporated. tissue engineering and nanotechnology. All things considered, gels constitute a cornerstone of current drug delivery research with continuous developments extending their potential in medicine and industry.

Keywords: Gel, Polymer, Nanotechnology, *in situ* gel, Phytosomal Gel, Liposomal Gel

INTRODUCTION

The Latin words "Gelu," which means "frost," and "gel are," which means "freeze" or "congeal," are the origin of the word "gel" and "jelly," while "gel" itself is derived from the word "gelatin." This source provides an example of the basic idea that a liquid will solidify into a solid-like material that is elastic and retains certain liquid characteristics but does not flow. The word "gel" was initially employed as a classification in the late 1800s when researchers attempted to classify semisolid materials according to their phenomenological characteristics rather than their chemical composition. At the time the analytical methods needed to determine chemical structures were unavailable(1). Topical gels are used to treat and cure topical ailments. They are a homogenous, semi-solid combination Gels' greater hydrophilia allowed for the rapid release of the drug or active component. A gel is made up of two parts. It is a three-dimensional cross-linked substance that has a proportionately large volume of liquid medium to create a stiff network that immobilizes the liquid phase without interruption. The gel's structural network is made up of both inorganic particles and organic macromolecules (2-4). Topical formulation decreases gastrointestinal pain, boosts the medicine's bioavailability, and prevents the drug from being metabolized in the liver. Topical medications function exactly where they should. The primary category of semi-solid preparations has seen an increase in the usage of topical gels in pharmaceutical and cosmetic formulations (5-9). Topical delivery techniques have several advantages over parenteral and oral approaches, such as lowering systemic side effects, preventing first-pass metabolism, and improving patient compliance. A practical drug delivery option among the several topical preparations is gels (10-13). More patient compliance, constant drug delivery, fewer side effects, and avoidance of the hepatic first pass impact are only a few benefits of the topical/transdermal (TT) route over other drug administration methods (14, 15).

Gels are defined by the U.S.P. as a semisolid structure with a dispersion of big organic molecules or small inorganic particles that are encircled and penetrated by a liquid medium. Large organic molecules dissolve in the continuous phase to create flexible, randomly coiled chains, while inorganic particles remain scattered throughout the continuous phase without dissolving (16 -19). Among the many benefits of topical drug delivery are the removal of the hazards and drawbacks connected with injectable techniques, as well as the flexibility in physiological conditions like pH variations, absorption rates, gastric emptying time, and enzyme presence. Common illnesses like psoriasis have symptoms that are intended to restrict the medication's pharmacological effects or subsequent results to the skin's outermost layers or visible surface (20-23). The potential uses of *in-situ* formed hydrogels in the biomedical industry have recently drawn attention. It is possible to combine pharmaceutical compounds or cells into an aqueous solution (sol) and then inject it into a specific location, where it will undergo a sol-to-gel transition to form a hydrogel depot. Without requiring intricate fabrication procedures or surgical procedures, this method provides a simple insertion methodology. The potential of these *in-situ* produced gels has been investigated in several biomedical applications, encompassing as minimally Invading drug administration, three-dimensional cell culture, injectable tissue engineering, tissue sealants, surgical adhesives, and adhesion- avoidance coatings. For a hydrogel to form *in-situ*, a quick process for creating crosslinks that firmly hold the highly hydrated polymeric system in place within a significant amount of water is required. It is crucial to choose a biologically acceptable technique for the crosslinking process when assessing biomedical applications (24-27).

Gel Properties

An inert, safe gelling agent that does not react with other formulation ingredients is appropriate for use in pharmaceutical or cosmetic applications. The gelling agent used for the preparation needs to produce a solid enough consistency for storage, but shear forces from shaking the container, squeezing the tube, or applying topically can easily break it.

1. To prevent microbiological contamination, it should also have the right antibacterial qualities. In addition, the topical gel should not feel tacky (16-19).
2. The fact that gels are frequently categorized as soft solids is an additional mechanical characteristic. When assessing solid properties using a stress-strain relationship, the modulus—the ratio of stress to strain—is generally modest, ranging from a fraction of a pascal to several thousand pascals. However, tougher gels can be made.
3. The ability to deform is another important mechanical property of gels. These materials typically behave like solids over a wide range of strain without breaking, which is why they occasionally exhibit what is known as "rubber elasticity." Not all gels are elastic, though; some have a plastic response rather than a rubber-elastic one, and can be brittle (like agar gels) (28).
4. Polymeric gels have a lot of unique characteristics. Other notable characteristics of these gels include the mechanoelectric effect, swelling, syneresis, aging, electrostatic potential distribution, electrical oscillation, electrical contraction, swelling, pseudoplastic (non-Newtonian) rheological behavior, and interactions with oppositely charged surfactants. Above all, these gels exhibit stimuli-responsive behavior in response to external stimuli such electric fields, temperature, pressure, and pH. Therefore, in reaction to their external environment, polymeric gel systems can usually generate force or perform functions (29).

Gel Structure

The solid compositions of inorganic gels made from molecular precursors are typically less than10 vol%. Research on a particular kind of silica gel shows that pH. a gel with 5 vol% solids (30,31), these gels exhibit fractal properties at length scales below about 25 nm. Transmission electron microscopy on supercritically dried gels confirmed the discovery that these gels' networks are mesoporous, as indicated by their noticeably low permeability, which will be covered in more detail (32, 33). The silica gel networks are made up of nodes where three or four chains converge, as shown by the transmission electron microscopy photos. The distance between these nodes is several times larger than the chain thickness. Compared to organic gels, which usually have polymeric coils dotted between the nodes (34), inorganic gels are substantially stiffer due to this structural configuration. Entropic variables impact the elastic characteristics of organic gels, permitting significant volume fluctuations (35). On the other hand, when temperature, solvent, voltage, and other external variables change, inorganic gels show no change in volume. The fact that a sizable portion of the atoms—roughly half for a surface area of 500 m^2/g—are exposed at the surface is a crucial consequence of these gels' large surface area. Therefore, significant compositional changes may result from reactions that take place near the interface (36). It is possible to create inorganic gels, either single- or multi-component, with almost all the periodic table's elements. The gel network is usually composed of an amorphous hydrous oxide. Although some elements, such as zirconium, titanium, and silicon, easily form three-dimensional networks, the majority do not. Alumina gels are typically made up of chains of nanometer-sized particles that resemble AlOOH. This is a common tendency of many oxides to produce tiny particles that group together to form networks. However, the layered structure of tungsten oxide gels, which includes intercalated water, allows them to absorb and release water in a manner akin to that of calcium silicate hydrate (C-S-H) (37).

Classification of Gels

Depending on the type of solvent

Aqueous gels (hydrogels) and Water as a dispersion medium for gels made of gelatin, agarose, and polyvinyl alcohol

Non-aqueous gels, such as Xerogels or Organogels

Petroleum-based gels and lecithin gels are examples of organic solvents used as a medium.

Depending on the kind of network structure

Physical Gels held in place by non-covalent interactions (van der Waals, H-bonds, etc.). Agar and gelatin are examples of thermo-reversible Chemical Gels Networks of polymers cross-linked by covalent bonds. Epoxy resins and polyacrylamide gels are examples of thermo-irreversible items.

Using Smart Gels, which are responsive

Smart (stimuli-responsive) gels React to outside stimuli like
Temperature, such as PNIPAM hydrogels
pH—for instance, polyacrylic acid gels
Electrical and magnetic fields, such as ferrogel
Light: azobenzene-functionalized gels, for instance Non-Reactive Gels Lack of reaction to environmental changes

According to Origin

Made from natural polymers, such as agar, gelatin, and alginate, natural gels
Synthetic Gels Artificial polymers, such as polyacrylamide and poloxamer. (38)

Assessment Methods for Gels

Clarity

The following rating system is used to evaluate the formulation's clarity visually against both black and white backgrounds: +, ++, and +++ for turbid, clear, and very clear (glassy).

pH measurement

A digital pH meter is used to measure the pH levels of different gel compositions. 100 milliliters of distilled water is used to dissolve one gram of gel, which is then left to stand for two hours. Three separate pH readings were taken for each formulation, and the average results are computed.

Drug Content

A suitable solvent (100 ml) is mixed with one gram of the produced gel. After filtering the stock solution, appropriate dilutions are used to make aliquots of different concentrations, and absorbance is measured. Using an equation obtained from the calibration curve's linear regression analysis, the drug content is ascertained.

Viscosity Evaluation

Using a Brookfield viscometer, the prepared gel's viscosity is determined. The rotational speeds of the gels were 0.3, 0.6, and 1.5 revolutions per minute. Every speed is recorded along with the matching dial readings. By increasing the dial reading by the factor listed in the Brookfield Viscometer catalog, the viscosity can be determined.

Spreadability

This characteristic indicates the extent to which the gel spreads when applied to the skin or another area that is impacted. The medical effectiveness of a composition is also influenced by spreadability. By timing the amount of time, in seconds, it takes for two slides to separate from the gel between them under a specific force, spreadability can be determined. An indication of better spreadability is a shorter separation time (39). In this case, S represents spreadability, M represents weight on the top slide, L represents distance on the glass slide, and T represents time required for the slides to fully separate.

Evaluation of Extrudability

Collapsible tubes are used to hold the formulations until the gels had solidified inside the container. Each formulation is evaluated for extrudability by determining the weight in grams needed to extrude a 0.5 cm gel ribbon in 10 seconds.

Evaluation of Homogeneity : Following gel setting, each formulation is visually inspected to determine its homogeneity. This required looking at their appearance and determining whether any aggregates are present.

Evaluation of grittiness: Every formulation is inspected under a light microscope to look for any notable particle debris. The gel preparation satisfies the requirements for being free of grittiness and particle debris, which are crucial for any topical treatment.

Skin Irritation Assessment: For the skin irritation investigation, 400–500 gram guinea pigs of both sexes are used. Ordinary animal feed and unlimited available to water can be given to the animals, they will be kept carefully and monitored surroundings. The guinea pigs' back fur is shaved, and a 4 cm^2 section is marked on each side; the test site is on one side and the control is on the other. For seven days, a gel dose (formulation specific) is administered twice daily on guinea pig, and the application site should be watched for any indications of sensitivity. If any reactions are seen, they must be rated from 0 to 3, which means that there is no reaction, that there is mild patchy erythema, that there is slight but confluent or moderate patchy erythema, or that there is harsh erythema with or without edema.

Studies of *in vitro* diffusion

Research on in vitro diffusion release of the generated gels across a cellophane membrane can be investigated in vitro using a Franz diffusion cell. A gel sample weighing 0.5g in the cellophane membrane and 250 ml of phosphate buffer (pH 7.4) as the diffusion media must be used for the diffusion experiments. A constant temperature of 37 ± 1° C must be maintained. Each sample should be periodically extracted in five milliliters at intervals of one, two, three, four, five, six, seven, and eight hours to get best result assessment of polymer-controlled release efficiency in prepared gels. Each withdrawn sample is replaced with fresh dissolving medium (16).

Current Developments and New Applications for Topical Gels

Instead of contrasting prepared liposomal gels with liquid state liposomes, other researchers have assessed liposomal gels' efficacy by contrasting them with traditional gels or creams that include the free drug. Their findings demonstrated that whereas liposomal gels did not enhance systemic absorption, they did increase pharmaceutical retention in the skin. The outcomes of these investigations were solely attributed to the liposome effect, which is known to allow for targeted and controlled drug administration when applied topically, ignoring the influence of the gel matrix.

The categorization of liposomal gel.

Traditional liposomal hydrogels

Differentiated liposomal gels

- Transferosomal Gels
- Gels with an ethosomal
- Proliposomal Gels
- Phytosomal gels
- Gels made of vesicular phospholipid (VPG)
- M-i-L (microgel in liposomes)

Gels with Lecithin Microemulsion

- Microemulsion-Based Organogels Based on Lecithin (LMBGs)
- PLOs (Pluronic Lecithin Organogels)
- Hydrogels Based on Microemulsions Stabilized by Lecithin

A very creative and successful delivery method is liposomes. The biosimilar structures of these systems, which have advantageous properties, are a major advantage. It is possible to incorporate both lipophilic and hydrophilic medicinal drugs due to their amphiphilic properties. These carriers enable focused localization and site-specific release and are non-toxic and biodegradable. They can pass through a variety of biological obstacles that are usually difficult for traditional systems to do. However, rheological constraints frequently limit the utilization of liposomes

in topical products. The conventional method of lipid film hydration is traditionally used to create liposomes; however, solvent injection and the French pressure cell methods are also viable alternatives. By adding a gelling chemical to the aqueous phase, liposomes can be integrated into a gel system. Because of this, several gelling agents, such as carbopol, xanthan gum, poloxamers, gellan gum, and polyvinyl alcohol, have been researched.

Traditional liposomal hydrogels can be made by either adding gelling agents straight into liposome dispersions without the need for drug separation or by integrating pre-formed liposomes into a suitable gel matrix after any unentrapped drug has been removed. The latter strategy streamlines the method by doing away with intricate separation steps and reducing drug loss, giving the device a remarkably high encapsulation efficiency.

Modified liposomal gels have lately been demonstrated to be ineffective as transdermal delivery vehicles since traditional liposomes do not thoroughly enter the skin. According to research, they typically stay on the stratum corneum's outermost layers. It has been shown using confocal microscopy that unbroken liposomes cannot penetrate the granular layers of the epidermis. Additionally, problems including aggregation, fusion, leakage, or hydrolysis of the encapsulated medications may result in a limited shelf life for aqueous dispersions of these vesicular systems. The discovery of vesicles with enhanced properties that enable them to more effectively transport drugs to deeper layers of the skin (such as ethosomes and transfersomes) and to boost the vesicles' stability has been a significant advancement in vesicle research. (like pro-vesicles and phytosomes).

Gels Based on Transferosomes

An active substance is contained in transferosomes, which are extremely flexible hydrophilic lipid vesicles that are applied topically in an aqueous formulation. Phospholipids make up these vesicles, together with an edge activator, usually a single-chain surfactant with a large radius of curvature. The vesicles' lipid bilayers are broken down by edge activators, increasing their deformability and flexibility and allowing them to flow through the stratum corneum's pores (40-43).

Ethosomal Gels

Phospholipids make up ethersomes, which are soft lipid vesicles with a comparatively high alcohol (ethanol and isopropyl alcohol) content (20–45%) and water. The main reason for ethosomes' increased skin permeability is their higher ethanol concentration. The lipids in the ethosomes and the stratum corneum bilayer are thought to be fluidized by ethanol, which is acknowledged as an efficient permeability enhancer. These pliable, squishy vesicles can more easily pass through the lipid bilayer's disarray because to this fluidization. Studies have demonstrated that after treatments lasting 12, 24, and 48 hours, ethosomes do not irritate skin despite their high alcohol content.

Proliposomes Gels

Vesicular systems' inadequate stability is the main obstacle to their development for industrial and therapeutic applications. Proliposomes offer a versatile delivery system that improves stability and makes large-scale sterilizing easier. This technique has been applied to deformable liposomes as well as liposomes and niosomes to increase their stability. Traditional liposome production methods are combined with a water-soluble carrier to make proliposomal formulations, which turn the system into a dry, freely-flowing powder. By adding this dry powder to a suitable structural medium, it can subsequently be transformed into a gel. A prednisolone proliposomal gel was created recently, and its effectiveness as a topical medication for rheumatoid arthritis was evaluated. The results demonstrated the promise of the developed proliposomal gel for the successful treatment of rheumatoid arthritis by showing improved anti-inflammatory effects and prolonged drug release.

Phytosomal Gels

Phytosomal gels Flavonoids, glycosides, and phenolics are among the chemicals that make up the majority of phytoconstituents that dissolve in water. Their effectiveness is lowered as a result of their poor absorption when administered topically or consumed orally (44, 45). It was shown that these botanicals' bioavailability was greatly enhanced by complexing them with phospholipids, which led to improved and faster skin absorption.

Gels of Vesicular Phospholipids (VPG)

According to Brandl *et al*., vesicles or liposomes make up the lipid phase of vesicular phospholipid gels (VPGs), which are semisolid aqueous dispersions of phospholipids (46, 47). Whereas liposome hydrogels produce their gel structure by including hydrophilic polymers into the liposomal dispersion, VPGs obtain their gel-like consistency by densely packing vesicles.

M-i-L (Microgel in Liposomes)

This innovative technology is the most recent advancement in liposomal gels and has not yet been applied to the topical administration of medications. Hydrogel-supported lipid bilayers, gel core liposomes, lipobeads, liposome-nanogel assemblies, and microgel in liposomes (M-i-L) are some of the names used in the literature to describe this kind of liposomal gel. The core of the phospholipid bilayer vesicle that constitutes M-i-L is a hydrogel polymer. This design mimics natural cells and leverages the benefits of both features. Additionally, the polymer network inside the inner microgel reduces the likelihood of rapid breakdown and early drug release in the body by fortifying the lipid bilayer.

Gels using Lecithin Microemulsion

Lecithin microemulsion gels fall into one of two main categories based on their matrix structure.

Microemulsion-Based Organogels Based on Lecithin (LMBGs)

It is said that phospholipid-based LMBGs are transparent, viscoelastic, biocompatible, thermodynamically stable, and isotropic. In 1988, Scartazzini and Luisi released the first study on gel-structured water-in-oil microemulsions while examining the optimal conditions for soy lecithin to form reverse micelles. They noticed that organic soy lecithin solutions became noticeably more viscous when small amounts of water were added. In nonpolar environments, the naturally occurring surfactant lecithin can form backward micelle-based microemulsions thanks to its geometric properties. When given enough water, these microscopic reverse micelles can expand monodimensionally into elongated, flexible, cylindrical large micelles more than a critical concentration of lecithin. This gives the substance a gel or jelly-like consistency as the massive micelles create a continuous network that encloses the organic phase outside.

PLOs, or pluronic lecithin organogels

When significant amounts of high-purity lecithin are needed, obtaining it can be expensive and difficult. Because of their efficacy as cosurfactants and stabilizers, some study has investigated the addition of synthetic polymers, like pluronics, to lecithin-based microemulsion-based gels (LMBGs). By including pluronics as cosurfactants, these studies showed that organogelling may be accomplished with lecithin of lesser purity. A class of non-ionic block copolymers known as pluronics—also called poloxamers, poloxamer polyols, or lutrols—are made up of ethylene and propylene oxide. LMBGs containing pluronics are frequently referred to as pluronic organogels, poloxamer organogels, or pluronic lecithin organogels (PLOs).

Hydrogels Stabilized by Lecithin Microemulsions

The conversion of oil-in-water microemulsions into gels has recently improved their potential for cutaneous applications. This change was achieved by adding different hydrogel matrices or water-soluble polymers, including carrageenan, gelatin, carbomer 934, and carbopol. Only the water phase on the outside was gelled or thickened during this process; the inside microemulsion droplets stayed liquid. In general, lecithin-stabilized microemulsion-based hydrogels are water-continuous microemulsions in which lecithin acts as a surfactant to maintain system stability. These microemulsions are subsequently transformed into a gel state by use of one of the hydrogel matrices outlined earlier (39).

***In-Situ* gelling systems in Novel Drug Delivery System**

Over the past decade, in-situ gelling systems for intravenous, buccal, vaginal, ocular, and nasal delivery have been developed. Drug delivery techniques that use *in-situ* gelling have garnered a lot of attention in the last ten years

some of examples of various *in-situ* gelling system which was shown in Table No 1. A variety of endogenous triggers, including variations in pH, temperature, or the presence of ions, can cause these systems, which are in a sol-state prior to delivery, to convert into gels. They can be administered in several ways to aid in the local or systemic transportation of medications, and they are effective transporters of drug-loaded microparticles and nanoparticles. A variety of *in-situ* gelling natural, synthetic, and/or semi-synthetic polymers can be used alone or in combination to create these systems. Particularly helpful for extending the residence duration at the site of action or absorption are mucoadhesive polymers. *in-situ* gelling systems can also incorporate solid polymeric formulations, often produced by freeze-drying, that rapidly hydrate when exposed to biological fluids. Drug release can be controlled thanks to this gel formation (48).

Hydrogels

The 3-dimensional network of polymer chains sprinkled with water that fills the spaces left by macromolecules is what modern definitions of hydrogels define as systems consisting of two or more constituents. The amount of water stored in these structures at equilibrium may vary significantly depending on the specifics of the polymer or polymers utilized, as well as the type and density of the network connections. Hydrogels typically display a mass fraction of water significantly greater than that of the polymer when they are swelled. It is standard procedure to use synthetic polymers that are soluble in water when not cross-linked to produce significant swelling. There are numerous "classical" chemical methods for making hydrogels. Multi-step processes that involve the synthesis of reactive polymer molecules and their subsequent cross-linking—which may also involve reactions with appropriate cross-linking agents—are among these techniques, as are one-step processes like polymerization and the simultaneous cross-linking of multifunctional monomers. Polymer engineers may accurately control structural features like cross-linking density at the molecular level when designing and building polymer networks, in addition to tailoring properties like mechanical strength, biodegradability, and reactivity to chemical and biological stimuli(49-53).

Newly released research on exciting gel-based delivery systems.

In recent years, innovative drug delivery methods have demonstrated remarkable success in delivering medicinal chemicals with targeted and localized effects which is mentioned in Table 2. Furthermore, these technologies allow for controlled drug release at preset rates while minimizing negative effects. Gels are three-dimensional, semi-solid structures composed of polymeric matrices. They function similarly to solid systems, although having a higher proportion of liquid components than solid dispersions (54-56). In a variety of industries, including as biotechnology, food, medicine, and cosmetics, innovative gel systems have useful uses. The efficient release of medicinal compounds is made possible by the simple formulation of a gel-based delivery system. Furthermore, by ensuring that the therapeutic substance and the absorption site have intimate surface contact, these devices improve the delivery of molecules via a variety of pathways. In the past decade, scientists have made substantial progress in their comprehension of gel-based drug delivery methods. New gel-based systems that can initiate drug release in response to particular biological or environmental stimuli, including temperature, pH levels, enzymes, ultrasound, and antigens, have been made possible by these advancements (57-62).

A Thorough Examination Based on Submitted Patents

The world intellectual property organization (WIPO) oversees the Patent Cooperation Treaty (PCT), a global patent filing system that processes international patent applications pertaining to hydrogels. By emphasizing the inventions and patents pertaining to hydrogels, this study particularly describes as follows (63). The following Table 3 shows overall collective information about reported patents in this arena.

Prospects for Gel Applications in Biomedicine in the Future

Gel-based systems' prospects in biological domains is promising and continues to evolve with advancements in material science, nanotechnology, and biomedical engineering. Key future directions include:

Personalized Medicine: Development of stimuli-responsive gels that can be tailored to patient-specific conditions and genetic profiles for targeted drug delivery and regenerative therapies.

Smart Gels: Integration of sensors and actuators within gels to create "smart" systems capable of real-time response to physiological signals, useful in wound healing and chronic disease monitoring.

Tissue Engineering: Further enhancement of gels as scaffolds for tissue engineering, particularly for complex organs. The use of 3D printing with gel matrices opens avenues for organ regeneration and repair.

Minimally Invasive Therapies: Injectable and *in-situ* forming gels that solidify under physiological conditions offer less invasive therapeutic options and are likely to see greater clinical adoption.

Combination Therapies: Gels are anticipated to be essential in combinational delivery of therapeutics (e.g., drugs, genes, proteins) and diagnostics (theranostics), leading to improved efficacy and reduced side effects.

Biodegradability and Biocompatibility: Continued research on improving the biodegradability and biocompatibility of gel materials, especially for long-term implants and drug delivery systems.

CONCLUSION

Gels have become a highly adaptable class of materials with enormous promise for use in a wide range of biological applications. Due to their tunable physical, chemical, and biological properties. From methods for delivering drugs to tissue engineering scaffolds and wound dressings, their adaptability and functionality have positioned them as a cornerstone of modern biomedical innovations. As interdisciplinary research expands, integrating material science with biology and engineering, gels are poised to revolutionize personalized medicine, minimally invasive procedures, and regenerative therapies. Continued innovation, rigorous clinical evaluation, and regulatory alignment will be crucial for translating these promising materials from the laboratory to real-world medical applications.

ACKNOWLEDGMENT

The authors would like to express their gratitude to Dr. A P Basavarajappa, Director, Bapuji Pharmacy College for providing all the support required for the outcome of the paper.

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Table 1: Example of Various In situ Gelling System

Route	Pathology	API	Polymer/s	Key Findings	References
Ocular	Glaucoma	Pilocarpine	Gelatin-graft-poly(N-isopropylacrylamide) (GN) copolymer	Demonstrated prolonged intracameral high drug concentration in an animal model	41,42
Nasal	Allergic rhinitis	Mometasone furoate (MF)	Gellan gum	proved to be more effective in an animal model than nasal medication suspension.	43,47
Buccal	Oral mucositis	Benzydamine hydrochloride	trimethyl chitosan (TMC) and glycerophosphate (GP)	promote extended drug release and enhance	48,49

				resistance to physiological clearance processes, as shown in both ex vivo and in vitro investigations.	
GIT	inflammatory diseases	Budesonide (BUD)	Poloxamer F-127	The formulation demonstrated the ability to alleviate inflammatory damage in the intestinal mucosa (animal model)	50
Vaginal	Vaginosis	Metronidazole	Thiolated gellan gum (GG) through conjugation with 2-(2-Amino ethyldisulfanyl) nicotinic acid (AMENA)	increased mucosal surface adherence; notable antibacterial activity; and prolonged metronidazole release	51
Intravesical	Bladder cancer	Deguenil (D)	Drug-loaded N-[1-(2,3dioleoyloxy)propyl]N,N,Ntrimethylammonium methyl sulfate (DOTAP) and monomethoxyl poly(ethylene glycol)-poly(ε-caprolactone) nanoparticles incorporated in Pluronic F127	extended duration of drug residence; high drug concentration in the bladder (animal model)	52

Table 2: recently published studies on innovative systems for gel-based delivery.

kinds of Hydrogels	Constituency (polymers)	Active Pharmaceutical Ingredient	Disease	References
Thermo-responsive Hydrogel	7-ethyl-10 hydroxycamptothecin (SN-38) liposomal hydrogel	SN-38	Hepatocellular carcinoma	55
Photosensitive hydrogels	azobenzene and α-cyclodextrin-modified hyaluronic acid combined with gold nanobipyramids	doxorubicin (DOX)	human epidermal keratinocytes	56
pH-responsive hydrogels	poly(acrylic acid) hydrogel complexed with stabilized amorphous calcium carbonate	DOX	hepatocarcinoma	57
Redox-stimuli Hydrogels	dextrin nanogel	DOX	Breast Cancer	58
Magnetism-Responsive Hydrogels	Ferromagnetic vortex-domain iron oxide, chitosan, and poly(ethylene glycol)	DOX	Breast Cancer	59
Proniosomal Gel	Surfactant, Lecithin, and Cholesterol	Curcumin	Ocular Inflammation	60
Liposomal Gel	Cholesterol, Carbopol 934	Travoprost	Glaucoma and Ocular Hypertension	61
Injectable Hydrogel	Horseradish Peroxidase (HRP), H2O,Chitosan, Hyaluronic Acid (HA),	Dextrane, Tyramine	Cartilage Tissue Regeneration	62
Shear-sensitive hydrogels	hyaluronic acid, aldehyde groups, amino groups, HSPC lipid	celecoxib	reduce cartilage damage and inflammation caused by shear stress	63

Table 3: The patents pertaining to hydrogels.

IPC Code	Definition	Description	Patent Documents
C08J3/075	Macromolecular gels produced through processes in aqueous environments	This category includes patents related to the creation and processing of macromolecular gels, such as hydrogels, utilizing aqueous solutions, with a focus on advancements in gel formation techniques.	8865
A61L27/52	Hydrogels or hydrocolloids utilized in prosthetics or for coating prosthetic devices	This classification emphasizes innovations in hydrogels or hydrocolloids intended for medical devices and prosthetic coatings, highlighting their biocompatibility and essential characteristics for medical use.	8109
A61K9/00	Pharmaceutical formulations distinguished by their unique physical forms	This section pertains to pharmaceutical products where the physical form (such as tablets, gels, capsules, patches, etc.) plays a vital role in enhancing drug delivery, absorption, or administration.	6789
A61K9/06	Ointments and bases for ointments, including the equipment for their production	This category focuses on ointments as a form of medicinal preparation, encompassing formulation bases and the tools or methods employed in the production of topical drug delivery systems.	5561

G02C7/04	Optical components fabricated from organic materials, including plastics	This classification addresses optical components, such as lenses and prisms, made from organic materials like plastic, which are particularly significant for contact lenses and lightweight, durable optical instruments.	3942
A61K47/36	Medicinal preparations involving polysaccharides or their derivatives	This section emphasizes advancements in drug delivery mechanisms, wound care solutions, or tissue engineering that utilize polysaccharides such as gums, alginate, hyaluronic acid, or chitosan.	3865
C08J3/24	Crosslinking of macromolecules	This classification addresses the crosslinking of macromolecules, concentrating on the mechanical properties and crosslinking agents that improve material strength, elasticity, and thermal stability, frequently applied in hydrogels and vulcanization processes.	3639
A61L27/54	Biologically active materials used in medical or prosthetic applications	This area encompasses materials engineered for biological interaction in fields such as regenerative medicine, wound healing, or medical devices, often utilizing hydrogels or biocompatible polymers for the delivery of therapeutic substances.	3575
A6L26/00	Chemical aspects or materials used for liquid bandages	This category focuses on innovations concerning the chemical formulation and application of liquid bandages for effective wound care and protection.	2943

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

CASE STUDY ARTICLE

COVID 19 Vaccine Side Effects Among the Staff Nurses of Selected Hospitals of Central Gujarat, India : A Cross - Sectional Study

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Received: 29 Oct 2025 Revised: 20 Dec 2025 Accepted: 05 Jan 2026

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ABSTRACT

Vaccination is an effective way of fighting against infectious diseases. Governments have prioritized high-risk groups for receiving the initial batch of COVID-19 vaccines due to the limited availability of vaccines worldwide. Side effects may occur, which are common symptoms of the body's immune response. There is no significant evidence to suggest that any vaccine, including the COVID-19 vaccine, would cause severe adverse effects leading to long-term health issues. A non-experimental designed was applied for this descriptive study. As sample total double of hundred staff nurses was selected with the help of convenient nonprobability technique. Twenty-seven closed-ended questionnaires (dichotomous questions) were used for data collection.Data collection was done through face to face interaction. The data was analysed as per the objectives of study. The level of side effects of the COVID-19 vaccine among 200 staff nurses shows that 188 of them experienced mild side effects, 12 experienced moderate effects, and none of the participants had serious adverse effects from the COVID-19 vaccination. Overall, the majority of staff nurses experienced mild side effects. There were significant demographic variables associated with qualification (χ^2 = 19.125) and working experience (χ^2 = 13.097). According to this study, COVID-19 vaccinated nursing staff did not experience severe side effects. The majority of participants (94%) experienced mild side effects, while 6% reported moderate side effects from the COVID-19 vaccine.

Keywords: COVID-19, Vaccine,Staff nurse, Side effects.

INTRODUCTION

In 27 January 2020, the earliest COVID-19 instance was reported and from the March 2020 a nationwide lockdown was announced in the India. Near about one lakh cases of covid-19 was recorded by May 18, 2020. India government has commenced the vaccination drive from 16 January 2021 in all over country. In first step the vaccination drive focusing on health care workers. After emerging in China in a city named Wuhan, in November2019, the novel coronavirus illness (COVID-19) was deemed a worldwide pandemic in March month of 2020. The government has put in place a set of protocols and steps to assist stem the growth of COVID-19, which includes the social isolation, to use masks properly on nose, travel bans, lockdowns and regular hand washing with soap and water or sanitizer. Researchers and pharmaceutical companies have created safe and efficient vaccines to further curb the development of the disease and the deaths it causes. Health care professionals, elderly people, particularly those are having long-term co-morbid diseases, those who work in necessary services all are consider in high-risk populations. Due to contact with persons who may be exposed to COVID-19 such as healthcare providers, visitors and also close contact with COVID-19sufferers and their bodily secretions, staff nurses are at a significant risk of spreading the disease. [1,15]

In response to COVID-19 exposure, the COVID-19 vaccine protests. It may be challenging to perform daily duties while experiencing these side effects, but they should pass in a few days. Unfavourable effects might not occur in some people. Tracking of vaccinations in the past has revealed that, if the dose is given, side effects typically manifest themselves within 06 weeks. Because of this, the FDA mandated that each medicine for COVID-19 that has been approved be read at least 02 months (eight weeks) after the last dose. Vaccinations, it is one of the most effective and cost-effective public health interventions, save millions of lives every year. Starting in 2020 scientists and pharmaceutical enterprises are rushing to create vaccinations after the SARS-CoV-2 genetic sequence was decoded and the World Health Organization (WHO) declared the pandemic on March 11th, 2020. "The WHO Strategic Advisory Group of Experts (SAGE)",characterised vaccine reluctance as "delay in acceptance or refusal of vaccination despite availability of vaccination services". It is thought that among the publicfear to get vaccines and mistrust both are worldwide pose a significant barrier to the realisation of such a goal.In order to stop further deaths and stop the pandemic from spreading, the policymakers may be helped by the findings of the current study to launch proactive campaigns and carefully crafted strategies that emphasise the value of vaccination among the populace and encourage vaccination acceptability and uptake, particularly in patients who are weaker. [2]

Objective

- To evaluate the COVID-19 vaccine's side effects in the staff nurses.
- To associate the side-effects of COVID-19 vaccine with selected demographic variables of the staff nurses.

MATERIALS AND METHODS

This study adopted a quantitative research approach with a descriptive, non-experimental design. It was conducted in selected hospitals across central Gujarat, with a sample of 200 staff nurses chosen through convenience non-probability sampling. Data collection occurred over a two-month period, from November to December 2021, using twenty-seven closed-ended questionnaires (dichotomous questions) administered via face-to-face interaction. The analysis focused on identifying the side effects of the COVID-19 vaccine among participants and examining the relationship between demographic variables, such as qualification and work experience, and the occurrence of these side effects. The research proposal was submitted to the ethical committee for approval under proposal number IEC/CHARUSAT/21/69. The sample size was determined using power analysis (Z1−β), with an alpha error of 5% and a power (1−β) of 80%. The reliability of the research tool was assessed using Karl Pearson's technique, resulting in a correlation coefficient of r = 0.799. Participants were clearly informed about the purpose of the study. The tool was developed based on the study's objectives and the inclusion and exclusion criteria. It consisted of two sections: the

first section addressed demographic variables, while the second section focused on evaluating adverse reactions to the COVID-19 vaccine.

Procedure

This descriptive, non-experimental study was conducted using 27 closed-ended questionnaires administered to staff nurses in selected hospitals of central Gujarat. A total of 200 participants were selected using a convenience non-probability sampling technique. Prior written informed consent was obtained from each participant, ensuring voluntary participation and confidentiality of their information. A pre-validated tool, consisting of a demographic questionnaire and a survey on the side effects of the COVID-19 vaccine, was utilized. The data were coded and organized into a master sheet, then compiled and analyzed using both descriptive and inferential statistics. The side effects of the COVID-19 vaccine were presented as frequencies and percentages. [Figure-1]

Figure-1 is presenting side effects of COVID-19 vaccines frequency and percentage among the staff nurse of selected hospital of central Gujarat.

RESULT

Finding of study were presented under the following three sections

Section First: Findings belongs to demographic variables of the participants.

Section Second: Findings related to COVID-19 vaccines side effects in staff nurses.

Section Third: Findings of association between COVID 19 vaccines side effects and selected demographical variable.

Section I indicate that majority of participants (49%) belong to 25 to 30 age group, (27.5%) belong to below 25 age group, (15.5%) belong to 31 to 35 age group and (8%) belonged from above 35 age group. 31.5% were male participants, 68.5% were female. Regarding their qualification1% were completed M.Sc. Nursing, 5.5% completed their B.Sc. Nursing, 0.5% completed P.B. B.Sc. Nursing, 46.5% completed GNM and 46.5% completed ANM .Most of the staff nurses (53.5%) had a working experience of 1 to 5 years, (20%) below 1 year, (19.5%) 5 to 10 years and (7%) more than 10 years. 42.5% were unmarried and 57.5% were married. In Section II findings showed that majority of participants (94%) had mild, 6% had moderate and out of 200 participants' no one had severe consequences of the COVID-19 vaccination. The data presented in section III showed that there were significance association between the demographic variables (qualification and the working experience) with side effects of COVID-19 vaccine.(Table No. 1 & 2]

DISCUSSION

A descriptive, non-experimental design was carried out to assess the adverse effects of the COVID-19 vaccine among 200 staff nurses in selected hospitals in central Gujarat. The study found that out of 200 participants, 188 (94%) experienced mild adverse effects from the COVID-19 vaccination, 12 (6%) reported moderate adverse effects, and none of the participants had severe side effects. A study conducted by Abonouab Raid, Andrea Pokorna et al. in Germany supports these findings. In their trial, 92 participants were involved, with 94.6% reporting mild (local) adverse effects and 5.4% reporting moderate (systemic) effects. These studies indicate that while the COVID-19 vaccine may cause mild and moderate adverse effects, it does not lead to severe side effects.

Limitation of the study

This study has following limitations. This research was limited to only staff nurses of selected hospital of central Gujrat. It can be carried out on other health care worker of other hospital. This study was also limited with 200 sample only.

CONCLUSION

This study revealed that the majority of staff nurses experienced mild side effects from the COVID-19 vaccine, with very few reporting moderate effects. As healthcare professionals, nurses play a critical role as counselors and communicators, helping to educate the community about the importance of vaccination and supporting informed decision-making. The findings of this study can assist in addressing common misconceptions about the potential negative health effects of the COVID-19 vaccine. Additionally, the results may contribute to the future planning and implementation of vaccination programs, helping to improve public confidence in vaccines. Ultimately, this study provides valuable insights that can enhance nursing practices and support efforts to improve vaccine acceptance in the community.

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Table No. 1 Significance association between qualification with side effects of COVID-19 vaccine.

Qualification								
Variable	**Score (Mild side effects)**	**Score (Moderate side effects)**	**Score (Severe side effects)**	**Total**	**X2**	**df**	**P value**	**Level of significance**
M.Sc. Nursing	2	0	0	2				
B.Sc Nursing	7	4	0	11				
P.B. B.Sc Nursing	1	0	0	1	19.125	4	9.488	19.125>9.488 S
GNM	89	4	0	93				
ANM	89	4	0	93				
Total	188	12	0	200				

Table -2 Significance association between the working experience with side effects of COVID 19 vaccine.

Working experience								
Variable	**Score (Mild side effects)**	**Score (Moderate side effects)**	**Score (Severe side effects)**	**Total**	**X2**	**df**	**P value**	**Level of significance**
Below 1 year	33	7	0	40				
1 to 5 Year	102	5	0	107				
5 to 10 year	39	0	0	39	13.097	3	7.815	13.097>7.815 S
More than 10year	14	0	0	14				
Total	188	12	0	200				

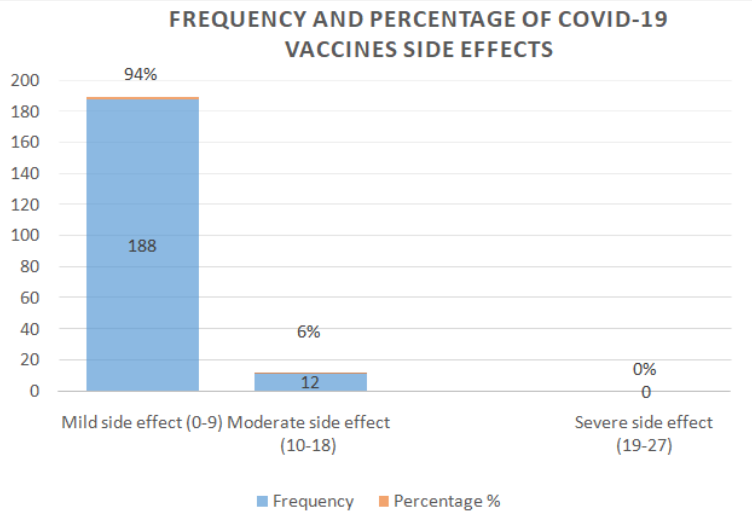

Figure-1: Frequency and Percentage of Covid-19 Vaccines Side Effects

RESEARCH ARTICLE

Leveraging AI / ML Concepts in Pharmaceutical Drug Development : Navigating Regulatory Compliance Pathways

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Received: 25 Nov 2025 Revised: 20 Dec 2025 Accepted: 22 Jan 2026

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ABSTRACT

By increasing prediction accuracy, speeding up decision-making, and streamlining procedures in discovery, preclinical testing, clinical trials, manufacturing, and pharmacovigilance, artificial intelligence (AI) and machine learning (ML) are revolutionizing the creation of pharmaceutical drugs. Rapid target selection, effective in silico screening, toxicity prediction, adaptive clinical study design, better patient recruitment, real-time production control, and early safety signal detection are all made possible by these technologies. Stronger regulatory control is now required as their influence grows. Important frameworks that offer structured guidance to guarantee transparency, dependability, and patient safety include the FDA AI/ML Action Plan, EMA Reflection Papers, Good Machine Learning Practice (GMLP), algorithm audit and governance expectations, predefined change control plans (PCCP), and risk complexity classification tools. Dataset integrity, validation proof, model versions, human review, and lifecycle monitoring are all prioritised in regulatory requirements for documentation. Even while AI/ML has greatly increased R&D efficiency, there are still issues with data quality, interpretation barriers, model bias, and altering international regulatory harmonization. In order to adopt AI/ML in pharmaceutical development in a secure, ethical, and legal way it is needed to remove these barriers.

Keywords: Artificial Intelligence, Machine Learning, Drug Development, Regulatory Compliance

INTRODUCTION

The fast development and integration of machine learning (ML) and artificial intelligence (AI) has created a revolutionary shift in the pharmaceutical sector. These technologies are now vital components of current drug development procedures, providing opportunities to accelerate in discovery, reduce failure rates, enhance diagnostic accuracy, and increase regulatory options. They are no longer experimental add-ons. AI-enabled pharmaceutical innovation has been made viable during the past ten years by the growth of biomedical data, the rise of deep learning algorithms and the availability of high-performance computing. As opposed to the genomic revolution of the early 2000s, this modification is clear at all phases of the drug development process, from early target identification to post-market surveillance. [1,2]

Background and importance of AI/ML in drug development:

Historically, the procedure of developing novel drugs has been time-consuming, expensive, and unsafe. Traditional methods mostly rely on labour-intensive wet lab analyses, multi-year clinical evaluations, and trial-and-error experimentation. Based on several types of studies, it might cost between US$1.5 and US$2.6 billion to bring an entirely novel molecular device to market, while it often takes over 10 to 12 years [3]. Especially in early discoveries and phase two clinical trials, where insufficient efficacy and unexpected toxicity can frequently result in failure, the rate of attrition is still high. In regard to this, AI/ML gives an innovative approach by quickly assessing huge data sets, detecting subtle patterns, estimating biological outcomes, and modeling outcomes of treatment even before human or animal studies start. [4,5]

The importance of AI/ML is most evident in early-stage drug discovery, where deep learning models now enable virtual screening of billions of compounds in hours, compared to the months required for traditional high-throughput screening. A show that DL-based molecular modeling improves lead identification by predicting physicochemical and ADMET properties with high accuracy [2,6]. Similarly, AI-driven target identification platforms use genomic mapping, protein-protein interaction networks and multi-omics integration to uncover disease mechanisms previously invisible to human-driven analysis. Beyond discovery, AI supports preclinical toxicology, clinical trial optimization, digital pathology standardization, and real-world evidence generation, making it a critical enabler of innovation throughout the development process. [7]

Scope of AI/ML in the entire phases of pharmaceutical development:

Each stage of pharmaceutical research is now being influenced by AI/ML technologies, to speed up, increase accuracy, and minimize costs. Using modern techniques like reinforcement learning and GANs, AI in the discovery of drugs speed up virtual screening, develops novel drugs, predicts the viability of synthesis, and improves therapeutic qualities [8,9]. While PBPK-AI integration increases dose prediction and translational accuracy, machine learning models in preclinical research predict toxicological, increase *in vitro-in vivo* correlation, reduce testing on animals, and simulate metabolic pathways [10]. While NLP technologies automate data mining and monitoring for increased efficiency and compliance, AI speeds up patient recruitment, improves adaptive trial design, allows the creation of digital biomarkers, and strengthens patient stratification during clinical development [11]. AI powers quality-by-design, real-time monitoring, anomaly detection, and predictive maintenance in manufacturing and quality control to guarantee constant product quality [12]. AI is supporting algorithm review, streamlining regulatory submissions, standardizing digital pathology, and automating documentation in regulatory affairs [13,14]. AI-powered pharmacovigilance in post-marketing surveillance uses social media, EHRs, and real-world data to identify safety signals more quickly and precisely [15].

Applications across the life cycle of drug development:

By allowing data-driven insights, cutting down on timelines, and increasing rate of success in discovery, development, and post-market surveillance, AI and ML are revolutionizing pharmaceutical research and development [1,19]. Key uses consist of:

Identification of targets and drug discovery:

- To find new therapeutic targets, AI models mine massive biological datasets (genomics, proteomics, chemical libraries).
- Deep learning speeds up the identification of lead compounds by predicting molecular interactions, binding affinities, and off-target effects.
- The creation of new chemical structures with optimal medicinal characteristics is made possible by AI-assisted de novo drug design [1,7,20].

Hit-to-lead optimization and composite screening:

- Compounds with a high chance of success are given priority by ML algorithms, which shortens the time and expense of experimental screening [2,21].
- To enable logical design choices, predictive models improve chemical and ADMET attributes [1,3].

Preclinical research:

- By predicting PK/PD, preclinical efficacy, and *in vitro*/*in vivo* toxicity, AI reduces the need for animal research.
- To find safety hazards early in development, machine learning algorithms simulate interactions between drug targets and drug systems [21,22].

Design of clinical trials and patient enrolment:

- AI maximizes statistical power, endpoints, dosage, and adaptive trial design.
- To effectively match patients, particularly for rare diseases, and enhance admission results, NLP and ML examine EHR and genomic databases.
- Site selection and test efficiency are further enhanced by virtual testing and simulation-based feasibility studies [11,23,24].

Finding biomarkers and making follow-up diagnoses:

- ML finds predictive biomarkers for response prediction and patient classification.
- AI aids in the creation of companion diagnostics to enhance therapy accuracy and lower unfavourable consequences [22, 24].

Production of pharmaceuticals and quality assurance:

- AI predicts batch quality, optimizes production parameters, and permits predictive equipment maintenance.
- In real time, deviations, anomalies, and quality flaws are detected using computer vision and machine learning.
- By forecasting demand and inventory needs, predictive analytics increases supply chain resilience [25,26].

Formulation development:

- AI forecasts the best formulation, stability, and adjuvant compatibility.
- ML minimizes the need for repeated trials for creating biological medications and solid dosage forms [29, 30].

Pharmacovigilance and post-market surveillance:

- To identify warning signs early on, AI keeps an eye on social media, real data, and accounts of unfavourable incidents.
- Long-term safety trends, ADR patterns, and possible recalls are identified using ML models.
- Automation improves regulatory compliance and pharmacovigilance reporting efficiency [23, 30].

Market approach and regulatory information:

- AI keeps an eye on competitive pipelines, clinical trial databases, and changes in international regulations.
- ML helps prioritize R&D by identifying unmet requirements and strategic possibilities in the therapeutic landscape [29, 30].

Regulatory compliance guidelines:

Strong regulatory compliance is necessary for the implementation of AI and ML in pharmaceutical drug development in order to ensure patient safety, efficacy, and data integrity. Regulatory routes integrate governance frameworks, risk assessment, best practices, agency-specific guidelines, and organized paperwork for post-market surveillance and approval [20, 31].

FDA action plan for AI/ML

- Guidelines for AI/ML-enabled software and other regulated applications of artificial intelligence in drug development are provided by the FDA's AI/ML Action Plan for Medical Devices (SaMD).
- AI systems must prioritize continuous learning, ongoing monitoring, and revalidation; pre-market assessment of model performance, reliability, and clinical efficacy.
- Requirements for submission include thorough documentation of datasets, algorithm logic, training and validation processes, performance measurements, and risk-reduction tactics [20,32,33].

EMA reflection papers:

- AI/ML applications inside the European regulatory environment are guided by EMA reflection papers.
- Focus on validation, reproducibility, ethical issues, and clinical study integration. Assists with RWD/RWE applications for submission to regulations.
- Documentation needs include risk-benefit analysis, data origin, validation outcomes, and model development records.
- Submission requirements: Clinical trial protocol and paperwork, including AI-assisted decision-making procedures, must demonstrate regulatory compliance [34].

Good Machine Learning Practice (GMLP):

GMLP provides best practices to guarantee the security, effectiveness, and control of AI/ML tools:

- Standardized procedures for model training, testing, validation, and data curation.
- Documentation includes change logs, modeling code, complete datasets, and performance measurements.
- Supports submissions by proving model interpretation, reproducibility, and FDA/EMA compliance [35].

Framework for algorithmic revision and model management:

Regulators anticipate governance and a defined framework:

- Algorithmic auditing guarantees impartiality, openness, and lack of prejudice.
- Development, deployment, and monitoring roles are outlined in model governance frameworks.
- **Documentation:** post-implementation assessments, monitoring logs, validation studies, and audit reports [35, 36].

Matrix for risk-complexity:

- AI/ML applications are categorized using a risk-complexity matrix based on system complexity and patient effect.
- Systems that are high-risk or high-complexity need to be rigorously validated and closely examined by regulators.
- Low-risk, low-complexity tools might need less supervision.
- Documentation: Validation reports, risk assessments, and mitigating techniques [31].

Submission and documentation specifications:

Regulatory bodies demand a lot of documentation:

- Data documentation, including sources, quality, and pre-processing.

- Model documentation: versioning, hyperparameters, and algorithm description.
- Metrics, robustness, bias analysis, and external validation are examples of validation documentation.
- Post-marketing monitoring plans, audit trails, and change logs are examples of governance paperwork.
- The submission package must contain risk evaluations, GMLP, PCCP, and FDA/EMA compliance [19, 20, 21, 37, 38].

METHODOLOGY

In order to understand how artificial intelligence (AI) and machine learning (ML) are applied in pharmaceutical medication development and how they satisfy regulatory standards, this study employed an organized methodology. Target discovery, virtual screening, medication design, toxicity prediction, patient recruiting, clinical trial planning, manufacturing control, and post-marketing safety monitoring were among the domains in which it looked at the application of AI/ML. To comprehend expectations for data quality, model validation, transparency, interpretability, performance monitoring, and lifecycle management of AI systems, key guidelines from the FDA, EMA, and ICH were examined. In order to evaluate the capabilities, hazards, and supporting data required for regulatory approval, the study also evaluated widely used AI/ML tools, such as deep learning models, natural language processing systems, chemical informatics platforms, and predictive toxicology software. Pharmaceutical firms' practical application of AI/ML is examined through real-world case studies, which emphasize both achievements and difficulties such data gaps, model interpretation, and regulatory ambiguities. The study found important patterns, benefits, gaps, and future directions by examining all of this data. AI/ML can speed up the identification of targets, enhance forecasts, reduce development times, streamline clinical trials, and enhance safety monitoring. But for these technologies to be used successfully, ethical and security issues must be addressed, transparency must be maintained, best practices must be followed, and legal requirements must be met. Overall, the study demonstrates that AI and ML have enormous potential to revolutionize medication development; nevertheless, for the innovation to be safe, effective, and responsible, cautious implementation guided by laws is required.

RESULTS

The results demonstrate that AI/ML enhances overall efficiency, speed, and accuracy throughout the whole drug development process. AI speeds up target identification and improves the efficiency of novel compound design in drug discovery. AI reduces the necessity for animal testing by predicting toxicity in preclinical phases. AI enhances patient recruitment, facilitates adaptive trial design, and streamlines data management during clinical trials. AI-based quality control and real-time monitoring make production more dependable. Regulations are made simpler by automated documentation and quicker compliance assessments. AI uses real-world data to help identify negative effects before a medicine is put on the market. In general, early research phases see the greatest acceptance of AI, but later stages continue to see an increase in demonstrable impact.

DISCUSSION

Case studies across drug development using AI/ML: [39,40,41]

Case study 1- Pfizer + IBM Watson- AI for Immuno-oncology drug discovery

- **Stage:** Preclinical / Target Discovery
- **Overview:** Pfizer leveraged IBM Watson's AI and NLP capabilities to rapidly analyze massive volumes of scientific literature, clinical trial data, and molecular databases. This enabled the identification of novel immuno-oncology drug targets much faster than traditional manual review.
- **Outcome:** Accelerated early-stage discovery and prioritized promising targets for experimental validation.
- **Significance:** Demonstrates AI's ability to mine unstructured biomedical data at scale, reducing time-to-target identification and enhancing decision-making.

Case study 2- Novartis- AI for virtual clinical trials & patient recruitment

- **Stage:** Clinical Trials
- **Overview:** Novartis implemented AI tools to analyze patient electronic health records and real-world data for identifying suitable participants, especially for rare-disease trials. Virtual trial simulations and predictive models optimized trial site selection and recruitment strategies.
- **Outcome:** Increased efficiency of patient recruitment and trial enrollment while reducing operational delays.
- **Significance:** Shows AI's ability to improve clinical trial design, enhance patient matching, and reduce trial costs.

Case study 3- GSK + Exscientia – The first AI-designed drug molecule

- **Stage:** Preclinical/drug design
- **Overview:** Excientia partnered with GSK to design a new small molecule drug using AI-powered generative chemistry and predictive modeling. Remarkably, the candidate reached Phase I clinical trials in less than 12 months compared to the traditional 4–5 years for similar molecules.
- **Results:** Demonstrated that AI can accelerate de novo drug design and reduce potential optimization timelines.
- **Significance:** Highlights the transformative potential of AI/ML by efficiently generating new therapeutic agents, setting a precedent for future AI-driven drug development programs.

Identified challenges:

- Data quality issues and model bias affect accuracy, fairness and regulatory acceptance.
- Limited interpretation of complex AI models, reduces trust in practitioners and regulators.
- Non-harmonised global regulations, creates uncertainty for multinational productions.
- Ethical and privacy concerns, especially around patient data use and algorithm transparency.
- Data fragmentation and lack of standardization hinders robust model training and reproducibility.
- Inadequate validation frameworks for adaptive and continuously learning AI/ML systems.
- Lifecycle management issues, including dataset management, version control, and real-time model monitoring.
- Cybersecurity vulnerabilities, such as adversarial attacks or unauthorized manipulation of AI models.
- Lack of skilled AI professionals in pharmaceutical and regulatory environments.
- Integration difficulties with older IT systems slow down digital adoption in R&D and production.

Future Scope:

The adoption of AI in drug development is expected to drive progress in several transformative directions:

- Regulatory analytics: Using AI to generate high-quality real-world evidence for post-approval monitoring.
- Digital twin system: Virtual simulation at patient and organ level to predict safety and efficacy.
- Unified learning model: Privacy-preserving collaboration across global institutions without sharing raw data.
- Explainable AI (XAI): Models with transparent, explainable outputs for clinical and regulatory acceptance.
- Fully Adaptive Clinical Trials: AI-powered, continuous update of trial designs based on incoming patient data.
- Global harmonization: Convergence of FDA, EMA, MHRA, PMDA and ICMRA guidelines for internationally aligned AI regulation.
- AI-powered precision medicine: Integrating genomics, multi-omics, imaging and wearable data to personalize therapy decisions.

The development of drugs is being altered by AI and ML. Pfizer found novel targets for cancer drugs more quickly by using AI. Novartis made recruitment quicker and simpler by using AI to identify the best patients for clinical trials. A novel medication created by GSK and Excientia using AI entered clinical trials in less than a year—much quicker than typical. However, there are obstacles including inadequate data quality, intricate AI models, privacy issues, disparate national laws, and a shortage of qualified experts. AI has the potential to enhance clinical research, construct digital patient models, advance precision medicine and expedite, secure and customize drug development.

In Conclusion, Artificial intelligence (AI) and machine learning (ML) are reshaping pharmaceutical drug development by increasing predictive accuracy, operational efficiency and scientific decision-making in target discovery, preclinical research, clinical trials and lifecycle management. Regulatory frameworks – including the FDA AI/ML Action Plan, EMA Reflection Papers, Good Machine Learning Practice (GMLP) and new governance models – play a critical role in ensuring transparency, reliability and patient safety by requiring rigorous documentation, validation, explainability and model lifecycle monitoring. Despite its benefits, AI/ML adoption faces challenges such as variable data quality, limited model interpretability, ethical risks, algorithm bias, and the absence of globally harmonized regulatory pathways. Overcoming these issues requires strong auditing, continuous monitoring, robust data management and alignment with regulatory expectations. As AI/ML increasingly integrates with real-world evidence, adaptive learning systems, digital biomarkers and personalized medicine, their potential to reduce development timelines and improve patient outcomes will continue to grow. Realizing this potential will depend on strong collaboration between industry, regulators, practitioners and technology developers to ensure the safe, compliant and responsible integration of AI into the pharmaceutical landscape.

ACKNOWLEDGEMENTS

I express my gratitude to the Chalapathi institute of pharmaceutical sciences for the support.

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Table 1: AI/Ml Tools In Drug Development [16,17,18]

Stage	AI/ML Tools	Application
Target identification and validation (preclinical)	• Deep learning models for predicting protein targets • Generative models (GAN, autoencoders) for the creation of molecules. • ML-based virtual screening on the CADD platform	• Identify high affinity drug targets • Reduce experimental costs and time • Accelerates hit discovery
Drug Screening and Lead Optimization	• Random Forest and Gradient Boosting for ADMET • Support vector machines (SVM) for activity prediction • ML-powered molecular docking score	• Prioritize compound libraries • Reduce wet lab testing • Rapidly predict toxicity and pharmacokinetics
Design and optimization of clinical trials	• XGBoost, neural network for prediction of patient outcomes • NLP for EPR-based rights extraction • Reinforcement learning for adaptive test design	• Improving test efficiency • Increase patient stratification • Predict test scores
Compliance and submission of regulations	• NLP-based document review system • AI-enabled ESG verification tools • ML-based data integrity checking tools	• Reduce submission errors • Ensure FDA/EMA compliance • Accelerate regulatory approvals
Post-market monitoring /pharmacovigilance	• Predictive analysis and anomaly detection models • NLP-based social media and literature mining • AI signal prioritization platform	• Early detection of adverse events • Real-time security monitoring • Better risk management

Table 2: AI/Ml Contributions In Drug Development

Drug Discovery	Accelerates Virtual Screening, Designing New Molecules, ADMET Predicts.
Pre-clinical	Predicting preclinical toxicity, reducing animal testing, improving dose modeling.
Clinical development	Improves patient recruitment, supports adaptive studies, enables digital biomarkers.
Manufacturing	Provides real-time monitoring, predictive maintenance and quality control.
Regulatory affairs	Automate documentation for regulatory matters and support compliance checks.
Post marketing	Enables early detection of adverse events using real-world and social media data.

Table 3: Current Landscape Of Ai/Ml Adoption Rates In Pharmaceutical R&D

Category	Percentage (%)
Experimentation	100
Scaling	45
Drug Discovery	80
R&D Use	70
Clinical Trials	55
Recent Adoption	75
Formal Policies	65
Measurable Value	35

Table 4: Impact of AI/Ml on Drug Development

Area / Stage	Percentage (%)
Discovery	45
Preclinical	30
Clinical Trials	25
Manufacturing	35
Regulatory Affairs	40
Pharmacovigilance	55

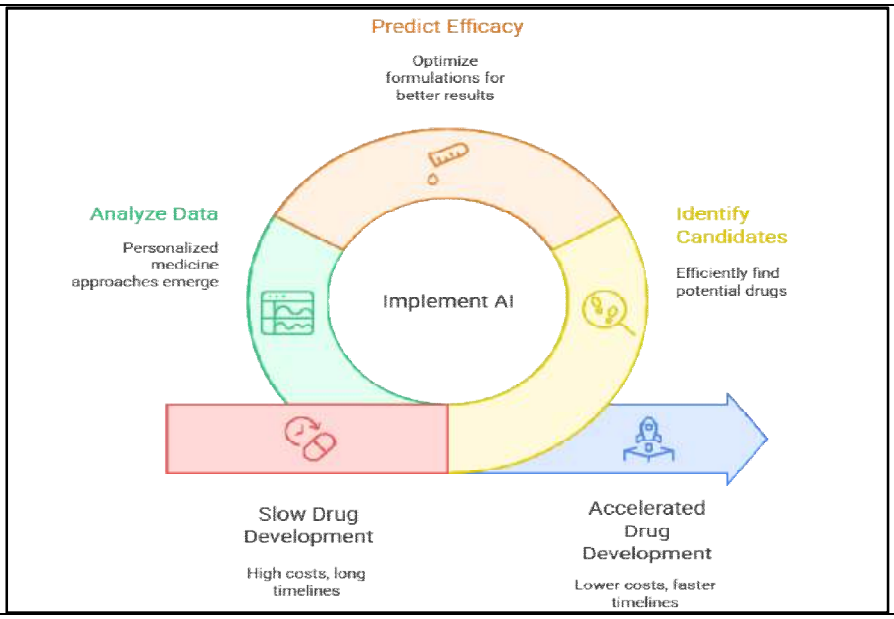

Fig. 1: AI in Pharmaceutical Drug Development

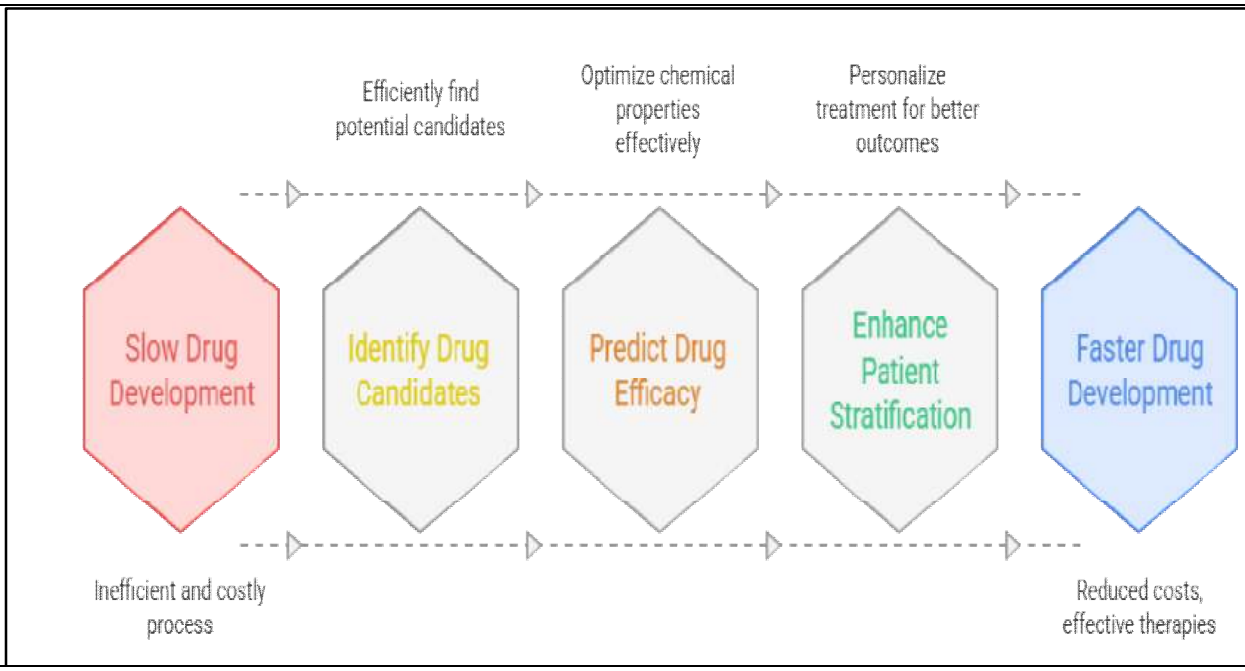

Fig. 2: ML in Pharmaceutical Drug Development

Data Acquisition
↓
Data Processing and Cleaning
↓
Natural Language Processing
↓
Feature Engineering
↓
Model Training
↓
Evaluation and Optimization
↓
Decision Support and Compliance Assessment
↓
Report Generation and Visualization
↓
Ongoing Monitoring and Updates

Fig. 3: AI/ML in regulatory management process

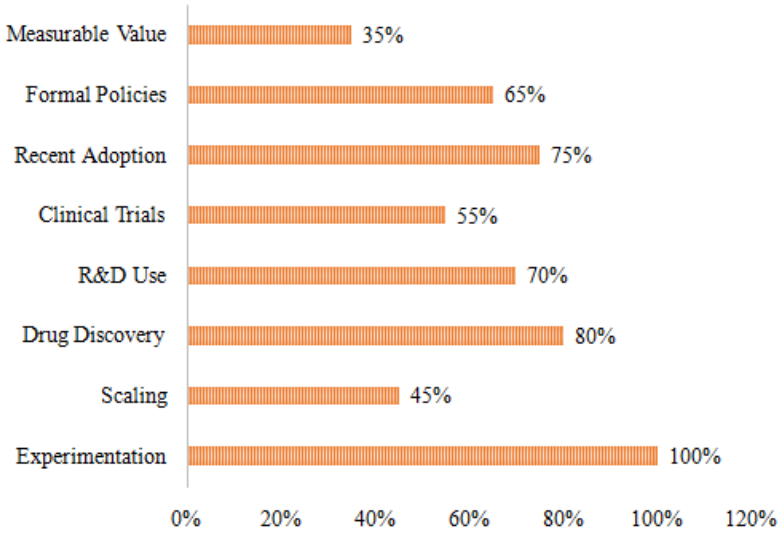

Fig. 4: Current Landscape of AI/ML Adoption Rates in Pharmaceutical R&D

The usage of AI and ML at various phases of pharmaceutical R&D is depicted in the figure. While scale and observable value are still low, adoption rates are highest during medication discovery, experimentation, and recent deployment. Overall, the graph shows that although the use of AI is expanding, there is still a lack of systematic integration and demonstrated impact.

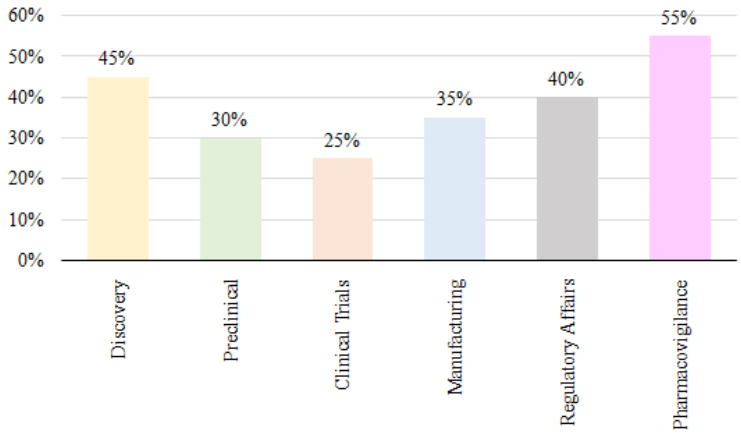

Fig. 5: Impact of AI/ML on Drug Development

The graph mentioned above illustrates how much AI/ML advances medication development at various phases. Efficiency gains are greatest in pharmacovigilance and discovery. Preclinical, clinical, production, and regulatory phases all exhibit discernible but less significant advancements.

RESEARCH ARTICLE

A Multi Photon Emission and Self-Defocusing Effect of Organic Non-Linear Photoluminescent Crystal : (E)-2-(((2-(2-hydroxyethoxy) ethyl) imino)methyl) -4-nitrophenol

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Received: 31 Oct 2025 Revised: 16 Dec 2025 Accepted: 09 Jan 2026

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ABSTRACT

A new organic Non-linear Optical crystal (E)-2-(((2-(2-hydroxyethoxy)ethyl)imino)methyl)-4-nitrophenol (E-2HM4N) has been synthesized by the slow evaporation techniques. Powder X-ray diffraction patterns have been utilized for obtaining structural optimism by assigning nuclear magnetic resonance chemical shifts while analyzing the resulting data. A preferred imine group of titled crystals is composed of a polar aliphatic tail and a polar aromatic head, and it self-assembles into crystals, forming a crystal structure. Nowadays, in fluorescence spectroscopy, imine-based biomaterials are used in many different ways. The invention specifically relates to the use of polar covalent imines because they enable deep light penetration into biological specimens and produce high-resolution optical Photoluminescence. The self-defocussing nature of the crystal is confirmed by the multi-emission peaks in photoluminescence which is due to the strong absorption in the UV Spectroscopy. The grown crystal's luminescence property displays green emission radiation with good imaging properties. For the imaging of various biological samples, many nonlinear optical techniques have been used, including multiphoton fluorescence and harmonic

generation. The title crystal has strong saturable absorption and a self-defocusing effect, as shown by third-order Non-linear Optical characteristics using a Z-scan method.

Keywords: Crystal Structure; UV; Photoluminescence; Z-scan-Self-defocusing;

INTRODUCTION

Franklin discovered the optical second harmonic generation signal in the early 1960s, very immediately after the creation of the laser. Since then, materials having large nonlinear optical (NLO) output have discovered widespread applications in laser sciences and technologies. The all-solid-state lasers used in applications like medical diagnosis now contain a key component made of NLO materials, which has played an important part in the development of these technologies [1]. The solid-state structure of organic compounds can be sensitively examined by non-linear optical properties, which have a variety of applications [2]. Organic non-linear optical (NLO) systems are receiving a lot of interest lately due to their improved stability and promising NLO response, which suggests they are suitable for third harmonic production. Because of the electronic structure in the π-conjugated state and the appearance of electron-donating and electron-accepting clusters on both sides of the system, organic substances exhibit significant non-linearity [3]. Non-centrosymmetric materials are of high attention so their possible developments in more areas such as third-order non-linear optical material [4]. Imines are compounds that form the well-known class of chemicals known as Schiff-bases during the condensation reactions between the amine and the aldehydes. Direct condensation was frequently used to process amine and aldehyde to produce Schiff-base compounds [5-6]. Schiff bases and their derivatives, particularly the amine family, have an intriguing area in drug research and development because of their bio-activities such as tumor, cancer, bacterial, and viral activities [7]. The advantage of having organic substances as NLO activities is that they may be engineered to have certain donor-acceptor groups to optimize desired NLO characteristics [8]. Organic materials display a variety of new NLO elements due to their broad structural design. It is desirable to produce broad organic frameworks with NLO characteristics via Schiff-based reactions.

NLO applications for Schiff base materials include optical devices, which include dynamic imaging techniques [6]. In particular, new sorts of researchers are interested in organic molecules with considerable NLO properties. The search for new advanced materials is an important area of contemporary research in numerous disciplines of science and the development of many new technologies. Non-linear optical (NLO) crystals have attracted a great deal of interest in recent years due to their potential applications in the domain of optoelectronics and photonic technologies [23]. While the engineering for enhancing second-order NLO efficiency is relatively well understood, the need for efficient third-order molecules and materials still exists. Third-order NLO organic goods are compared to inorganic spices in terms of dimensional convenience [9]. We discuss a method for exhibiting the structure of organic materials using entire nuclear magnetic resonance (NMR) Spectral analysis in the context of PXRD data [10]. Although the structure evaluation approach had its challenges, a favorable outcome was attained by merging the PXRD analysis and data from NMR spectra and resolving the issue by utilizing the DASH 4.0.0 software for structure optimization [11]. In this research work, we carried out the Synthesis, development, and characterization of novel organic crystal (E)-2-(((2-(2-hydroxyethoxy)ethyl)imino)methyl)-4-nitrophenol ($C_{11}H_{14}N_2O_5$) (E-2HM4N). UV-Vis Spectroscopy and photoluminescence characterization have been performed which results in a high-performing multi-emitting organic NLO material that should meet a variety of characteristics, one of which is the presence of a large third-order NLO with a non-centrosymmetric crystal structure. We thoroughly examine the non-linear refraction, non-linear absorption, and self-defocusing properties of the E-2HM4N crystal using Z-scan analysis.

MATERIALS AND METHODS

The compounds 2-hydroxy-5-nitrobenzaldehyde and 2-(2-aminoethoxy)ethanol are used in the current study as an analytical reagent (AR) with a 99% purity and the solvent Acetic Acid used for the synthesis was obtained from Sigma-Aldrich and set to utilize without further sterilization.

Synthesis and Crystal growth

Using slowly evaporating methods, an E-2HM4N single crystal was created using procedures from 2-hydroxy-5-nitrobenzaldehyde and 2-(2-aminoethoxy)ethanol. Initially, 2-hydroxy-5-nitrobenzaldehyde (0.3g, 0.001795 mol) was dissolved in acetic acid (10ml) by continuous stirring. 2-(2-aminoethoxy)ethanol (0.2g, 0.00190 mol) was added to this solution and continuously stirred for an hour at 30 °C. The liquid then became yellow after that. A single crystal was extracted from the liquid after a 30-day development period. Figure 1 depicts the E-2HM4N single-crystal picture. In Fig. 2, the reaction plan is displayed.

RESULT AND DISCUSSION

Single-Crystal and Powder X-ray Diffraction

Single Crystal X-ray Diffraction Measurements of E-2HM4N were gathered using a Bruker Kappa APEXII diffractometer. The data structure determination was recorded by BrukerD8 Venture. The E-2HM4N crystal structure becomes the Monoclinic crystal system with non-centrosymmetric space group Pc. The estimated lattice parameters are a = 7.25Å, b = 8.37Å, c= 11.70Å, α = 90.00°, β = 94.92°, γ = 90.00° and V = 707A^3. X'Pert Pro-PAnalytic was used to collect PXRD analyses while employing CuKα radiation (λ=1.5406nm) at 40 kV and 30 mA power. Over a two-dimensional 2Θ range of 10° to 80°, a PXRD diffraction pattern was gathered. Powder X-ray diffraction analysis was used to solve the crystallinity of the E-2HM4N compound from the fine powder form of the crystal. The crystallinity of the developed crystal is noticeable from the observed sharp and intense peaks [12]. Fig. 3 shows PXRD data of E-2HM4N crystal. The formed crystals were ground into a powder and studied using PXRD. PXRD gives detailed information about the crystallinity nature and purity of the crystal. PXRD gives more accurate information rather than SC-XRD [13].

Structure Determination

The structure is directly determined using both PXRD data and Chemical shift data [11]. A user-friendly piece of software named DASH is used to solve crystal structures using X-ray powder diffraction data. We used DASH 4.0.0 software to determine crystal structure using the input module optimized by 'opt hf/3-21g geom=connectivity' keywords using Gaussian 16W, revision c.01, software [14]. H_{22}-O_7 ……. N_{12} intramolecular hydrogen bonds are observed in the structure (dashed blue line). For the indexing, the greatest powder pattern was utilized [13]. E-2HM4N crystal in the Monoclinic system with space group Pc. The structural organization is favorable to interesting NLO properties of the crystal. The crystal structure of E-2HM4N was deposited in the Cambridge-crystallographic data center (Deposition Number: 2231805) [15]. Experimental crystallographic parameters are given in Table 1. The Molecule structure of the E-2HM4N crystal is in Figure 4.

^{13}C NMR and ^{1}H NMR Spectral Studies

Bruker AMX NMR Spectrometer has been used to record data for ^{13}C and ^{1}H NMR (300 MHz). Tetramethyl silane (TMS) is employed at ambient temperature and DMSO is used as the solvent. NMR spectroscopy has been used to examine conformational changes in a variety of ring compounds [16]. The obtained spectra are shown in Figures 5 and 6. The corresponding shift of ^{13}C NMR and ^{1}H NMR signals are collected and illustrated in Table 2. NMR Spectra of 2-hydroxy-5-nitrobenzaldehyde and 2-(2-aminoethoxy)ethanol were collected from the spectral database and compared in Table 2. The peak of the DMSO solvent can be seen at 40.236 ppm. The aromatic ring's carbon atom was blamed for the chemical shift seen at 140.143 ppm, 131.078 ppm, 124.703 ppm, 122.573 ppm, and 118.846 ppm. The CHO resonance peak was obtained at 189.353 ppm. The peak's up-field shift from 194.61 ppm to 118.846

ppm demonstrates that water molecules were removed during the production reaction of the chemical E-2HM4N. The carbon atom that is attached in the (phenol) OH group of 2-(2-aminoethoxy) ethanol causes the triplet that was seen at 39.735 ppm, 39.568 ppm, and 39.401 ppm. ^{13}C NMR spectrum of E-2HM4N Crystal (Fig. 5). ^{1}H NMR describes the E-2HM4N crystal spectrum as shown in Figure 6. At 2.500 ppm, the solvent signal becomes visible. The signals collected strongly revealed that the water molecule was eliminated from the interaction between NH_2 and CHO, which produces a CH=N group. E-2HM4N. Thus, the confirmation was done by the down-field shift of the NH_2 signal from 1.7 ppm to 2.493 ppm. Due to the formation of the signal CH=N, which was shifted toward higher ppm, the signal NH_2 in pure 2-(2-aminoethoxy)ethanol is at 1.7 ppm. The resonance induced by the proton CH=N groups shifted to a higher ppm.

UV VIS NIR Spectroscopy

The observed transmittance graph of the E-2HM4N crystal is shown in Fig. 7. Derived optical bandgap is 2.03eV.The E-2HM4N crystal's band gap supports the need for high-quality nonlinear optical applications [19]. The E-2HM4N crystal has good transmittance over the whole visible and near-infrared area, as can be seen from the spectrum [12]. For NLO application, the crystal should be transparent to all of the interfering wavelengths [17].

Refractive index

The Refractive index is the ultimate property of an optical material. Transmittance (T) and refractive index of the crystal in terms of transmittance are expressed as (Swanepoel method 1983),

$n = [N + (N – S^2)^{1/2}]^{1/2}$

Where,

$N = 2S \frac{Tmax-Tmin}{TmaxTmin} + \frac{S^2+1}{2}$,

Where T_{max} and T_{min}, are the transmittance max and the correlating minimum at that wavelength (λ). It used a well-recognized part of the mathematical equation.

$S = \frac{1}{Ts} + \left(\frac{1}{Ts} - 1\right)^{1/2}$

The refractive index was calculated as n = 1.5204 of E-2HM4Nat 387.5 nm, suggesting that the material will enhance the performance of optical properties[18]. Figure 10 shows the refractive index with the wavelength of the E-2HM4N crystal. The refractive-index decreases as wavelength increases. The higher band gap transmission in the overall region and lower refractive index make the crystal suitable for good pharmaceutical applications [19]. The refractive-index of the E-2HM4Ncrystal (Figure 8).

Photoluminescence Study

One of the useful technologies to give direct information on the molecular-level physical characteristics of materials is photoluminescence spectroscopy. Photoluminescence spectroscopy is one of the effective tools to provide direct information about the physical properties of materials at the molecular level. Figure 9 displays the Photoluminescence spectrum of the E-2HM4N crystal. The spectrum shows stable and strong emission peaks at 360nm, 491nm, and 521nm which was due to the excitation in UV VIS light at 620nm. It also revealed that E-2HM4N crystal had violet, blue, and green emission. The green fluorescence that the NLO crystal produces at 521 nm suggests that it would make a strong candidate for nonlinear optical applications [20].The self-defocusing characteristics of the NLO crystal have been established by the multi-emission peak. The high fluorescence emission displayed by the chemical in the title suggests that it would be a viable candidate for NLO applications [21].The availability of further emissions peaks supports the E-2HM4N crystal's high degree of crystallinity and structural magnificence [22].

Z-Scan measurements

The calculated linear refractive index value is 1.5204. The NLO community immediately embraced the Z-Scan examination as a standard method for finding out nonlinear variations in refractive index and nonlinear optical absorption. E-2HM4N crystals' nonlinear absorption and refractive index. The study of nonlinear refraction by the Z-scan method depends on the position (Z) of the samples under investigation along a focused Gaussian laser beam.

Depending on whether nonlinear refraction is negative or positive, the sample results in either extra focusing or defocusing. The Z-scan method [24] is a straightforward yet very precise way to get the nonlinear absorption coefficient β and the nonlinear index of refraction n2. The real portion of the third-order susceptibility is proportional to the nonlinear index of refraction. [Re$\chi^{(3)}$] and the nonlinear absorption coefficient is proportional to [Im$\chi^{(3)}$]. A 103 mm focal length lens was utilized to focus a 532 nm diode-pumped solid-state laser for the Z-scan investigations. At the focal point, the estimated values for intensity ($I_\circ$) and beam waist ($\omega_\circ$) were 0.33 μm and 0.0136 MWcm^{-2}, respectively. The experimental setup's Rayleigh range ($Z_\circ = \pi\omega_\circ/\lambda$) was determined to be 1.32 mm, meeting the requirement of $L < z_\circ$ for thin sample estimation. The schematic of the experimental setup used is shown in Fig. 10. A 1 mm wide optical cell with the E-2HM4N sample in an acetic acid solution has been moved along the propagation laser beam's axial route, across the focal region. By feeding the Si photodiode detector into the dual channel detector measurement unit, the transmission of the beam via an aperture positioned in the far field was measured. An aperture was replaced with a lens to catch all of the laser beam transmitted through the sample for an open-aperture Z-scan. Figure 11 gives a closed, open, and ratio of the closed-to-open normalized *Z*-scan of the E2HM4N sample in Acetic Acid solvent at 62% transmittance. The closed aperture Z-scan data shows a peak followed by a valley-normalized transmittance, indicating a negative sign for the refraction nonlinearity, or self-defocusing. The local temperature variation in the refractive-index is the cause of the self-defocusing effect. The open aperture Z-scan pattern showed transmission minimum at focus, indicating the reverse saturable absorption (RSA). The refractive-index of material's strong electromagnetic radiation changes, resulting in the nonlinear optical process of self-focusing [9]. Table 3 contains the third-order NLO parameters.

The measurable quantity ΔT_{p-v} can be defined as the difference between the normalized peak and valley transmittances, $T_p - T_v$. The variation of this quantity as a function of $|\Delta\phi_o|$ is given by

$$\Delta T_{p-v} = 0.406(1-S)^{0.25}|\Delta\phi_o| \quad (1)$$

where $\Delta\phi_0$ is the on-axis phase shift at the focus. S the aperture linear transmittance is given by

$$S = 1 - \exp(-2\, r_a^2/\omega_a^2) \quad (2)$$

with r_a denoting the aperture radius and ω_a denoting the radius of the laser spot before the aperture.
The on-axis phase shift is related to the third-order nonlinear refractive-index (n_2) [25] by,

$$|\Delta\phi_0| = k n_2 L_{eff} I_0 \quad (3)$$

where $L_{eff} = (1-e^{-\alpha L})/\alpha$, with L the sample length, α is the linear absorption-coefficient I_O is the intensity of the laser beam at focus $z = 0$, and k is the wave number($k=2\pi/\lambda$)

The imaginary parts of the third-order nonlinear optical susceptibility [χ^3] are estimated using the value of the nonlinear absorption-coefficient β obtained from the open aperture Z-scan data and using the relations:

$$q_o(z) = \frac{\beta . I_o . L_{eff}}{(1+\frac{Z^2}{Z_o^2})} \quad (4)$$

$$\beta = \frac{2\sqrt{2}.\Delta T}{I_o . L_{eff}} \quad (5)$$

$Z_R = k\omega_0^2/2$ is the diffraction length of the beam, ω_0 is the beam waist radius at the focal point.

The following relations can be utilized for calculating the portions, both real and imagined, of the third-order nonlinear optical susceptibility [26] using the experimentally measured nonlinear refractive index n2 and nonlinear absorption-coefficient β.

$$\mathrm{Re}\,\chi^3(esu) = 10^{-4}\,\frac{\varepsilon_o c^2 n_o^2}{\pi} n_2 (\frac{cm^2}{W}) \quad (6)$$

$$I_m \chi^3(esu) = 10^{-2} \frac{\varepsilon_o c^2 n_o{}^2 \lambda}{4\pi^2} \beta(\frac{cm}{W}) \quad (7)$$

where ε_0 is the vacuum permittivity, and c is the light velocity in vacuum.
The absolute value of the third-order nonlinear optical susceptibility is given by the relation

$$\left|\chi^3\right| = \left[(R_e(\chi^3))^2 + (I_m(\chi^3))^2\right]^{1/2} \quad (8)$$

The nonlinear parameters calculated are tabulated in Table 3

CONCLUSION

The New Crystal is identified in the amine family and its structure was solved and deposited in CCDC. The structural Property Relationship approach found the relationships between chemical structure and related structural properties including the target property of the studied crystal (Bio-imaging) for in-vitro bio-imaging applications and being ideal for lung cancer disease diagnosis. The linear refractive index is calculated from the Swanepoel method and the nonlinear refractive index is calculated from the Z-scan method. It is concluded that Schiff-based molecular crystal contains recognizable molecules within the structure and is held together with intermolecular hydrogen-bonding by the result obtained. In Photoluminescence spectroscopy NLO property of the Schiff-based crystal was well investigated through violet, blue, and green emissions. The generated E-2HM4N crystal will be the potential candidate in bio-imaging which was investigated by the multi-emission peak in Photoluminescence Spectroscopy and in the Z-scan analysis with the value of 2.3866 x 10^{-6}esu.

Electronic supplementary Information

CCDC 2231805 contains supplementary Crystallographic Data of E-2HM4N, that can be obtained freely from the Cambridge crystallographic data center via www.ccdc.cam.ac.uk/data_request/cif.

Credit authorship contribution Statement
The idea and design of the study were contributed to by all authors. preparation of materials, gathering of data, conceptualization, methodology, software, and writing—creation of the first draft by J. Priyanka., Supervision, Reviewing and Editing, Project Administration by R. Ida Malarselvi, Resources by G. Vinitha, Validation by C. Ramachandra Raja, Visualization by R. Priscilla and all authors commented on previous versions of the manuscript. The final manuscript was read and approved by all authors.

DATA AVAILABILITY

No data was used for the research described in the article.

FUNDING

No particular funding from public, private, or nonprofit organizations was given to this research.

ACKNOWLEDGMENTS

As part of this work, SCXRD, and NMR Spectroscopy characterization techniques were conducted in Sophisticated Analytical Instruments Facility (SAIF), Indian Institute of Technology, Madras, Chennai – 600 036, Tamil Nadu, India. UV-Vis-NIR spectroscopy characterization technique was conducted at Sathyabama University, Chennai, Tamil Nadu, India. PXRD and Photoluminescence characterization was conducted at the University Science

Instrumentation Centre (USIC), Alagappa University, Karaikudi - 630 003, Tamil Nadu, India. Also, the authors place on record special thanks to Dr. G. Vinitha, For giving them a third-order nonlinear testing facility to record Z-scan measurements, thanks to VIT, Chennai.

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Table 1: Experimental crystallographic parameters of E-2HM4N Crystal

Empirical Formula	$C_{11}H_{14}N_2O_5$
Molecular Weight	245.24g/m
Crystal System	Monoclinic
a	15.82830Å
b	10.19290Å
c	10.36370Å
α	90°
β	106.8866°
γ	90°
Unit Cell Volume	1599.945A^3
Spacegroup	Pc
Z	2
Dx	0.528 g cm^{-3}
Temperature	303K
2Θ	10.0° – 80.0°
Radiation, λ/ Å	Cu – Kα, 1.5406

Table 2: The chemical shift values of E-2HM4N Crystal in ppm for ^{13}C NMR and ^{1}H NMR

NMR	Atom	E-2HM4N chemical shift in ppm	A pure 2-hydroxy-5-nitrobenzaldehyde	Pure 2-(2-aminoethoxy) ethanol	Assignments
^{13}CNMR	(C1)	189.535	194.61		CHO
	(C2)	166.124	166.18		C-OH
	(C3)	140.143	140.73		C-H
	(C4)	131.078	131.69		C-H
	(C5)	124.703	129.81		C-H
	(C6)	122.573	119.49		C-H
	(C7)	118.846	119.03		C-H
	(C8), (C9), (C10), (C11)	39.902, 39.735, 39.568, 39.401		41.61	C-NH_2
^{1}H NMR	(H1)	8.414	15.2		OH
	(H2)	8.408	10.19		CH
	(H3)	8.356	8.25		CH
	(H4)	8.351	8.40		CH
	(H5)	8.338	7.26		C=N imine
	(H6), (H7), (H8)	8.332, 7.184, 7.166		5.4	R-OH
	(H9)	3.371		3.54	CH2
	(H10)	2.493		1.7	NH2

Table 3: Optical parameters of E-2HM4N Crystal

Linear refractive index - n_o	1.5204
Non-linear refractive-index - n_2	2.70x10^{-9} cm^2/W
Non-linear Absorption coefficient – β	1.43x10^{-4} cm/W
third-order nonlinear susceptibility - χ^3	2.3866 x10^{-6}esu

Fig. 1: Grown crystal of E-2HM4N Crystal

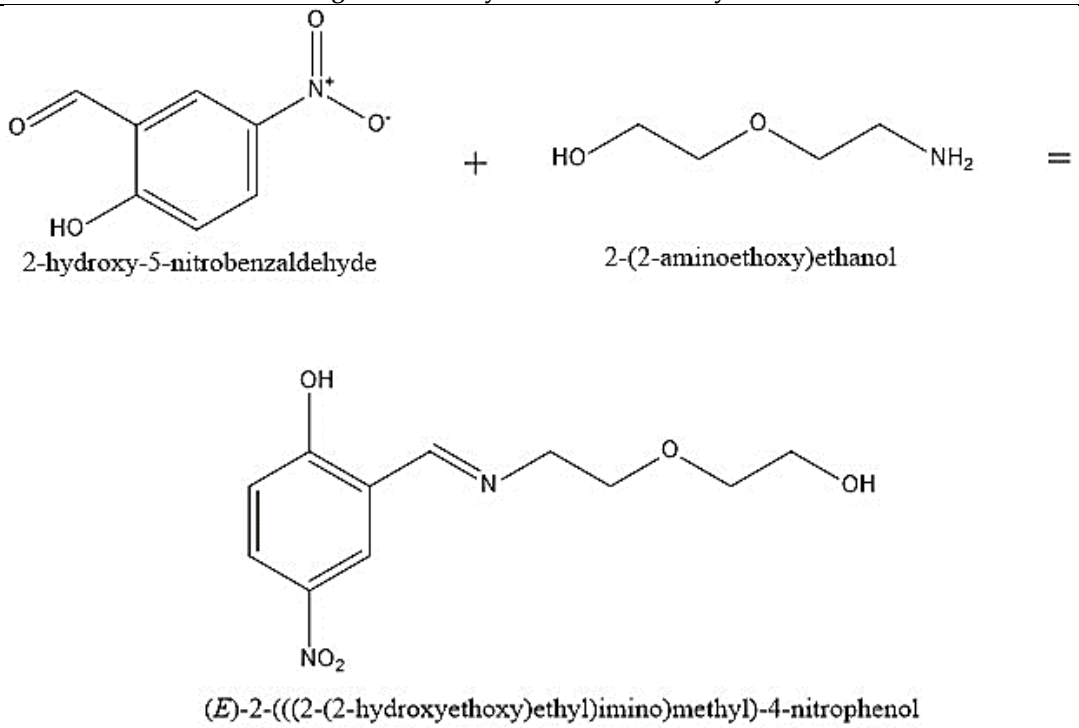

Figure 2: Reaction Scheme of E-2HM4N crystal

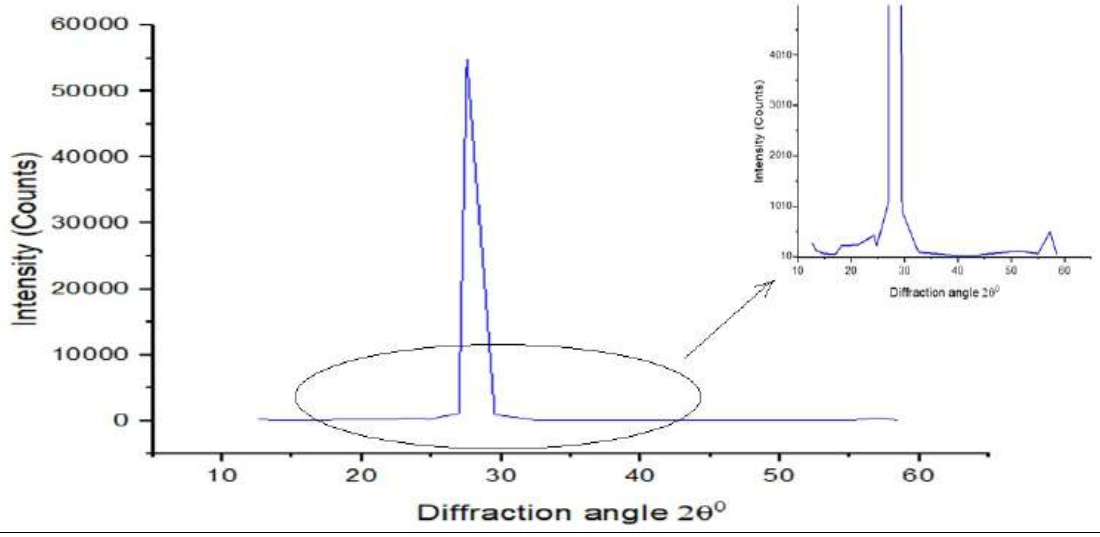

Figure 3: PXRD of E-2HM4N crystal used to determine the structure

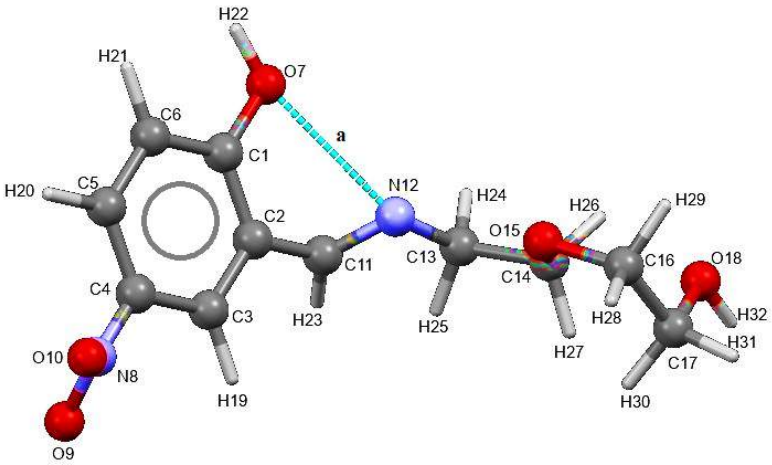

Figure 4: Molecular Structure of E-2HM4N Crystal

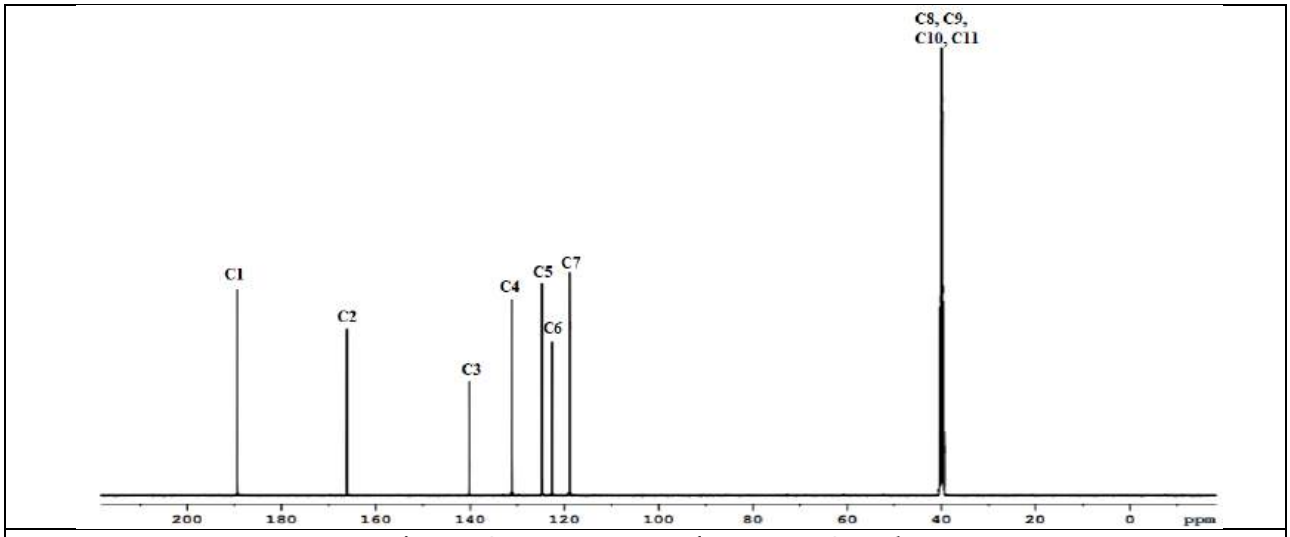

Fig. 5: ^{13} C NMR spectrum of E-2HM4N Crystal

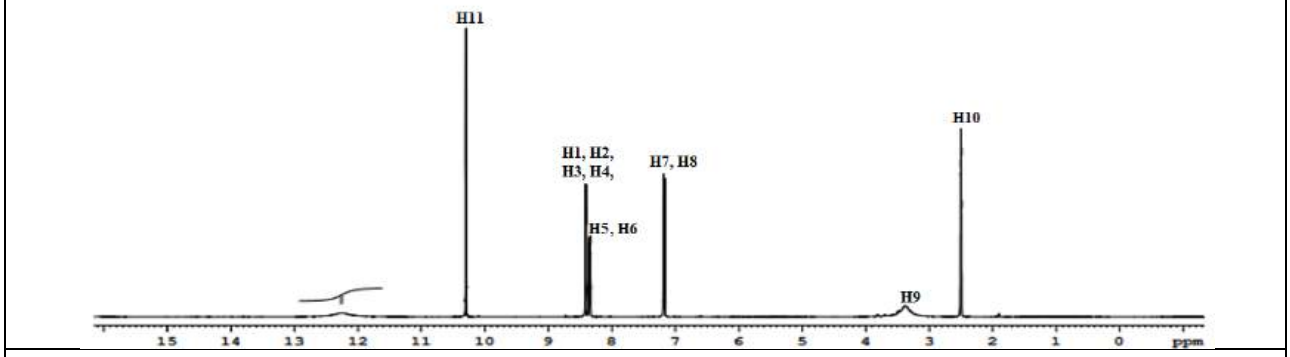

Fig. 6: ^{1}H NMR spectrum of E-2HM4N Crystal

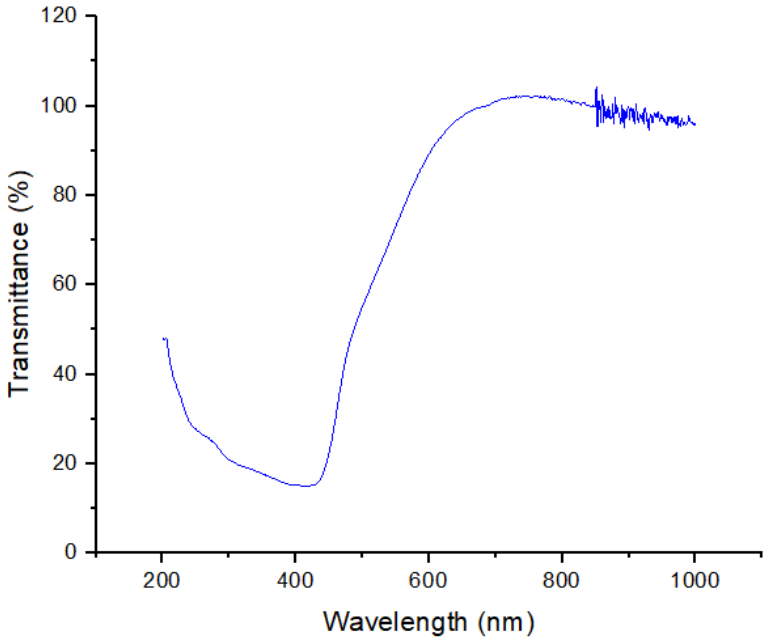

Figure 7: UV VIS NIR spectrum of E-2HM4N crystal

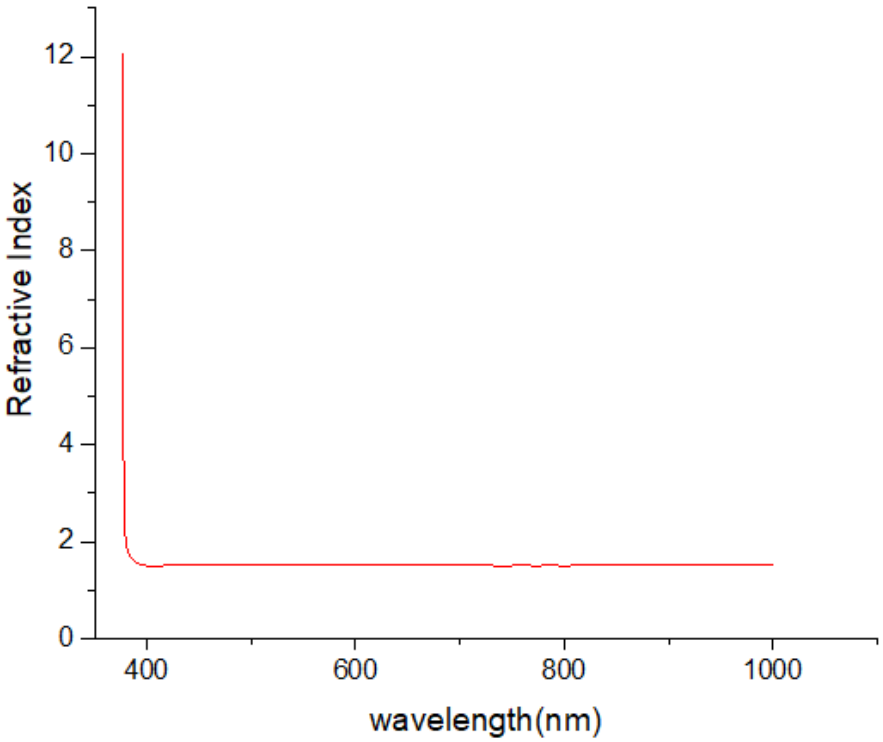

Figure 8: The refractive-index of the E-2HM4Ncrystal

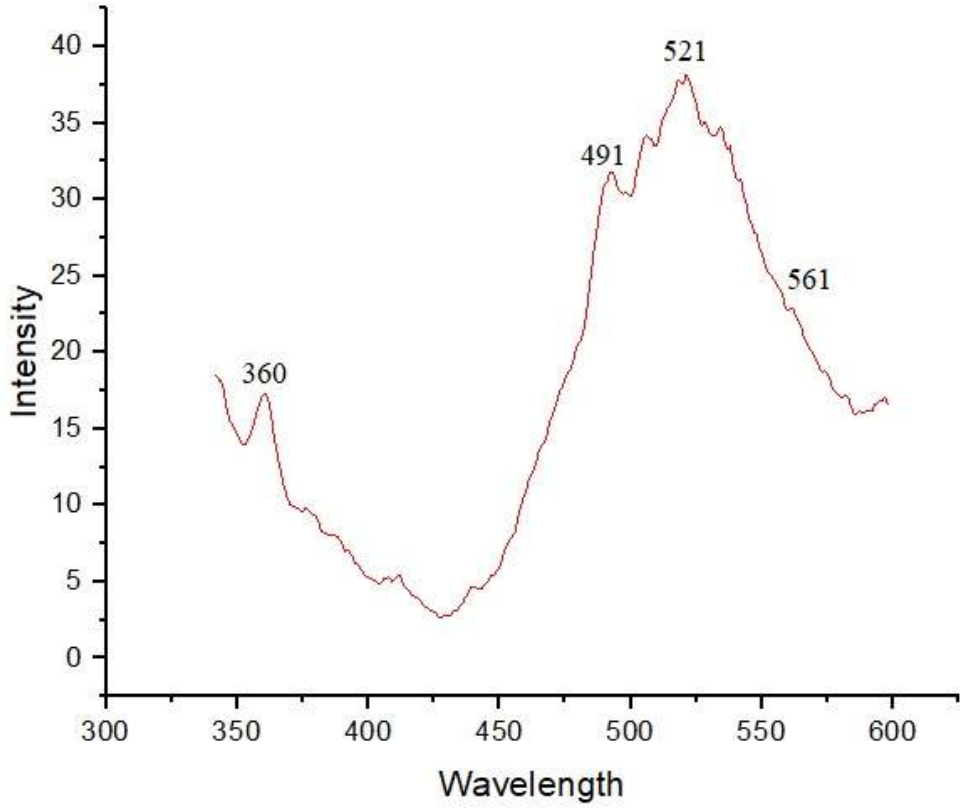

Figure 9: PL spectrum of E-2HM4N crystal

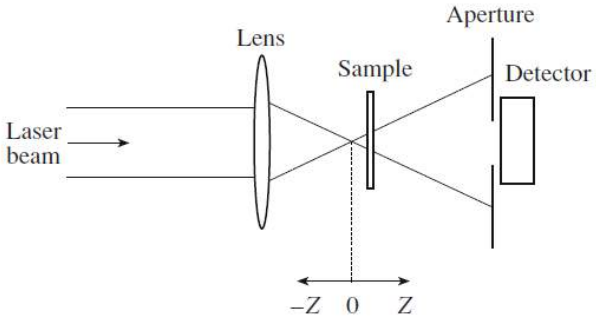

Fig.10: Schematic of experimental setup for z-scan

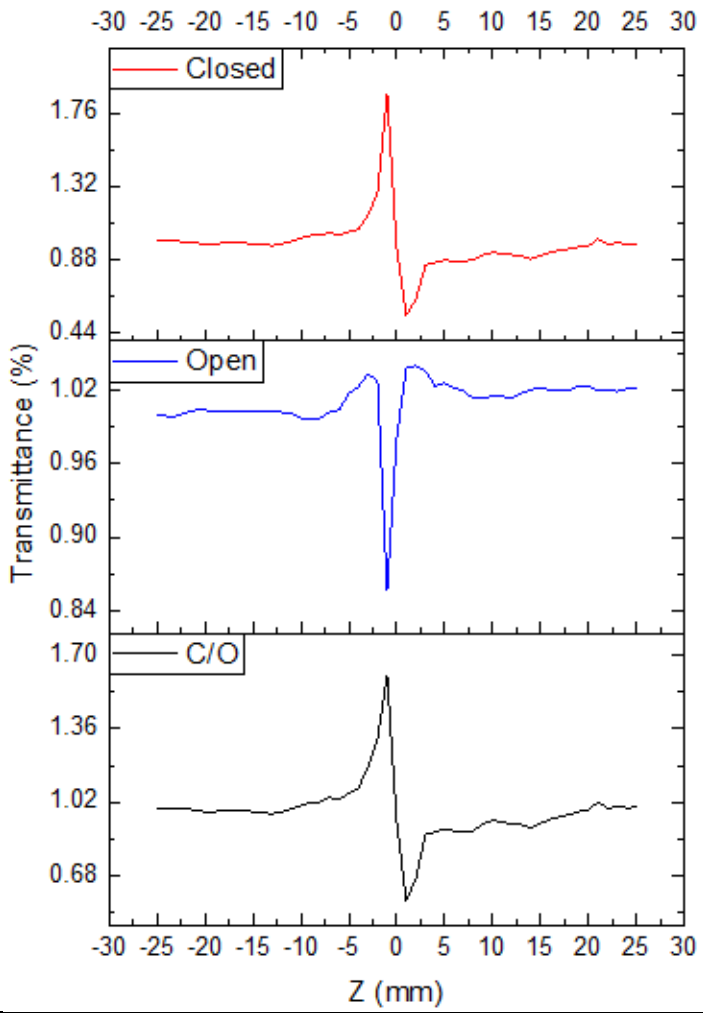

Figure 11: Z-scan closed and the open aperture tract of E-2HM4N

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

A Hybrid Single Valued Neutrosophic TOPSIS Decision Model for Resillient Crop Selection under Uncertainty

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Received: 05 Oct 2025 Revised: 09 Dec 2025 Accepted: 22 Jan 2026

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ABSTRACT

A crucial element in securing agricultural sustainability, resource efficiency, and revenue generation is crop selection. Despite inadequate and ambiguous information, farmers and decision-makers must weigh several competing factors, including yield, water needs, pest resistance, market price, and maturity duration. It is frequently challenging for traditional multi-criteria decision-making (MCDM) methodologies to adequately model this indeterminacy. In a bid to overcome this difficulty, this research combines the Technique for Order Preference by Similarity to Ideal Solution (TOPSIS) for agricultural crop selection with Single-Valued Neutrosophic Sets (SVNS).Using agricultural performance data spanning ten years, a case study was carried out with four crops: wheat, maize, soybeans, and cotton. After converting raw data into neutrosophic decision matrices and normalizing them, the suggested SVNN-TOPSIS framework calculates distances and closeness coefficients to establish the ordering of alternatives and identifies weighted positive and negative ideal solutions. The results showed that the technique can capture uncertainty and give strong decision support, with soybeans being the most appropriate crop, followed by maize, wheat, and cotton. This work enhances agricultural decision-making by providing a realistic and adaptable assessment model that takes into account ambiguity, inconsistency, and partial knowledge. In furtherance of improving crop selection's rationality, the results demonstrate the promise of neutrosophic MCDM techniques in more general agricultural and environmental planning contexts.

Keywords: Multi-Criteria Decision-Making (MCDM), Single-Valued Neutrosophic Sets (SVNS), TOPSIS, Positive Ideal Solution (PIS), Negative Ideal Solution (NIS), Agricultural Crop Selection; Uncertainty Modeling.

INTRODUCTION

Agricultural crop selection is a fundamental decision-making problem that directly influences farm productivity, resource utilization, and economic sustainability. Farmers and policymakers are often confronted with the challenge of choosing the most suitable crop among several alternatives, considering multiple and often conflicting criteria such as yield potential, water requirements, pest resistance, market price, and maturity period. Traditional decision-making approaches are often inadequate in capturing the uncertainty, vagueness, and indeterminacy inherent in such real-world agricultural problems. Hence, advanced MCDM techniques are increasingly being employed to provide systematic and rational solutions.

Among the various MCDM methods, the TOPSIS is widely recognized for its simplicity and effectiveness. It ranks alternatives by simultaneously minimizing the distance from the PIS and maximizing the distance from the NIS. However, classical TOPSIS operates on crisp or fuzzy data, which may not adequately represent the indeterminate and incomplete information present in agricultural environments. To overcome this limitation, the neutrosophic set theory, introduced by Smarandache, extends fuzzy logic by incorporating three independent components: truth-membership (T), indeterminacy-membership (I), and falsity-membership (F). The SVNS is a practical form of this theory, capable of handling real-life uncertain and imprecise data. Integrating SVNS with TOPSIS allows for a more comprehensive evaluation framework where expert judgments and agricultural data can be expressed with greater flexibility. This study proposes a novel approach to agricultural crop selection by applying the SVN-TOPSISmethod. A case study involving four crops—Wheat, Maize, Soybean, and Cotton—evaluated against five critical criteria over a ten-year dataset is conducted. The methodology demonstrates how neutrosophic modeling effectively captures uncertainty in decision-making and provides a rational ranking of crop alternatives. The results highlight the potential of SVNN-based MCDM techniques in supporting agricultural planning and policy formulation, ensuring that decisions are robust, data-driven, and reflective of real-world complexities.

Angammal[1] highlighted the significance of combining agricultural decision-making with neutrosophic techniques by proposing a multi-attribute neutrosophic optimization technique for the best crop selection in Ariyalur District. In order to better address uncertainty, Xu and Peng [2] extended traditional MCDM approaches by creating an enhanced technique based on TODIM and TOPSIS under multi-valued neutrosophic sets. Using generalized SV non-linear bipolar neutrosophic settings, Garai and Garg [3] examined water resource management issues in the Purulia agricultural field, offering insights into farming sustainability. In order to model agricultural land selection and provide a framework for decision support in land allocation, Ashraf and Abdullah [4] used sine trigonometric single-valued neutrosophic information.Abdel-Basset [5] presented a bipolar neutrosophic multi-criteria decision-making framework for professional selection that goes beyond agriculture and exhibits adaptability in other application domains. To increase the accuracy of ranking alternatives in single-valued neutrosophic environments, Garg [6] introduced a TOPSIS-based approach and a novel divergence measure. Prior to this, Ye [7] created a multicriteria decision-making technique employing correlation coefficients under SVN, while Chi and Liu [8] expanded the TOPSIS method for MADM using interval neutrosophic sets. Alzahrani et al. [9] used neutrosophic multi-criteria decision-making to investigate the best location for a women's institution, with a focus on spatial planning in the face of uncertainty. Gaussian SVN numbers were first presented and their uses in multi-attribute decision-making were illustrated by Karaaslan [10].

An alternative viewpoint for MADM difficulties was provided by Garai [11], who suggested a ranking technique based on possible mean under SVN. SVNS were officially established by Wang et al. [12], which served as the basis for later models. Earlier, Smarandache [13] laid the theoretical foundation for indeterminacy-based decision-making by introducing neutrosophic logic as a unifying topic in logics. One of the earliest links between fuzzy logic and agriculture was made by Yong [14], who used fuzzy TOPSIS to pick plant locations. Singh and Mallick [15] developed a fuzzy-based MCDM approach for green chamber farming, which helped advance sustainable

agriculture operations. From a historical perspective, uncertainty modeling in mathematics and decision sciences was first introduced by Zadeh [16] with the introduction of fuzzy sets. This field was later expanded by Hwang and Yoon [17], who proposed TOPSIS and other conventional MADM approaches. By modeling a neutrosophic agility index, Kavitha and Hepzibah [18] provided a fresh mathematical framework for assessment. Using MCDM approaches, Shafeena Miraclinl and Hepzibah [19] carried out an extensive investigation on the inequalities that affect women in society. Lastly, the foundation for contemporary decision-making techniques was reinforced when Opricovic and Tzeng [20] compared compromise solutions in MCDM, specifically *VIKOR and TOPSIS*.Collectively, these studies [1-20] demonstrate the ongoing development of decision-making methods from fuzzy sets to neutrosophic environments and their applications in agriculture, resource allocation, and social sciences, with single-valued neutrosophic TOPSIS emerging as a strong tool for dealing with uncertainty in complex systems.

Previous Research

The application of MCDM techniques to agricultural decision-making has been extensively studied. In crop planning, irrigation scheduling, and resource allocation, traditional techniques like AHP (Analytic Hierarchy Process), MOORA (Multi-Objective Optimization by Ratio Analysis), and TOPSIS (Technique for Order Preference by Similarity to Ideal Solution) have been used effectively. To cope with the ambiguity in agricultural data and expert opinions, fuzzy set theory has also been incorporated into MCDM in numerous research. Fuzzy AHP and fuzzy TOPSIS, for instance, have been used to assess crop options according to risk, cost, and yield criteria. However, because of shifting soil conditions, shifting markets, and changing climates, indeterminacy—or incomplete or inconsistent information—is highly common in agriculture and is only partially captured by the fuzzy framework, which focuses on ambiguity. In an effort to get around this, new studies have started investigating neutrosophic sets, which are fuzzy and intuitionistic fuzzy sets extended by adding three independent parameters: falsehood (F), indeterminacy (I), and truth (T). While neutrosophic techniques have been used in fields including risk analysis, supply chain management, and healthcare, they are still hardly used in agricultural crop selection.

Novelty of This Work

This research introduces a SVN TOPSISmodel for agricultural crop selection, which represents a novel contribution in the following ways:

1. SVNS and TOPSIS integration for agriculture The SVNS framework lends the evaluation more realistic by simulation of indeterminacy in agricultural data, in contrast to fuzzy techniques.
2. Use of longitudinal (10-year) data: The strategy utilizes use of ten years' worth of crop performance data to make sure that choices are made based on long-term agricultural patterns rather than the circumstances of a single year.
3. Extensive evaluation criteria: The study offers a comprehensive framework for decision-making by taking into account important factors such yield, water demand, insect resistance, market price, and maturity duration.
4. Validation of a practical case study: The suggested method shows its suitability for actual agricultural planning and policymaking by ranking the four main crops (wheat, maize, soybeans, and cotton).
5. Advancement of MCDM literature: By tackling a significant real-life issue—crop selection—where ambiguity, inconsistency, and uncertainty coexist, the study broadens the use of neutrosophic MCDM.

Neutosophic logic and MCDM technique are thus combined in a novel approach that has not been thoroughly investigated in agricultural decision-making, offering a more adaptable and trustworthy assessment tool.

METHODOLOGY

Preliminaries

Fuzzy Set

Let M' be a non-empty set.

$\mathcal{N} \subseteq M'$ is defined as,

N = $\{(m, \mu_{\mathcal{N}}(m)) | x \in M'\}$, where $\mu_{\mathcal{N}}(m)$: $M' \rightarrow [0, 1]$is the membership function of the fuzzy set $\mathcal{N}$.

Neutrosophic Set

Smarandache devised the mathematical model known as a Neutrosophic Set, which ellaborates the idea of a fuzzy set by giving each element three components:

$$\mathcal{A} = \{\langle m, T(m), I(m), F(m)\rangle / m \in \mathrm{U}\}$$

Where for each element$x \in$ U

- $T(m) \in [0,1]$ - truth-membership degree
- $I(m) \in [0,1]$ - indeterminacy-membership degree
- $F(m) \in [0,1]$ - falsity-membership degree

$$\mathbf{0} \leq T(m) + I(m) + F(m) \leq 3$$

Single Valued Triangle Neutrosophic number (SVTN)

A SVTN number $\tilde{A}^N$= ⟨(o,p,q); $w_{\tilde{a}}$, $u_{\tilde{a}}, y_{\tilde{a}}$⟩, whose TM, IM, and FM are given below:

$$\mu_a(m) = \begin{cases} \dfrac{(m-o)w_{\tilde{a}}}{p-o}, o \leq m \leq p \\ w_{\tilde{a}}, m = p \\ \dfrac{(q-o)w_{\tilde{a}}}{(q-p)}, p \leq m \leq q \\ 0 \quad , otherwise \end{cases} \quad \vartheta_a(m) = \begin{cases} \dfrac{(e-m+u_{\tilde{a}}(m-o))}{p-o}, o \leq m \leq p \\ u_{\tilde{a}}, m = p \\ \dfrac{(m-p+u_{\tilde{a}}(q-m)}{(q-p)}, p \leq m \leq q \\ 0 \quad , otherwise \end{cases}$$

$$\gamma_a(m) = \begin{cases} \dfrac{(p-x+y_{\tilde{a}}(m-o))}{p-o}, o \leq m \leq p \\ y_{\tilde{a}}, m = p \\ \dfrac{(m-p+y_{\tilde{a}}(q-m)}{(q-p)}, p \leq m \leq q \\ 0 \quad , otherwise \end{cases}$$

Case Study

Plenty of nations, particularly emerging ones, continue to rely substantially on agriculture for economic stability, rural livelihoods, and food security. In a particular season, choosing which crop to grow is one of the most important choices that farmers and politicians must make. In addition to farm productivity and profitability, this choice affects sustainability in terms of soil fertility, insect management, water use, and climate change resilience.

Crop selection is inherently a **MCDM problem**, as farmers must simultaneously consider diverse and often conflicting factors such as:

- **Yield potential** (ensuring higher productivity),
- **Water requirement** (vital in regions with scarcity or irregular rainfall),
- **Pest and disease resistance** (reducing dependency on pesticides),
- **Market price and economic returns** (ensuring profitability),
- **Maturity period** (matching cropping cycles with climatic and market windows).

In actuality, indeterminacy and uncertainty make it difficult to evaluate these criteria. Because of shifting insect dynamics, soil heterogeneity, unpredictable climate variations, and shifting market pricing, agricultural data gathered over a number of years may be imprecise or incomplete. This indeterminacy cannot be well captured by conventional decision-making methods, such as statistical models or even fuzzy MCDM procedures. A more thorough decision-support framework that takes truth, uncertainty, and falsehood into consideration at the same time in the evaluation process is therefore desperately needed. In order to solve this, the current work suggests using SVN-TOPSIS for agricultural crop selection. This allows decision-makers to efficiently evaluate crop options in imprecise and uncertain contexts.

Agricultural Crop Data (2015–2024)
The chosen agricultural crops are given in fig.2

Study Area
This study focuses on agricultural crop selection in India, one of the world's major agrarian countries, where agriculture plays an important role in rural livelihoods and national food security. India cultivates a wide range of crops across several agro-climatic zones, however determining the best crop is frequently hampered by variations in rainfall, soil fertility, insect incidence, and market dynamics. Four representative crops were examined for evaluation: wheat, maize, soybean, and cotton, each of which plays an important part in the Indian agricultural system.

- **Agricultural systems:**
  Wheat - A basic food crop and the second most significant cereal in India after rice, primarily farmed in the northern states.
  Maize- A versatile grain crop grown in a variety of states with diverse agro-climatic conditions.
  Soybean- A key oilseed crop that contributes to both domestic consumption and exports, with a high concentration in central India.
  Cotton– A valuable cash crop that is widely grown in western and southern India. It is important to the textile industry, although it is water-intensive and pest-prone.

The agricultural crops data are provided in the **Table 1**.

Data Sources by Criterion
The dataset used in this study spans 2015-2024 and was generated from *Ministry of Agriculture & Farmers Welfare (Government of India), FAOSTAT, and ICAR (Indian Council of Agricultural Research)* reports, as well as expert input from agricultural experts. The research region covers a ten-year period, capturing both temporal variability (year-to-year changes) and spatial variability (across distinct agro-climatic zones), ensuring that crop evaluations reflect long-term agricultural performance rather than short-term variations.This region was chosen as the research location not just for its economic and food security relevance, but also because it exemplifies the uncertainty and complexity that characterizes agricultural systems in developing countries. The paradigm described here can be used to various places across the world, as long as similar agricultural data is available. The data source and the processing methods are given in **Table 2**.

Step 1 SVN decision matrix
Alternatives (Wheat, Maize, Soybean, Cotton)
Criteria ($\mathcal{G}_1$ Yield, $\mathcal{G}_2$Water, $\mathcal{G}_3$ Pest, $\mathcal{G}_4$ Price, $\mathcal{G}_5$ Maturity). (T, I, F). Represented in **Table 3**.
Step 2 Normalization
We normalize each component (T, I, F) **per criterion** using vector normalization is represented in **Table 4**.
Step 3 -Weighted Normalized SVN matrix $\mathcal{W}j$=0.30,0.20,0.20,0.20,0.10 is given in Table 5.
Step 4- PI ($\mathcal{A}+$) and NI ($\mathcal{A}-$) per criterion (T, I, F)
For each criterion:

- $\mathcal{A}^+$ = (max T, min I, min F)
- $\mathcal{A}^-$ = (min T, max I, max F)

PIS - $\mathcal{A}$+(per criterion)
The Positive Ideal solutions is given in Table 6.
NIS - $\mathcal{A}$−(per criterion)
The Negative Ideal solutions is given in Table 7.
Step 5–Distancesto $\mathcal{A}$+and $\mathcal{A}$−(Euclidean across all criteria & components)
Computed for each alternative are given in Table 8.
Step 6 -Final Ranking (by CC, higher is better)
Ranking of the crops are represented in Table 9.
Ranking (best → worst):
Soybean > Maize > Wheat > Cotton.
Graphical representation of the ranking is given in the Fig.3.

RESULTS AND DISCUSSION

Using a decade of agricultural data, four crops—wheat, maize, soybeans, and cotton—were assessed using SVN-TOPSIS framework based on yield, water requirement, pest resistance, market price, and maturity period. The most appropriate crop was determined by the proximity coefficients, which gave soybeans the best ranking, followed by maize, wheat, and cotton. While maize was constrained by higher water requirements, soybeans thrived because of their balanced output, moderate water requirements, steady market price, and good insect resistance. Cotton placed lowest due to its high-water consumption, slower maturity, and vulnerability to pests, whereas wheat performed moderately.The SVN-TOPSIS method produced a complex and trustworthy ranking by successfully capturing climate, market, and expert uncertainty. Because SVN-TOPSIS takes truth, indeterminacy, and falsity into account, it can make more accurate decisions under uncertainty than traditional TOPSIS. These findings provide farmers and policymakers with practical advice on how to allocate resources and choose crops in a sustainable manner.

CONCLUSION

This study evaluated four key crops—wheat, maize, soybeans, and cotton—based on market price, maturity period, yield, water requirements, and pest resistance using the Single-Valued Neutrosophic TOPSIS approach. Cotton came in last because of its high-water requirements and vulnerability to pests, whereas soybeans were the most appropriate crop because of their balanced performance across a number of categories. In contrast to conventional TOPSIS, the SVN-TOPSIS framework produced a dependable and nuanced ranking by successfully capturing uncertainty in the market, climate, and expert knowledge. Farmers and politicians can use these findings as useful assistance when choosing crops and allocating resources in a sustainable, data-driven manner.

Future Direction

The results of the research indicate the value that the SVN-TOPSIS framework is for agricultural decision-making, especially when managing uncertainty resulting from expert opinions, market swings, and weather variables. Going future, a number of approaches can improve this research's robustness and usefulness. First, localized crop recommendation systems that are suited to particular agro-climatic zones may be developed with the aid of additional crops and regional variances. Second, incorporating dynamic elements like trends in water shortages, soil fertility variations, and climate change projections could enhance long-term decision-making. Third, hybrid models that further enhance crop selection under numerous uncertainties may be produced by integrating SVN-TOPSIS with other MCDM techniques, such as fuzzy PROMETHEE or AROMAN. Furthermore, using field monitoring and real-time market data can enable farmers to receive advice that are flexible and responsive. Lastly, these techniques can be used to more comprehensive agricultural planning, which includes scheduling irrigation, allocating resources, and developing pest control plans, in addition to crop selection. In addition to boosting sustainability and productivity,

such developments would fortify policy-level food security decision-making in the face of escalating economic and environmental difficulties.

Conflicts of Interest

The authors declare no conflict of interest.

Data Availability

All data that supports the findings of this study is available in the reputable Indian government surveys.

ACKNOWLEDGEMENTS

The authors are Thankful to the unknown referees for their valuable suggestions in improving the quality of manuscript.

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Table 1: The agricultural crops data

Year	Crop	Yield	Water Req.	Price	Pest Resist.	Maturity (days)
2015	*Wheat*	3.2	420	190	7	120
2015	*Maize*	4.5	520	180	6	110
2015	*Soybean*	2.8	380	400	8	100
2015	*Cotton*	2.5	600	150	5	160
2016	*Wheat*	3.4	410	200	7	118
2016	*Maize*	4.6	515	185	6	109
2016	*Soybean*	3.0	370	410	8	98
2016	*Cotton*	2.6	590	160	5	158
2017	*Wheat*	3.6	400	210	8	117
2017	*Maize*	4.7	510	190	7	108
2017	*Soybean*	3.1	365	420	9	97
2017	*Cotton*	2.7	580	170	6	157
2018	*Wheat*	3.7	395	220	8	116
2018	*Maize*	4.8	505	195	7	108
2018	*Soybean*	3.2	360	430	9	96
2018	*Cotton*	2.8	575	175	6	155
2019	*Wheat*	3.8	390	230	8	115
2019	*Maize*	4.9	500	200	7	107
2019	*Soybean*	3.3	355	440	9	95
2019	*Cotton*	2.9	570	180	6	154
2020	*Wheat*	3.9	385	240	9	114
2020	*Maize*	5.0	495	210	8	106
2020	*Soybean*	3.5	350	450	9	94
2020	*Cotton*	3.0	565	190	6	153
2021	*Wheat*	4.0	380	250	9	113
2021	*Maize*	5.2	490	220	8	105
2021	*Soybean*	3.6	345	460	9	94
2021	*Cotton*	3.1	560	200	7	152
2022	*Wheat*	4.1	375	260	9	112
2022	*Maize*	5.3	485	230	8	105
2022	*Soybean*	3.7	340	470	9	93
2022	*Cotton*	3.2	555	210	7	151

2023	*Wheat*	4.2	370	270	9	112
2023	*Maize*	5.4	480	240	8	104
2023	*Soybean*	3.8	335	480	9	93
2023	*Cotton*	3.3	550	220	7	150
2024	*Wheat*	4.3	365	280	9	111
2024	*Maize*	5.5	475	250	8	103
2024	*Soybean*	3.9	330	490	9	92
2024	*Cotton*	3.4	545	230	7	149

Table 2: Data Source by criterion.

Criterion	Data Type	Source	Processing
Yield (kg/ha)	Quantitative	FAOSTAT; Ministry of Agriculture & Farmers Welfare (Agricultural Statistics at a Glance)	Averaged over 10 years; normalized to remove unit variations
Water Requirement	Quantitative	ICAR agronomic guidelines; FAO irrigation reports	Expressed as mm/season; converted into relative values for comparison
Pest Resistance	Qualitative	ICAR crop science reports; Expert judgments from agricultural scientists	Converted into linguistic scales (High, Medium, Low) and mapped to SVNN values
Market Price (₹/kg)	Quantitative	National agricultural market bulletins; FAOSTAT	10-year average price with inflation adjustment
Maturity Period	Qualitative	ICAR reports; Expert validation	Expressed in days to maturity; normalized into SVNN scale

Table 3: SVN decision matrix

Crop	$\mathcal{G}_1$	$\mathcal{G}_2$	$\mathcal{G}_3$	$\mathcal{G}_4$	$\mathcal{G}_5$
Wheat	(0.2772,0.3500,0.3728)	(0.5417,0.3500,0.1083)	(0.5250,0.3500,0.1250)	(0.1178,0.3500,0.5322)	(0.4366,0.3445,0.2189)
Maize	(0.6500,0.3500,0.0000)	(0.2152,0.3500,0.4348)	(0.2750,0.3500,0.3750)	(0.0545,0.3500,0.5955)	(0.5736,0.2896,0.1368)
Soybean	(0.1402,0.3500,0.5098)	(0.6500,0.3500,0.0000)	(0.7464,0.2536,0.0000)	(0.6500,0.3500,0.0000)	(0.6887,0.3113,0.0000)
Cotton	(0.0000,0.3500,0.6500)	(0.0000,0.3500,0.6500)	(0.0000,0.3500,0.6500)	(0.0000,0.3500,0.6500)	(0.0000,0.3500,0.6500)

Table 4: Normalization

Crop	$\mathcal{G}_1$	$\mathcal{G}_2$	$\mathcal{G}_3$	$\mathcal{G}_4$	$\mathcal{G}_5$
Wheat	(0.3848, 0.5000, 0.4113)	(0.6205, 0.5000, 0.1372)	(0.5508, 0.5326, 0.1643)	(0.1777, 0.5000, 0.5168)	(0.4379, 0.5303, 0.3130)
Maize	(0.9023, 0.5000, 0.0000)	(0.2465, 0.5000, 0.5507)	(0.2885, 0.5326, 0.4929)	(0.0822, 0.5000, 0.5783)	(0.5753, 0.4458, 0.1956)
Soybean	(0.1946, 0.5000, 0.5625)	(0.7445, 0.5000, 0.0000)	(0.7831, 0.3859, 0.0000)	(0.9806, 0.5000, 0.0000)	(0.6908, 0.4792, 0.0000)
Cotton	(0.0000, 0.5000, 0.7172)	(0.0000, 0.5000, 0.8233)	(0.0000, 0.5326, 0.8544)	(0.0000, 0.5000, 0.6312)	(0.0000, 0.5388, 0.9294)

Table 5: Weighted normalized SVN matrix

Crop	$\mathcal{G}_1$ (0.30)	$\mathcal{G}_2$ (0.20)	$\mathcal{G}_3$ (0.20)	$\mathcal{G}_4$ (0.20)	$\mathcal{G}_5$ (0.10)
Wheat	(0.1154, 0.1500, 0.1234)	(0.1241, 0.1000, 0.0274)	(0.1102, 0.1065, 0.0329)	(0.0355, 0.1000, 0.1034)	(0.0438, 0.0530, 0.0313)
Maize	(0.2707, 0.1500, 0.0000)	(0.0493, 0.1000, 0.1101)	(0.0577, 0.1065, 0.0986)	(0.0164, 0.1000, 0.1157)	(0.0575, 0.0446, 0.0196)
Soybean	(0.0584, 0.1500, 0.1688)	(0.1489, 0.1000, 0.0000)	(0.1566, 0.0772, 0.0000)	(0.1961, 0.1000, 0.0000)	(0.0691, 0.0479, 0.0000)
Cotton	(0.0000, 0.1500, 0.2152)	(0.0000, 0.1000, 0.1647)	(0.0000, 0.1065, 0.1709)	(0.0000, 0.1000, 0.1262)	(0.0000, 0.0539, 0.0929)

Table 6: Positive Ideal Solution

Criterion	$\mathcal{A}^+$(T,I,F)
$\mathcal{G}_1$	(0.2707, 0.1500, 0.0000)
$\mathcal{G}_2$	(0.1489, 0.1000, 0.0000)
$\mathcal{G}_3$	(0.1566, 0.0772, 0.0000)
$\mathcal{G}_4$	(0.1961, 0.1000, 0.0000)
$\mathcal{G}_5$	(0.0691, 0.0446, 0.0000)

Table 7: Negative Ideal Solution

Criterion	$\mathcal{A}^-$(T,I,F)
$\mathcal{G}_1$	(0.0000, 0.1500, 0.2152)
$\mathcal{G}_2$	(0.0000, 0.1000, 0.1647)
$\mathcal{G}_3$	(0.0000, 0.1065, 0.1709)
$\mathcal{G}_4$	(0.0000, 0.1000, 0.1262)
$\mathcal{G}_5$	(0.0000, 0.0539, 0.0929)

Table 8: Distance for each Criterion

Alternative	Sum ofC_{ij}^{+}	$D^+ = \sqrt{\sum C_{ij}^{+}}$	Sum ofC_{ij}^{-}	$D^- = \sqrt{\sum C_{ij}^{-}}$
Wheat	0.082958	**0.28802549**	0.094666	**0.30767965**
Maize	0.088099	**0.29765452**	0.134684	**0.37773494**
Soybean	0.073057	**0.27121502**	0.177292	**0.42106046**
Cotton	0.279371	**0.53976039**	0.000000	**0.00000000**

Table 9: Final Ranking

Alternative	D^+	D^-	CC
Soybean	0.27121502	0.42106046	0.608227
Maize	0.29765452	0.37773494	0.559285
Wheat	0.28802549	0.30767965	0.516497
Cotton	0.53976039	0.00000000	0.000000

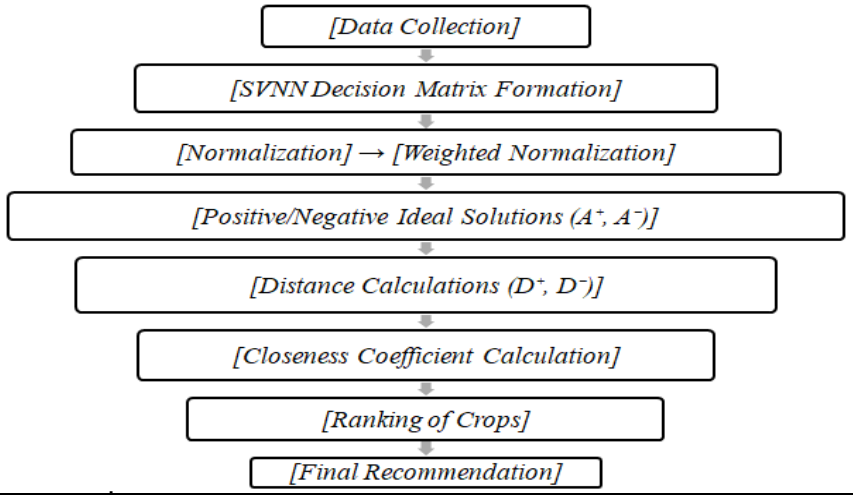

Fig 1: Framework Visualization

Fig.2 Chosen Agricultural Crops

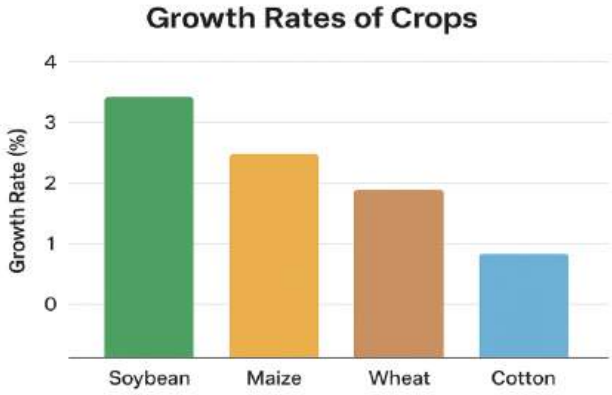

Fig.3 Graphical Representation

RESEARCH ARTICLE

Design, Molecular Docking and ADMET Analysis of Quinazolinone Derivatives as Potential Dual AChE/ BChE Inhibitors for Alzheimer's Disease

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Received: 06 Nov 2025 Revised: 07 Dec 2025 Accepted: 21 Jan 2026

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ABSTRACT

Alzheimer's disease is a progressive neurodegenerative disorder marked by cognitive and memory impairment. Inhibition of acetyl cholinesterase remains a key therapeutic strategy; however, increased butyrylcholinesterase activity in advanced stages of the disease highlights the need for dual-target inhibitors. This has prompted the design of quinazolinone derivatives targeting both enzymes. This study aims to evaluate the inhibitory potential of designed quinazolinone-based derivatives against AChE and BChE using computational drug-design methodologies. Eighteen quinazolinone derivatives and the standard drugs Donepezil and tacrine were screened against acetylcholinesterase and butyrylcholinesterase using *insilico* approaches. Molecular docking was performed using Schrödinger Maestro v11.2 with Glide XP, while ligand preparation and optimization were carried out using LigPrep. Active-site identification was conducted using SiteMap, and binding free energies were calculated using the Prime MM-GBSA module. ADME/T properties were predicted using QikProp to evaluate drug-likeness, CNS permeability, and compliance with Lipinski's Rule of Five. Docking studies identified APM2 and APM3 as the most potent compounds against AChE and BChE, exhibiting higher G scores (−11 to −10 kcal/mol) than the standard drugs Donepezil and Rivastigmine. Prime MM-GBSA analysis revealed favorable binding energies for selected derivatives, while ADME/T predictions indicated good oral absorption, acceptable drug-likeness, and compliance with Lipinski's rule. The study

highlights quinazolinone derivatives as promising dual AChE/BChE inhibitors for Alzheimer's disease. Polar and alkyl amine interactions were found to influence binding affinity, providing a rational basis for the design of novel disubstituted quinazolinones as potential anti-Alzheimer agents.

Keywords: Alzheimer disease, acetylcholinesterase inhibitors, butyrylcholinesterase, Quinazolinone derivatives, Cholinergic pathway, Computational drug design.

INTRODUCTION

Neurodegenerative disorders are characterized by progressive dysfunction of the central nervous system, leading to neuronal loss and cognitive decline. Among age-related dementias, Alzheimer's disease (AD) is the most prevalent, presenting with impairments in memory, thinking, and behavior and progressively worsening over time. Key pathological biomarkers of AD include amyloid-β (Aβ) plaques and hyperphosphorylated tau (p-tau), which have been major targets in drug development, exemplified by recently approved anti-amyloid therapies such as lecanemab and donanemab for early-stage disease [1-3]. Acetylcholinesterase (AChE) is a serine hydrolase responsible for hydrolyzing acetylcholine (ACh) at cholinergic synapses and neuromuscular junctions. Its active site, located deep within a narrow aromatic gorge, contains a catalytic triad (Ser200, His430, Glu327) critical for enzymatic activity and ligand binding [4-6,19]. Structural features of this gorge, particularly key aromatic residues, play an essential role in substrate recognition and inhibition.

Butyrylcholinesterase (BChE), a tetrameric glycoprotein with a broader and more flexible active-site gorge, differs from AChE due to substitution of aromatic residues with smaller aliphatic amino acids. This structural variation allows BChE to hydrolyze a wider range of substrates [11,17,18]. Importantly, while AChE activity declines during AD progression, BChE activity increases, making it a dominant modulator of cholinergic transmission in later disease stages [7-10,12-14]. Current AD therapy largely relies on AChE inhibitors to enhance cholinergic neurotransmission; however, only 30–40% of patients show a favorable response, and efficacy declines as the disease progresses [13,14]. Consequently, multi-target-directed ligands (MTDLs) that inhibit both AChE and BChE have gained attention for improved therapeutic outcomes and potential disease-modifying effects, including delayed Aβ aggregation [15-17,21]. Nitrogen-containing heterocycles, particularly quinazolinone derivatives, have attracted considerable interest due to their broad pharmacological activities, including anti-cholinesterase effects [22-25]. Related scaffolds such as coumarins, sulfonamides, and quinolines have also demonstrated anti-Alzheimer potential through enzyme inhibition and additional mechanisms such as antioxidant and anti-inflammatory actions [20].

Advances in computer-aided drug design (CADD), including molecular docking and MM-GBSA free-energy calculations, have significantly accelerated early drug discovery by enabling prediction of binding affinity and identification of key molecular interactions prior to synthesis [26,27,30]. In this context, the present study employed Glide docking and Prime/MM-GBSA rescoring to identify promising quinazolinone-based dual AChE/BChE inhibitors with favorable bind.

MATERIALS AND METHODS

Acetyl cholinesterase and butyrylcholinesterase have several structures in the PDB database in different resolutions. AChE with the pdb 4EY7, resolution (2.35Å) and BChE (PDB ID 6EZ2), resolution (2.7Å) were selected based on the sequence Similarity. The initial X-ray crystallographic coordinates of PDF (PDB ID: 4EY7) and (PDB ID 6EZ2), were downloaded from Protein Data Bank (http://www.rcsb.org). The proteins were subjected to the [Protein Preparation Wizard, Schrodinger, LLC, New York, NY, 2017-1]. A small but promising group of 18 compounds database consisting of quinazolinone scaffold were created. The ligands were subjected to ligand preparation using the LigPrep module in the Schrodinger Suite [LigPrep, Schrodinger, LLC, New York, NY, 2017-1]. The module refined

the structures, energy-minimised the conformations, adjusted the spatial arrangements software helps with the identification of the receptor grid according to our needs. The site map application was used to find, visualise and evaluate protein binding sites [31-32]. Glide (Schrodinger, Inc.) methodology: In this study, two enzymatic targets with the co-crystallised ligand molecule (Donepezil) bound to the AChE structure (4EY7) and Carbamylated BChE (rivastigmine metabolite/intermediate) bound to butyrylcholinesterase BChE (6EZ2) were used to generate receptor grids, serving as a framework for docking-based virtual screening. The designed chemical scaffolds were subsequently positioned within the AChE & BChE, binding pocket, as defined by this grid, using the Virtual Screening Workflow (VSW) provided in the Schrodinger suite. A flexible docking approach was employed to model receptor flexibility, simulate the inherent plasticity of the active site and incorporate conformational changes in the binding pocket.[30-34] The docking scores summarized in Table 2 and all the molecules binding pose in the site is shown in the Fig. 3.

Prime MM-GBSA methodology: This application calculates the free energy binding between the receptor and a ligand in its complex. The protein-ligand binding free energies during the last 2 ns were calculated using the Prime/MM-GBSA module of Schrödinger suite [Suite] to get the averaged binding property. Residues in binding pockets of the protein were treated as flexible and the ligand partial charges were assigned by the initial charges.The binding free energy ΔGbind was estimated using the equation [Lyne, P.D]: ΔGbind = Gcmplex – (Gprotein + Gligand) [33-34].

Drug likeliness analysis

Pharmacokinetic properties—likewise absorption, distribution, metabolism, excretion, and toxicity (ADMET) — play a major role in initial phases of drug design and development. The analysis of these parameters provides specific insights into the drug-likeness of molecules, providing knowledge on how a compound will behave in a biological system. By integrating these evaluations early in the preclinical phase, researchers can more competently identify molecules with balanced set of physicochemical characteristics and optimal pharmacokinetics (PK) and pharmacodynamics (PD) behavior, thereby prioritizing compounds with higher therapeutic potential and increasing success rates early in the development pipeline [34]. In this study, the QikProp module of the Schrodinger suite [QikProp, Schrodinger, LLC, New York, NY, 2017-1] was used to assess the drug-likeness profiles of the top-scoring designed molecules. QikProp settings determine which molecules are flagged as being dissimilar to other 95% of the known drugs. The Qikprop helps us in analyzing the pharmacokinetics and pharmacodynamics of the ligands by accessing the drug like properties Predicted significant ADME/T properties such as permeability through MDCK Cells (QPlogMDCK) (Irvine, J. D), QikProp predicted log IC_{50} value for blockage of K+ channels (QPlogHERG), QikProp predicted gut-blood barrier (QPPCaco) (Luco, J. M.) and violations of the Lipinski's rule of five (LROF) (Lipinski, C. A). The molecular properties are provided in Table 1, Glide and Prime MM-GBSA rescoring values are listed in Table 2. The ADME properties were predicted so as to calculate oral bioavailability, dermal penetration, CNS penetration, metabolism and Toxicity. The results are shown in the table 3.

RESULTS AND DISCUSSION

Docking analysis demonstrated stable binding of the quinazolinone derivatives within the active sites of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), mediated by key hydrogen bonding and hydrophobic interactions. Catalytically important residues, including Gly116, Gly117, Ser198, Ser203, His447, and Glu334, were consistently involved in ligand stabilization, comparable to interactions observed with the reference drugs Donepezil and Rivastigmine (Fig. 7–10). The designed quinazolinone derivatives exhibited superior binding affinities relative to the reference compounds, with G-scores ranging from −11 to −3 kcal/mol for AChE and −10 to −4.9 kcal/mol for BChE. Among them, APM2 and APM3 emerged as the most promising dual inhibitors, supported by favorable MM-GBSA binding energy values. Complex stabilization was primarily driven by hydrogen bonding with residues Gly116, Gly117, Ala202, Gln223, and Ala208, along with hydrophobic interactions within the enzyme gorge (Fig. 7–

10). ADME profiling revealed that all selected quinazolinone derivatives complied with Lipinski's Rule of Five and Rule of Three. The compounds exhibited molecular weights below 500 Da, acceptable hydrogen bond donor and acceptor counts, predicted human oral absorption exceeding 70%, and favorable lipophilicity and brain–blood partition coefficients. These pharmacokinetic properties, summarized in Table 3, indicate good oral bioavailability and central nervous system penetration. Overall, APM2 and APM3 demonstrate strong potential as drug-like dual AChE/BChE inhibitors for Alzheimer's disease.

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Table 1: Binding Database index of Molecules along with their Molecular properties, Molecular formula, Molecular weight, Log P value and their IUPAC nomenclature:

Sample	Molecular formula	MW	LOG P	IUPAC
APP2	$C_{20}H_{15}O_2N_3$	329.35	3.46	(4-hydroxyphenyl)-3-(6-methylpyridin-2-yl)-3, dihydroquinazolin-4-one
APP3	$C_{20}H_{14}NO_2Cl$	347.80	4.41	2-(4-chlorophenyl)-3-(6-methylpyridin-2-yl)-3, dihydroquinazolin-4-one
APP4	$C_{19}H_{14}N_4O_3$	358.35	4.13	3-(6-methylpyridin-2-yl)-2-(3nitrophenyl)-3, dihydroquinazolin-4-one
APP5	$C_{20}H_{15}N_3O_3$	345.35	3.17	2-(2,4-dihydroxyphenyl)-3-(6-methylpyridin-2-yl)-3,4-dihydroquinazolin-4-one

APP6	$C_{20}H_{14}O_6N_5$	419.353	2.44	2-[3-(6-methylpyridin-2-yl)-4-oxo-3,4-dihydroquinazolin-2-yl]-4,6-dinitrobenzene-1-olate
APM1	$C_{21}H_{20}O_4N_3$	381.43	2.61	5-{2-[2-(diethylazaniumyl) ethyl]-4-oxo-3,4-dihydroquinazolin-3-yl}-2-hydroxybenzoate
APM2	$C_{22}H_{18}O_4N_4$	402.409	3.86	2-({2-[3-(3-carboxylato-4-hydroxyphenyl)-4-oxo-3,4-dihydroquinazolin-2-yl] ethyl} amino) pyridin-1-ium
APM3	$C_{24}H_{19}O_5N_3$	431.447	3.54	2-hydroxy-5-(2-{2-[(4-methoxyphenyl) amino] ethyl}-oxo-3,4-dihydroquinazolin-3-yl) benzoate
APM4	$C_{24}H_{19}O_7N_3$	481.479	2.92	2-hydroxy-5-(1-oxo-3-{2-[(4-sulfonatophenyl) amino] ethyl}-1,2-dihydroisoquinolin-2-yl) benzoate
APM5	$C_{24}H_{20}O_5N_3$	417.42	3.37	2-hydroxy-5-(2-{2-[(4hydroxyphenyl) amino] ethyl}-4-oxo-3,4dihydroquinazolin-3-yl) benzoate
APM6	$C_{25}H_{19}O_4N_3F_3$	469.419	5.92	2-hydroxy-5-[4-oxo-2-(2-{[4-(trifluromethyl) phenyl] amino} ethyl)-3,4-dihydroquinazolin-3-yl] benzoate
APD1	$C_{27}H_{20}O_4N_2$	432.481	4.85	2-(4-methoxyphenyl)-3-{4-[(E)-2-phenyldiazen-1-ylphenyl}-3,4dihydroquinazolin-4-one
APD2	$C_{26}H_{18}N_40_2$	418.454	1.48	2-(4-hydroxyphenyl)-3-{4-[(E)-2-phenyldiazen-1-yl] phenyl}-3,4-dihydroquinazolin-4-one
APD4	$C_{26}H_{17}O_3N_5$	447.452	1.47	2-(3-nitrophenyl)-3-{4-[(E)-2-phenyldiazen-1-yl] phenyl}-3,4-dihydroquinazolin-4-one
APD6	$C_{26}H_{18}N_6O_6$	508.449	3.65	2,4-dinitro-6-(4-oxo-3-{4-[(E)-2-phenyldiazen-1-yl] phenyl}-3,4-dihydroquinazolin-2-yl) benzene-1-olate
APT5	$C_{15}H_{11}O_3N_5$	321.295	3.42	2-(2,4-dihydroxyphenyl)-3-(1H-1,2,4-triazol-3-yl)-3,4-dihydroquinazolin-4-one
APT6	$C_{15}H_90_6N_7$	395.29	2.68	2,4-dinitro-6-[4-oxo-3-(1H-1,2,4-triazol-3-yl)-3,4,4a,8a-tetrahydraquinazolin-2-yl] benzene-1-olate
APT4	$C_{15}H_{10}O_3N_6$	334.293	1.58	2-(3-nitrophenyl)-3-(1H-1,2,4-triazol-3-yl)-3,4-dihydroquinazolin-4-one

Table 2: Molecular docking score and interaction profiles of screened quinazoline derivatives with AChE (PDB:4EY7).and BChE (PDB ID: 6EZ2)

S. No	CPD CODE	GLIDE DOCKING SCORE (Kcal/mol)		Prime MMGBSA DGbind (Gbind=Kcal/)		NUMBER OF H-BOND	
		AChE	BChE	AChE	BChE	AChE	BChE
1.	APM3	-10.71	-10.7	-28.57	-30.45	1	2
2.	APM2	-11.03	-10.5	-67.54	-33.91	1	2
3.	APT5	-9.966	-8.3	-27.36	-28.7	1	2
4.	APP4	-11.27	-8.2	-24.813	-65.76	0	1
5.	APM4	-8.645	-7.9	-67.76	-30.21	1	1
6.	APT4	-8.638	-8.4	-29.34	-44.12	2	2
7.	APP5	-8.155	-4.9	30.90	-19.14	2	1
8.	APP2	-10.19	-7.1	-43.304	-67.41	0	2
9.	APP6	-3.811	-6.9	-14.679	-24.74	1	1
10.	APP3	-9.384	-6.6	-42.523	-30.34	0	-
11.	APT6	-7.918	-4.9	-21.148	-28.52	1	-
12.	APM6	-6.128	-4.2	-65.408	-61.23	1	-

13.	APD2	-6.117	-6.2	-37.386	-36.32	0	-
14.	APD1	-6.022	-6.02	-27.24	-30.45	1	-
15.	APD4	-5.651	--6.7	-31.45	-38.24	1	-
16.	APM5	-5.395	-8	-30.87	-35.72	2	1
17.	APM1	-3.67	-7.5	-54.52	-60.28	1	2
18.	Donipiz	-9.2	-8.3	-	-	3	1
19.	Rivasti	-7	-8.2	-	-	2	2

Table 3: ADME properties of 2,3 disubstituted quinazolinones

Code	CI log Swat	%Human oral abs	R of 3	QPPCaCo	Log S	QPLog Khsa	Log KP	Qplog BB	MDCK	QP log HERG	metab	Stars
APP2	-4.9	100	0	918.25	-4.7	0.26	-1.9	-0.5	451.1	-6.0	2	0
APP3	-5.4	100	0	3044.6	-5.1	0.324	-1.0	0.16	403.1	-6.0	1	1
APP4	-5.2	93.08	0	516.71	-4.2	0.091	-2.4	-0.8	242.32	-5.9	2	0
APP5	-4.9	89.83	0	468.46	-4.2	0.12	-2.4	-0.9	217.96	-5.7	3	0
APP6	-5.9	53.24	0	35.37	-4.5	0.11	-4.7	-2.1	13.34	-5.9	4	1
APM1	-3.7	51.03	1	12.02	-3.7	-0.06	-5.3	-1.2	5.84	-4.3	3	0
APM2	-5.7	72.46	0	26.45	-5.3	0.098	-3.2	-1.9	12.42	-5.1	4	0
APM3	-6.2	76.59	0	33.25	-5.6	0.212	-3.1	-1.9	15.90	-4.9	5	0
APM4	-5.9	33.59	1	0.42	-4.9	-0.46	-5.5	-3.5	0.18	-3.3	4	2
APM5	-5.9	62.46	1	10.10	-5.1	0.044	-4.0	-2.4	4.38	-4.9	5	0
APM6	-7.3	81.76	1	33.90	-6.6	0.451	-3.2	-1.6	64.03	-4.9	6	1
APD1	-6.8	100	0	1394.8	-4.5	0.346	-1.0	-0.4	708.8	-6.1	2	2
APD2	-6.6	100	0	691.5	-4.9	0.495	-1.5	-0.7	332.03	-6.3	2	2
APD4	-7.0	100	1	340.7	-6.2	0.509	-1.8	-1.3	154.51	-7.9	2	1
APD6	-7.7	44.28	0	33.8	-4.4	0.273	-4.2	-2.1	12.74	-5.7	4	1
APT5	-4.2	68.74	0	93.7	-3.3	-0.23	-4.0	-1.5	38.29	-5.3	2	0
APT6	-5.2	32.49	1	7.3	-3.5	-0.27	-6.2	-2.8	2.44	-5.4	3	2
APT4	-4.1	68.94	0	104.5	-3.2	-0.36	-3.9	-1.4	43.06	-5.5	1	0
Range	-6.5 – 0.5	<80%H >25%L	Max 3	<25 p, >500 great	-1 to - 5	-1.5 to +1.5	–8.0 to –1.0	-3 to 1.2	<25 poor,>500 great	Conc.below-5	1- 8	1-4

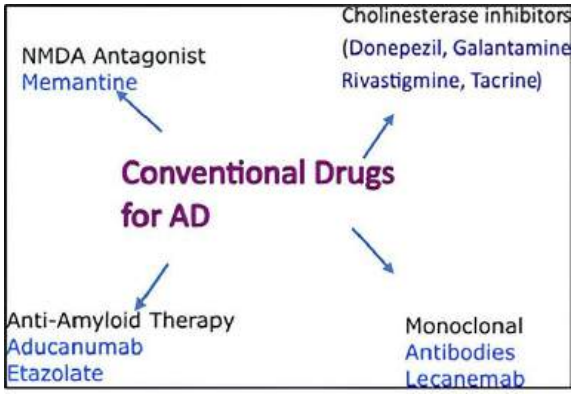

Fig.1: Methods of treatment

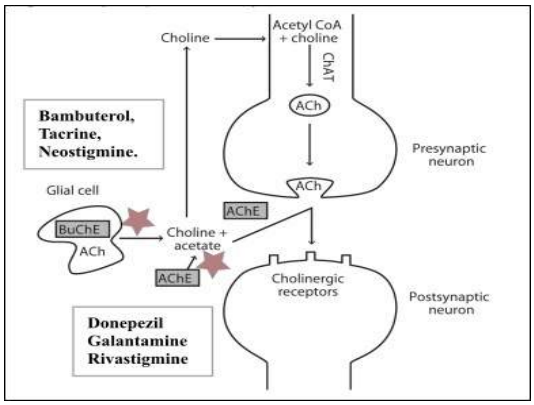

Fig. 2: Mechanism of AChE and BChE

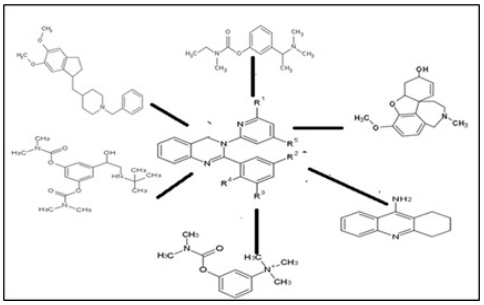

Fig. 3: Quinazolinone scaffold

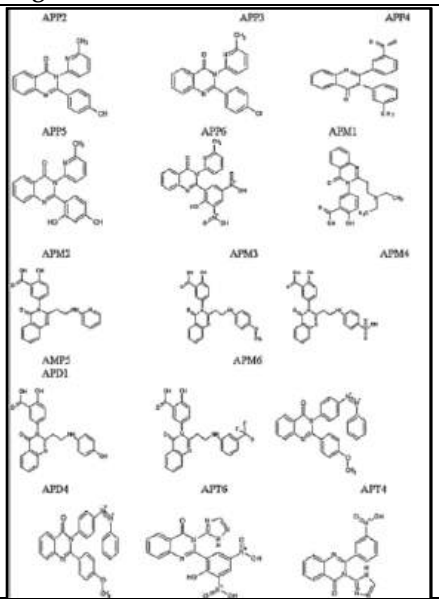

Fig.4.: Library of Compounds

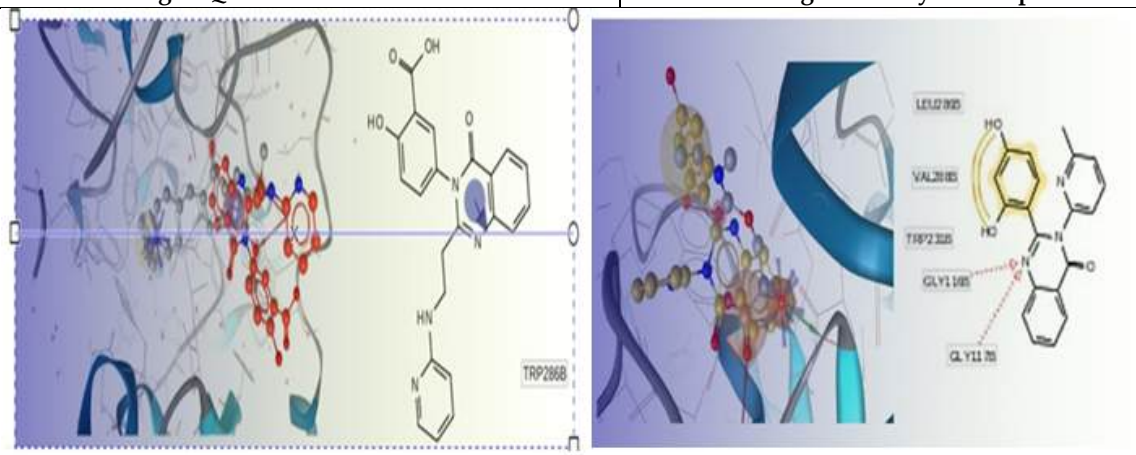

Fig 5 and 6: Interaction of compound APM3, APT4 with BCHE (PDB:6EZ2) protein active site both 2D and 3D diagrams

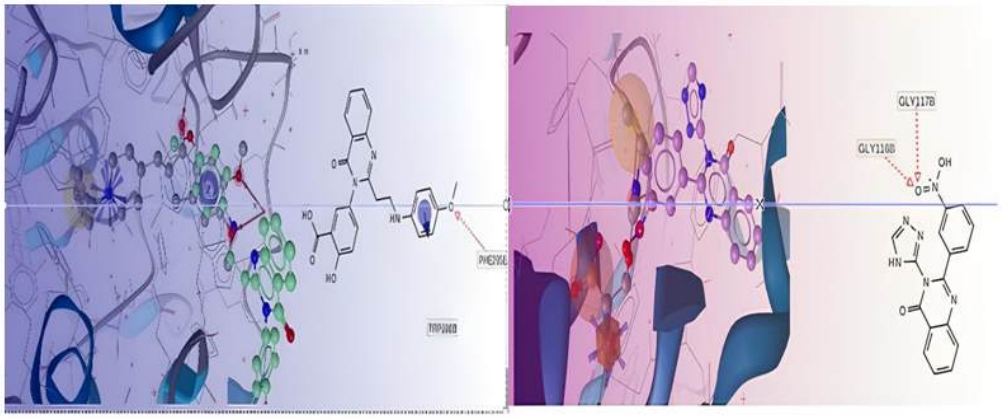

Fig:7 Interaction of compound APM2, APP2 with ACHE (PDB:4EY7) protein active site 3D diagram

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

RESEARCH ARTICLE

Exploring the Role of Organic Dyes and Binary Oxides in Tuning Bandgap Energy for Dye Sensitized Solar Cells

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Received: 20 Nov 2025 Revised: 01 Dec 2025 Accepted: 26 Dec 2025

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ABSTRACT

Dye-sensitized solar cells (DSSC) are among the most advanced solar cell technologies due to their exceptional properties, such as low cost and environmental friendliness. A good DSSC requires the proper combination of constituent materials, which significantly influences their performance. Strategies for identifying suitable material components in DSSC device configuration are required. In this article, we present information on the potential material combinations used to create DSSCs, with a focus on composite electromagnetic wave absorption properties. The composites were made using simple doctor blade techniques, with different Fe_2O_3 doping being too successful. Bandgap energy modulation for dye-sensitized solar cells (DSSCs) using organic dyes and binary oxides. A crucial factor affecting light absorption and the ensuing creation of charge in DSSCs is bandgap energy. In order to understand the synergistic effects of different combinations of organic dye and binary oxides on bandgap tuning, structural, optical, morphological, and electrochemical properties of the materials are analyzed through systematic exploration. Flexible counter electrodes and photoanodes made of novel materials were developed for the efficiency of DSSCs.

Keywords: Tunable bandgap energy, FESEM, Binary oxides, Electrolyte

INTRODUCTION

DSSCs, also known as "Gratzel cells," were fabricated for the first time in 1991 by O'Regan and Gratzel and are considered third-generation solar cells. [1] The construction and mechanism of a DSSC photoelectrochemical system. The general structure of such cells comprises a photo anode as a working electrode, a counter electrode, and an electrolyte filled in the space between the photoanode and counter electrode. The photoanode is made up of transparent conductive glass coated with transparent conductive oxide (indium- or fluorine-doped tin oxide; ITO and FTO, respectively), on which a dye-coated metal oxide semiconductor (thickness, 10–20μm) is applied [2]. The metal oxide semiconductor layer has two functions, namely support for the sensitizer and a carrier of photo-generated electrons from the dyes to the external circuit. Most of the reviews in the field of solar cells are dealing with the preparation of nanostructured electrode materials in DSSCs, but the crystal growth technique has been successfully employed for a purified form of material that exhibits better properties. [3] The generation of energy is one of the most important scientific and technological challenges in the 21st century. The commercially available solar cells are currently based on inorganic silicon semiconductors.[4] The demand for silicon will skyrocket within the next decade and the price of silicon will rise dramatically. Organic solar cells, therefore, appear to be a highly promising and cost-effective alternative for the photovoltaic energy sector. [5] In this context, dye-sensitized solar cells (DSSC) have attracted considerable attention in recent years. The structure, crystallinity, and surface morphology of photoanode materials can influence the efficiency of the DSSCs or Key parameters. Direct solar light conversion into electrical energy is one option for the use of renewable energy.[6] Nanocrystalline materials have garnered a lot of interest from researchers throughout the world in recent years due to their remarkable optical, electrical, and mechanical capabilities compared to their bulk-phase counterparts.[7] Many efforts have been made in recent years to include metals with typical optical properties inside semiconductor devices. Therefore, the next stage toward propelling DSSCs as a future energy device would be to improve efficiency and device stability, as well as to reduce material and manufacturing costs[8]. An injected-like Dye-Sensitized Solar Cell's key components are a photoanode, electrolyte, and counter electrode. The majority of the photoanode is made of fluorine-doped tin oxide (FTO) glass, which absorbs a sensitizer like a 5-methylsalicylaldehyde with 2-(2-aminoethoxy) ethanol dye. The composition of the electrolyte is I^-/I^{3-} redox. Graphite and semiconductor binary metal oxides of Fe_2O_3 and $BaCrO_4$ were combined to create a counter electrode. The dye molecules absorb photons with sufficient energy when exposed to the sunshine to begin the transfer of electrons from their ground states to excited ones. Once in the semiconductor binary oxide film's conduction band, these excited electrons are subsequently transported to the conductive substrate, allowing current to flow to the counter electrode.[9] It is expected that the low cost of commercially fabricating DSSCs along with their good performance will replace conventional solar cells very sooner. Research is going on for improving the efficiency and viability of the cell. DSSCs are still at the start of their development cycle. Efficiency gains are possible and have recently started a more widespread study. Binary metal Oxide electrodes using Fe_2O_3 are Good semiconducting material compared to $BaCrO_4$. The conducting material Fe_2O_3 has high semi-conducting material easily conducting electrons at the time $BaCrO_4$ also worked in binary metals it easily conducted in the FTO glass. Its conductivity worked in UV – Visible. The dye UV – Visible range is 200nm – 585nm but compared to binary metal oxide is 200nm – 800nm it confirmed the active cell are highly conductive materials. The working electrode and counter electrode both have high electron-conducting properties, but efficiency is low because the photoanode's surface was passivated in some areas at the time the electrons were carried there. Passivation is avoided in this ongoing effort because of the new procedures' great efficiency. Materials are excellent at conducting electrons, but efficiency is low because the working electrode and counter electrode conducted electrons during a time when some of the surfaces were passivated. In this upcoming development, passivation is eschewed in favor of more efficient ways. The novelty of work we formed the solar cell with the Tunable band gap energy of the binary metal oxide with dye molecules.

EXPERIMENTAL

Materials

Pure compounds from 5-Methylsalicylaldehyde, 3-cholroaniline, metal oxides Fe_2O_3 and $BaCrO_4$, and solvent ccl_4 acetic acid, hydrochloric acid used for the synthesis were purchased from Sigma-Aldrich as Analytical reagents with 99% of purity. I^-/I^{3-} iodide solution used as Redox electrolyte.

Synthesis of Dye preparation

The 5- Methyl salicylaldehyde, which has been dissolved in 5ml of CCl_4 and the 5ml of acetic acid, was grown into a single crystal using slow evaporation methods. Drop by drop, with stirring process continued for an hour at ambient temperature, 0.18 (0.00141) of 3-Chloroaniline was added to this solution. The mixture deepened to golden at this point. With a slow evaporation technique, crystal forms after two weeks of standing. The dye's chemical response, as shown in fig.1

Chemical Reaction

$C_7H_5NO_4 + C_4H_{11}NO_2 \longrightarrow C_{11}H_{14}N_2O_5$

Chemical Structure

Chemical structure of Dye – [E-3CM4M] (Fig.1).

Synthesis of Binary Oxides Fe_2O_3 / $BaCrO_4$ preparation

The electrodes made from the synthesized nanoparticles were used to get the findings presented in this study and pure Fe2O3 nanoparticles were combined in 0.1 g (0.00062 mol) of powder, which was then dissolved in 1 ml of hydrochloric acid, to create a slurry solution using a standard sample preparation method. The particle dispersions in the mortar were combined with 0.1 g (0.00039 mol) of barium chromate powder, 1 ml of hydrochloric acid, mixed with Fe_2O_3, and hydrochloric acid was added dropwise. Thin film processing was used to create the finished Fe_2BaCrO_7paste. The area that was going to be coated with FTO thin film was marked using Scotch tape. The entire FTO substrate was covered with a homogeneous layer of paste. Fe_2BaCrO_7 0.15g was spin-coated for 20 seconds at a speed of 3000 revolutions per minute (RPM). The films were then annealed to increase their crystallinity. The samples were first dried at room temperature for half an hour.

Preparing the electrolyte

We extracted Graphene from the HB pencil to make counter electrodes. To obtain a dark shade of Graphene for one of the counter electrodes, the conductive side of one FTO-coated glass was held over the point of HB pencil for 30 seconds. Iodide/triiodide has been a redox couple being used all through the entirety of the DSSC analysis, and it has proved that the most adaptable redox couples thus far, combination gives conversion efficiency is 11 – 12% and having good life span.

Assembling the Cell and Cell Performance DSSCS

We can easily fabricate an unsealed DSSC and measure its PV performance. A spacer film, such as polyethylene (15- to 30-µm thickness), is placed on the dye-coated TiO2 photoelectrode and then the electrolyte solution is dropped on the surface of the TiO2 electrode using a pipette (one or two drops). The counter electrode is placed on top of the TiO2 electrode, and then the two electrodes are fastened together with two binder clips. If a low melting point polymer film such as Surlyn is used instead of the spacer film, we can fabricate a sealed cell after packaging of the cell using a resin (e.g. ethylene vinyl acetate, EVA) for long-term stability. Since Gratzel and coworkers reported high performance of a DSSC in 1991, many ¨ workers worldwide have tried to reproduce their result. Some reported performances are shown in Table 15.1. These cells were fabricated using a Ru complex photosensitizer, N3 dye, and a nanocrystalline Fe_2BaCrO_7 electrode. In many cases, the light condition is AM1.5

Characterization

X'Pert Pro-Panalytic was used to capture powder X-ray diffraction using Cu K X - radiation (=1.5406) at 40kV and 30mA power. The X-ray Diffraction pattern was gathered in the 2 regions between 0 and 100. DASH 4.0.0 was used to monitor the lattice parameters. Perkin Elmer Lambda 950 UV VIS NIR Spectrometer having Deuterium lamp source was used to collect optical transmission data at room temperature between 200nm and 1100nm with a precision of 0.05nm and an accuracy of 0.08nm. The sample's absorption bands are visible between 200 and 800nm. One of the frequently used techniques for visualizing the microstructure and shape of materials is field emission scanning electron microscopy. Technical requirements 1.5nm nominal precision at 10 kV (Zeiss Sigma 300). I- V traits displayed by a 20 W source parameter is 2450 from Keithley (SMU). The SMU has a maximum current source of 1 A, a maximum voltage source of 200 V, and a measurement resolution of 0.01/10 (Current/Voltage).

RESULTS AND DISCUSSIONS

Powder X ray diffraction (PXRD) study

Powder X-Ray diffraction was recorded on the X'Pert Pro- Pana lytic system using Cu Kα X-radiation ((λ=1.5406Å) at 40 kV and 30 mA power. X-Ray diffraction patterns were collected over the 2θ range 10° - 80°. The Rietveld refinement method and the simulated annealing structure solution have been used in the DASH 4.0.0 program to solve crystal structures. Structural affirmation accomplished by well-defined strong XRD Bragg's diffraction pattern with assigning NMR chemical shifts and its data analysis. The structure is shown in Figure 3. PXRD of Dye Figure.2. The diffraction analysis of this growth inter-planar line spacing corresponds to scattering planes. PXRD data of photo anode (Dye) is shown in Fig 4. Major Diffraction Peak located in monoclinic phase at 2Ɵ values of with relatively very high intensity. From PXRD fig 2. Lattice parameters like crystalline size, Dislocation density, and lattice strain using Debye's Scherrer formula are shown in Table.1 [10].

Powder X ray diffraction (PXRD) analysis (Table 1).(Fig 3).

UV-Visible-NIR_ spectroscopy of Dye

The main impacts on coloring effectiveness sensitive solar cells for the light scattering and greater dye absorption [11] Figure 4. Depicts the dye film's UV-visible absorption spectrum. These data indicate that the dye material absorbs between 200nm to 575nm.

UV – Visible NIR spectrum of E-3CM4M Dye (Figure 4).

The dye's band gap energy is 2.15eV, confirming the semiconducting of material.

UV –Vis-NIR- Spectroscopy for Binary metal oxides

The Fe_2O_3 based DSSC with the $BaCrO_4$ layered dispersion of light was studied using UV-visible absorbance spectra. Soaking the photo anode helped remove the loaded dye. Displays a dye with UV-visible absorbance spectrum that was isolated from Fe2O3 using $BaCrO_4$ and an electrolyte. Semiconducting material validated the UV - Visible study by adjusting band energy gap. The bandgap energy spectrum of Fe_2O_3 oxide is 2.5eV, whereas the energy band gap of $BaCrO_4$ is 2.3eV. The band energy gap of the combined counter electrode Fe_2BaCrO_7 is 1.65eV. The UV spectrum is depicted in Figures 5(a), 5(b), and 5(c) [12]. Figure 5(a). UV – VIS - NIR spectrum of Fe_2O_3. Figure 5(b). UV – VIS - NIR spectrum of BaCrO4 Figure 5(c) - UV – VIS - NIR- spectrum of binary metal oxide (Fe_2BaCrO_7)

Field emission scanning electron microscopy:

The particle hasshape in nano dimensions became apparent. As shown in Figure 6. The dye granules had an average diameter of 2-20 μm. In 1m microphotographs, the fractured surface fragments are visible. Gas molecules cause the electron beam to be disturbed, and the resulting secondary and backscattered electrons, which are used to image the particles, appear to be 2 m in size. Particle studies are conducted in a strong vacuum. [13]. Field Emission Scanning Electron Microscopy (Figure 6).

Electrochemical Measurements for DSSC Cell

I - V characteristics

I -V characteristic using solar simulator conditions. The characterization performed using the solar simulator at cell electrical performance as analyses under one sun illumination and under dark conditions, the measurements to I-V parameters of the cell from tabulated 2. The observed in the low to high medium voltage and current-range of cell [14]. The photo-anodes absorbed to the electrolytes it's conducted to cathode device fabrication confirmed the fill factors and hence cell performance achieved. The optimization of the device fabrication parameters are maximum voltage, maximum current, and fill-factor confirmed by I- V curves. I _V characteristics of DSSC (Table. 2) (Fig 7).

CONCLUSION

The Synthesis of novel materials, the development of fabrication of DSSCs their properties and performance in real devices and latest development of tunable bandgap material for solar energy conversion. We produce photo anode in with the technique of crystal growth for purified version and used powder as organic dye photo anode were analyzed by PXRD, UV and FESEM to understand the structural, optical and morphological behavior of the dye material. The dye samples' UV–vis spectra revealed high absorption, Result indicates that the Fe_2O_3 and $BaCrO_4$ composites exhibit improved absorption performance compared to individual components, The findings shed light on the mechanisms underlying bandgap energy modulation in DSSCs, offering insights into the design and optimization of next – generation photovoltaic devices for enhanced energy conversion efficiency DSSCs.

ACKNOWLEDGMENT

The Authors would like to thank Spin Coating, PXRD, UV – Vis Spectroscopy, FESEM, Cyclic Voltammetry, and I- V Characterization techniques were carried out Centre for Nanoscience and Nanotechnology, Sathyabama Institute of Science and Technology, Chennai, and University Science Instrumentation Centre (USIC), Alagappa University Karaikudi – 630 003, Tamil Nadu India.

Supplementary Crystallographic Data

CCDC contains the supplementary Crystallographic data for E-3CM4M which can be obtained free of charge from the Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif.

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Table 1: Powder X ray diffraction (PXRD) analysis

Crystallite Size (D)	41.5nm
Dislocation Density(δ)	5.806×10^{14}lines /m^2
lattice strain (ε)	0.15353681
a, b, c	8.69 Å, 5.89 -Å, 7.48Å

Table 2: I _V characteristics of DSSC

DSSC cell	V_{oc}(mV)	J_{sc}(mA/cm^2)	(FF)	η%
5MMC + Fe_2O_3 +$BaCrO_4$	0.668	7.056	0.559	2.6

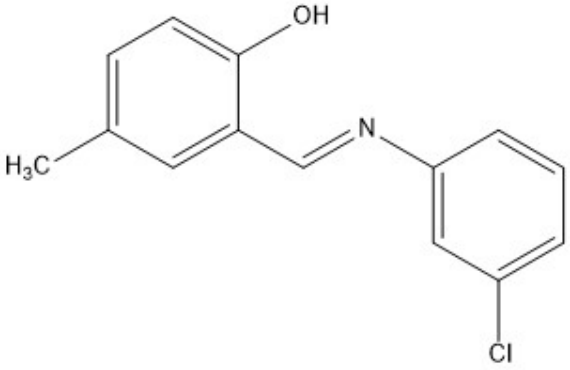

Fig.1: Chemical structure of Dye – [E-2HM4N]

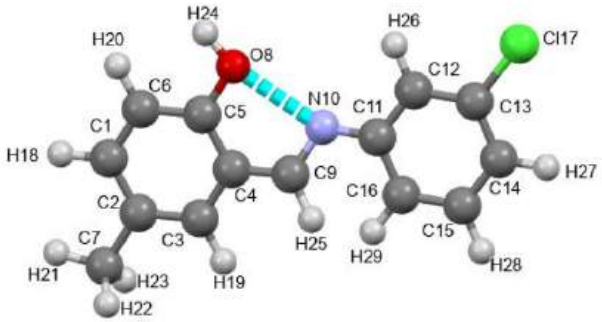

Figure 2: PXRD of Dye

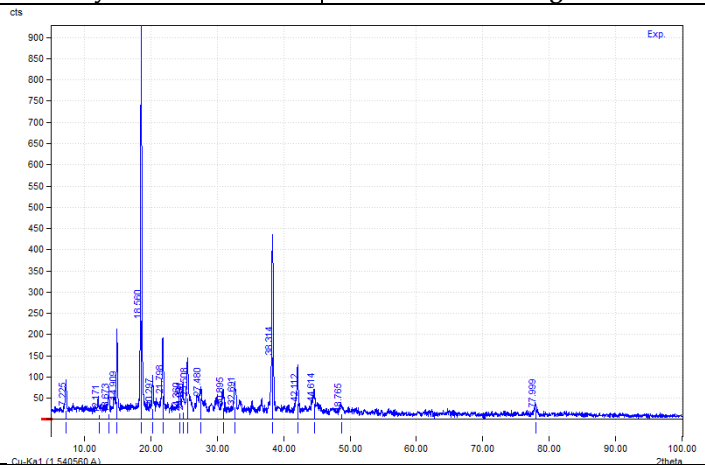

Figure 3: Powder X ray diffraction (PXRD) analysis

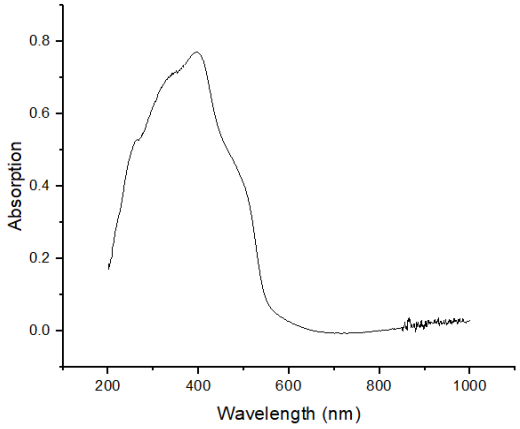

Figure 4: UV – Visible NIR spectrum of E-2HM4NDye

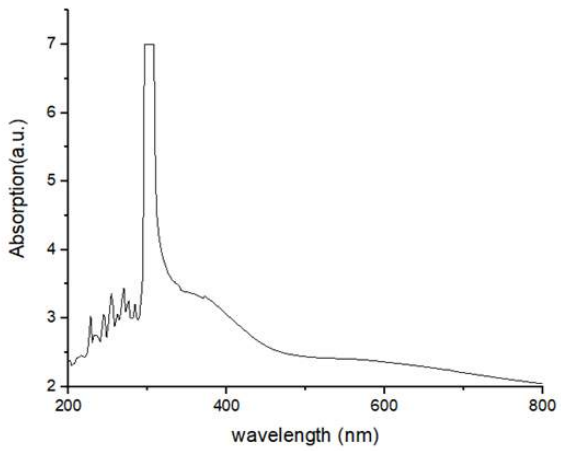

Figure 5(a). UV – VIS - NIR spectrum of Fe_2O_3

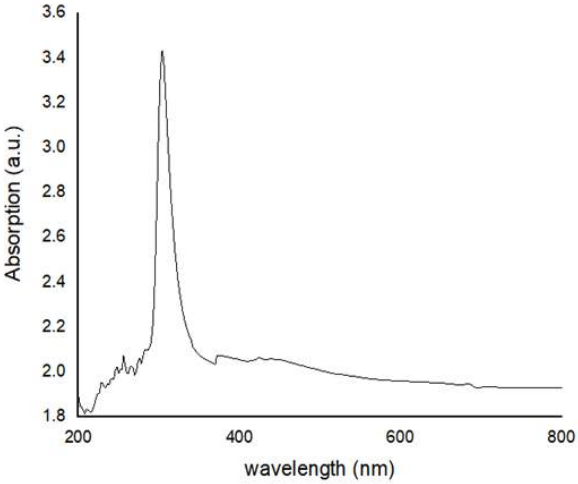

Figure 5(b). UV – VIS - NIR spectrum of $BaCrO_4$

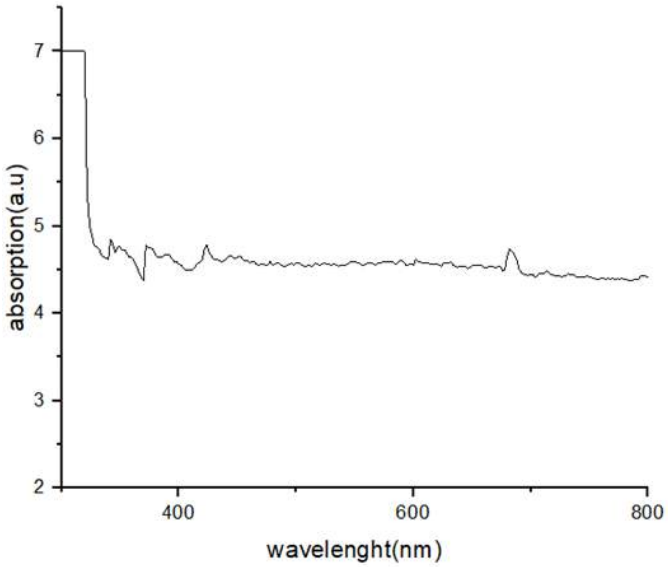

Figure 5(c) - UV – VIS - NIR- spectrum of binary metal oxide (Fe_2BaCrO_7)

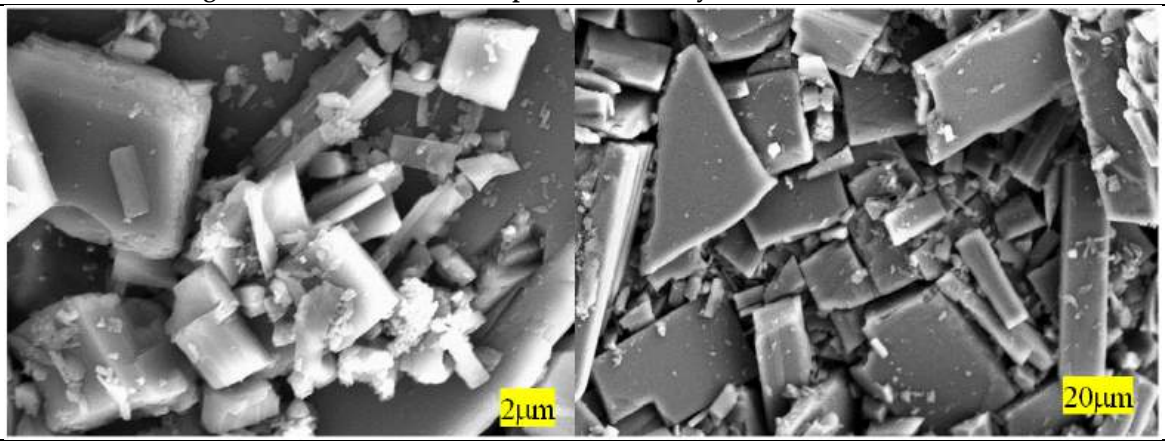

Figure 6: Field Emission Scanning Electron Microscopy

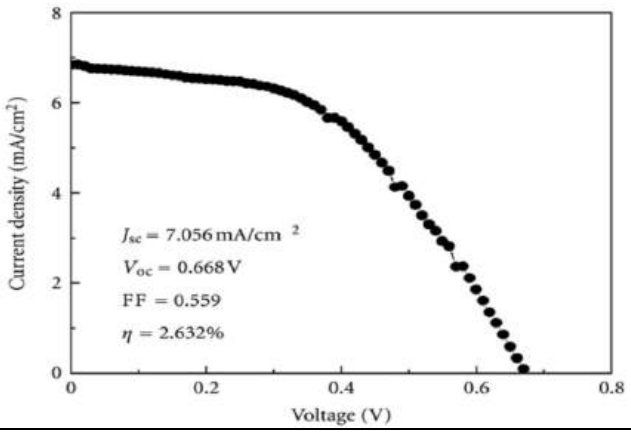

Fig. 7: I _V characteristics of DSSC

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Vol.16 / Issue 94 / Feb / 2026 *International Bimonthly (Print) – Open Access* *ISSN: 0976 – 0997*

REVIEW ARTICLE

Impacts of Climate Change on Molluscs : An Integrative Review of Environmental Stressors and Species Resilience

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Received: 18 Aug 2025 Revised: 20 Nov 2025 Accepted: 26 Jan 2026

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ABSTRACT

Molluscs, the most vulnerable species to climate change, play an ecological role in nutrient cycling and filtration of water, and they support the food web and help in the economy of the country. This review highlights the research conducted with mollusc species to assess their durability against various environmental gradients. The physiological process, which includes shell construction, reproductive mechanisms, and larval development, is disrupted when sea surface temperature increase. The sea surface temperature increased in natural ways such as radiation and seasonal changes, and it is also caused by human activity such as pollution, deforestation, etc. The equilibrium of the ecosystem is changed mostly by the process of ocean acidification. Beyond their ecological impact, it also affects the economy of the country by reducing the total population of the mollusc species, and this causes low commercial production of them. The population loss of this organism would affect the food web of the ecosystem and the employment of the people who work in the mollusc shell-based industries. When the sea level rises, it impacts the mollusc by reducing the availability of food and habitat shift; the species that depends on the sandy beaches would lose their habitat. These impacts cause the reduced annual production of molluscs such as mussels, oysters, etc. This paper aims to deliver the information about the reasons for climate change, the challenges faced by the mollusc and the measures to prevent the loss of organisms that are economically important for the country.

Keywords: Anthropogenic activities, global warming, bivalvia, salinity, aquaculture.

INTRODUCTION

Climate change occurs mostly due to anthropogenic activity, especially through industrial activity, burning of fossil fuels, and deforestation, which leads to the emission of greenhouse gases such as carbon dioxide, methane, etc., causing the accumulation of heavy metals in the environment and ocean acidification (OA). The rise in the level of carbon dioxide and decrease in the level of pH pave the way for ocean acidification (Allison et al., 2011). Due to industrial revolution, the carbon dioxide level in the atmosphere has increased by up to 400 ppm (Lamichaney and Maity., 2021.), and the pH level has decreased by 30% (Fortunato, 2015). It affects the majority of the marine organisms by means of calcification. It causes a greater impact on the phylum Mollusca because they are the most vulnerable (Przeslawki et al., 2005). Phylum Mollusca is the second largest phylum in the animal kingdom (Kershaw, 1983). Climate change has a greater impact on marine, estuarine, and freshwater organisms. It causes greater ecological and economic consequences (Parker et al., 2013). Due to elevated carbon dioxide exposure in the sea, it challenges the aquaculture by affecting the larval development, reproduction, metabolic activity, and production of molluscs such as clams and oysters (Cooley et al., 2012; Byrne, 2010). The impacts include shell weakening, larval mortality, growth reduction, heat stress, and salinity stress (Dickinson et al., 2013). The mortality of the mussel increases when the temperature gets higher than 29 ℃ (Dailianis, 2011). These changes will cause mismatched food availability in the marine and freshwater ecosystems. There is also a positive impact on the mollusc but the negative impacts are more prominent. The mollusc species, which inhabit freshwater and marine environments, may potentially get introduced into previously uninhabited areas by migrating into the deeper or cooler habitats, and the poleward range shifts will introduce the organism into a new ecosystem (Saupe et al., 2014). Some bivalves have greater resistance to lower temperatures because of the presence of antifreeze proteins in their hemolymph (Husmann et al., 2011; Zhang et al., 2024).

The physical processes in the aquatic systems, like the major ocean currents, are changing due to global warming. It changes the temperature of the water; the mortalities of the seed and the adult mollusc occur when the temperature changes from 28-31 ℃ (Rodrigues et al., 2015). The mollusc can be cultured in both temperate and tropical environments through semi-intensive line and raft cultivation using mussels and scallops in marine and brackish water (Allison et al., 2011). Molluscs are used as decorative items and also for pharmaceutical purposes (Murphy and Kerton, 2017; Romano et al., 2022; González and Vallejo, 2023;). The population in developing countries greatly depends on the mollusc because it has protein content, which is used for consumption and has a higher commercial value (Roy et al., 2008).

Impacts of Salinity

Salinity is a key abiotic factor, that can directly influence the life cycles of aquatic species (Madhavi et al., 2014). The adult *Mytilopsis leucophaeata* is extremely resilient to changes in the salinity and temperature (Verween et al., 2007). For *Abra ovate, Cerastoderma glaucum,* and *Caspiohydrobia species*, the ideal salinity gradient with Aral salt composition was between 17 and 27 psu (Krupa and Grishaeva, 2019). The survival rate of the larva *Crepidula plana* was greater in all temperatures, but at lower salinity the larva was intolerant (Zimmerman and Pechenik, 1991). At 16.7 psu the juveniles of *Donax trunculus* show higher tolerance to lower salinity (Reyes-Mart*ínez et al., 2020)*. When the external seawater salinity level decreases from 30 to 25 psu, it does not affect the salinity of the water in the pallial cavity of the gastropods; even after 2 to 12 hours of isolation, the salinity level is constant in the pallial cavity of *Crepipatella dilatata,* and the same happens to *Ostrea chilensis* (Chaparro et al., 2009). The veliger larva of the *Crepipatella peruviana* shows reduced velar activity when exposed to 20 and 15 salinity, but when the adults are exposed to the external environment, which has salinity value ranges from 32 to 25, and after some time when the value is declined to 15, the salinity value of the water inside their mantle cavity remains at 25 which means that the adult can isolate themselves from the external environment (Montory et al., 2016). Low salinity might worsen the detrimental effects of high CO_2 levels on the biomineralisation and growth energy balance of the eastern oyster, the *Crassostrea virginica*, a common

estuarine bivalve (Dickinson et al., 2012). The juveniles of *Mercenaria mercenaria* show a higher mortality rate when exposed to lower salinities (Dickinson et al., 2013).

Temperature Rise in Marine and Freshwater:

The major environmental factor is the temperature and it changes depending on the season and the year. The changes in the climate, mainly the temperature, will affect the distribution and the survival of the intertidal species in the upcoming few decades (Somero, 2010). When SST increases, it affects the different life stages of the species and the physiology of the species such as less potential to develop their organic protective layers, i.e., the shell, and a decrease in the growth rate and survival rate (Gazeau et al., 2013). The metabolic rate of the mollusc will be higher at warmer temperatures (Brodersen et al., 2011). The cold-water mollusc species may switch to more thermophilic places when the water temperature rises (Daufresne, 2004). The adult molluscs are more vulnerable to the temperature rise, and the mortality rate is 100% in the summer when the temperature rises to +3 °C (Rodrigues et al., 2015). The embryo of the *Aplysia californica* shows high mortality at temperatures above 30°C and below 10 °C (Verween et al., 2007).When the thermal level of the water increases more than 4 °C some species, which include *Crassostrea gigas,* show robust activity (Gibson et al., 2011). *Haliotis coccoradiata,* an abalone that is highly vulnerable to slight increases in temperature, which causes deleterious effects because abalone has a specific level of tolerance to the temperature (Gilroy and Edwards, 1998). When the temperature of the water increases, it helps the development of the oysters, and the reverse happens when the acidification increases (Parker et al., 2010).

Regulation of reproduction by temperature:

Reproduction can be directly impacted by temperature in both quantitative and qualitative ways (Gust et al., 2011). It has been projected that climate change will raise the average world temperature and influence how species interact with one another (Kalinda et al., 2017). Temperature is one of the most significant abiotic factors. The terrestrial gastropods are highly impacted by the environment they live in and depend on the environment for their development and for reproductive life (De Vaufleury, 2001). Fabioux et al. (2005), did an experiment by examining the gametogenic cycle of *C. gigas,* where the temperature played a vital role in their gonial mitosis regulation. When the temperature phase gets changed, it will affect the annual reproductive cycles of the mollusc because the temperature phase depends on the photoperiod and the mean sea temperature (Olive, 1995). The alteration in the external environment will mostly impact the larval forms; they are the most susceptible to the environmental alterations (Claudi and Evans, 1993). An experiment is done with the *Aplysia californica* to prove that the reproductive system of the *A. californica* is reliant on the photoperiod and the temperature because their results show that the species lay more eggs when they are kept in short days in warm water compared to long days in warm water (Wayne and Block, 1992). The fertilization rate is increased in the oysters when treated with elevated levels of temperature at 8°C, and the reverse happens when treated with temperatures more than 12°C (Parker et al., 2010). The absolute water temperature and seasonal day length cycles will affect the production of egg capsules of *Rapana venosa* (Harding et al., 2008). Increasing temperature shows negative impacts on the early ontogenic stages of the *Armina maculata* (Pires, 2012).

Ocean Acidification

Impact on Mollusc Shell Formation:

The ocean acidification plays an interrelated role with climate change and its impacts. The mollusc shell plays an important role, which provides protection from predators, and it provides its shell for other living organisms for attachment (Gutierrez et al., 2003). The seawater chemistry gets altered by the OA caused by industrial activity (Cooley et al., 2012) and the increased carbon dioxide level will affect the shell which is made up of $CaCO_3$ .The shell hardness and the rigidity of the oyster, *Magallana angulata*, will be reduced because of the exposure to ocean acidification (Meng et al., 2018). The species of mollusc such as mussels and oysters, need their shell for a defence mechanism from predators (Kroeker et al., 2014).

The shell of the adult mollusc is constructed with aragonite, or in some cases it is made up of both calcite and aragonite, but it occurs in specific taxa (Addadi et al., 2006). The shell of the mollusc shows reduced aragonite

thickness in their shell, and the structure of the shell is changed when they are grown under ocean acidification state (Fitzer et al., 2015). Since 2005, the survival of the oysters has been reduced in the hatcheries that are present on the Northwest coast of the USA, and this is caused by the ocean acidification that occurs in the deep water and on the ocean shore (Barton et al., 2012). Even under a very low level of pH, the shell of certain species of the mollusc is developed (Gazeau et al., 2013). Some species can maintain their shell structure, but they utilise more energy. The ocean acidification causes lasting larval life in the water; this causes predation on the larvae because they have a less developed shell over them (Ross et al., 2011). The calcification of the mollusc is decreased due to the alteration of the proteins needed for the calcification when the water is acidified (Dineshram et al., 2021). The inhibition of shell growth and the abnormalities in their morphology are caused in *C. gigas* by the acidification in the ocean by elevated levels of CO_2 (Barros et al., 2013). The ocean acidification has more effects on the survival of the molluscs in the marine environment, and it also affects the developmental process and the framework of the shell (Gazeau et al., 2013; Kroeker et al., 2014). The transcription of arginine kinase and the cavortin downregulation would affect the calcification of the oyster (Ducker and Falkenberg, 2020).

Population Consequences:

Ocean acidification threatens the population of the shelled mollusc by changing their resistance of the shell (Zhang et al., 2024). The population of healthy oysters is threatened by bioerosion and by ocean acidification, and this affects their restoration ability (Böök et al., 2024). On the coast of British Columbia, they conducted a survey, and the results show that the mollusc population has decreased up to 80% since 1978 (Hankewich and Lessard, 2006). Due to ocean acidification, the food web would be changed, and the species would lose their habitat to live in which reduces the population density, and the people who are dependent on the mollusc would lose their food and employment (Newell, 2004). The population of the *Limacina helicina* is reduced in the polar ecosystem, and these changes will impact their ecosystem (Comeau et al., 2009). When the larval equilibrium gets disturbed because of ocean acidification, this causes an alteration in the adult population of the mollusc (Ross et al., 2011). Under ocean acidification, the mollusc species *Saccostrea glomerata* population is reduced, and the commercial production of these rock oysters is reduced because of the inappropriate biomineralisation process (Fitzer et al., 2019). The estuarine bivalve population will decreases when the mortality of the young ones increases due to the elevated carbon dioxide level in the water caused by anthropogenic activity (Guinotte and Fabry, 2008). The elevated level of carbon dioxide in the water has a direct negative impact on molluscs and the tolerance to the CO_2 level is different for different species i.e., species-specific (Kurihara, 2008).

Impacts on the Reproduction of Molluscs:

The reproductive life of the mollusc is broadly affected due to the changes in the seawater chemistry. The marine shelled mollusc had a wide range of cellular processes, and this organism is affected by the ocean acidification (Böök et al., 2024). This phylum includes two important classes: Bivalvia and the Gastropoda, which are especially sensitive to ocean acidification (Qian et al., 2024). When the oysters get overexposed to the ocean acidification during gametogenesis, the reproduction will be disturbed (Boulais et al., 2017). The sperm motility, fertilisation success rate and the qualities of the gamete are impacted when the extracellular pH is decreased (Boulais et al., 2018).

The distribution of the reproductive resources will be affected when the sex-specific growth, distribution of energy, and tissue regeneration are changed due to the ocean acidification (Padilla-Gamiño et al., 2022). All the life stages of the oysters are directly affected by the ocean acidification (Lemasson et al., 2017). The *Tritia reticulata* shows increased mortality when they are exposed to water with a lower pH level for only two days, and at the pH level of 7.5, they showed notorious expressions (Oliveria et al., 2020). Even when the larvae of the *C. gigas* and *Mytilus galloprovincialis* are treated with carbon dioxide, they form a convex hinge in their shell when reared at the pH of 7.8 and 1000 μ atm pCO_2, and this feature is used in the embryo toxicology bioassays to identify the irregular development of the veliger larva (His et al., 1997). When the parent *Saccostrea glomerata*, exposed during their reproductive state to the lower pH condition, their larvae show a greater performance in their physiology (Parker et al., 2010). The total number of post-fertilisation (18 hours) D-hinge oyster larvae is reduced when the female is exposed to the lower pH before their reproductive stage (Venkataraman et al., 2019). The gametes of the *C. virginica* exposed to lower pH and the result of

this experiment shows that the survival rate of the larvae is higher, but they show increased levels of defects, and the height of the shell is lessened (Clements et al., 2021).

Sea Level Fluctuations and Habitat Loss:

When the volume of the ocean increased and the melting of ice increased, these phenomena led to the cause of global sea level rise (Bellard et al., 2013). The tropical oceanic islands, which are located in the central Pacific affected by the Cenozoic sea level fluctuation, harmed the bivalve population's survival (Paulay, 1990). Climate change paved the way for the sea level rise; it disturbs the estuaries and their intertidal habitats (Dixon et al., 2023). Deforestation by humans caused the extinction of fauna (Richling and Bouchet, 2013). The beds of the shellfish and their habitats have been destroyed by overfishing, developments in the coastal areas, and pollution (Gibson et al., 2001). Most of the coastal marine ecosystems are facing habitat loss because of more human activities. The sea level fluctuations mostly affected the habitats in the soft sediments and the bivalves in the soft bottom compared to the bivalves in the hard bottom (Paulay, 1990). Due to the construction of the boardwalk bridge, people gained access to enter the subtropical mangrove forest; it disturbed the assemblage of molluscs and their habitat (Skilleter and Warren, 2000). There are 46 endemic land snail species recorded based on the details collected in the museum in Gambier Island, and the snails belong to the families Euconulidae, Endodontidae, Assimineidae, and Helicinidae (Bouchet and Abdou, 2003). The global sample of land snails was collected in 2015, and it shows that about 3000-5100 species of the mollusc have become extinct due to the destruction of their habitat and the impacts of climate change (Régnier et al., 2017). The cause of extinction and altered distribution of the species in the late Cenozoic is due to the occurrence of sea fluctuation (Harzhauser and Neubauer, 2021).

Economic Impacts

The commercial fisheries, particularly the calcifying shellfish species, are at a greater threat due to ocean acidification. The reduction in the harvests of commercially important species is caused by ocean acidification, and it directly affects humans, through the social and economic connections (Cooley and Doney, 2009). Ocean acidification will also affect the capture fisheries in the coastal environments (Narita et al., 2012). Shellfish aquaculture is affected due to climate change and also by the pollution caused by humans (Allison et al., 2011). The anthropogenic source of pollution is greater due to increased human population and coastal development, which results in the lower sanitary quality of nearshore waters, and the shellfish cultured in the water are not suitable for consumption (Langan, 2009). The major threats faced by the *conus* species under the risk of extinction are pollution and habitat loss due to the spillage of petrol and other developmental activities in the coastal regions (Peters et al., 2013). The ocean acidification caused by climate change poses a greater threat to the future bivalve aquaculture by affecting the carbonate mineral saturation level and disturbing the formation of the shell (Vaughn and Hoellein, 2018). Ocean acidification and sea warming are caused by the increasing greenhouse gas effects, and this has a greater effect on the economy of the Mediterranean Sea and poses threats to the mollusc habitats as well as endemic species in the sea (Campos Rodrigues, 2016). Due to over greenhouse gas emissions by human activity causes, more carbon dioxide levels in the marine ecosystem and this lead to the alteration in the marine ecosystem, which directly affects the production and supply of the marine resources, which also affects the economic values, and the population who depends on the marine resources is changed (Tisdell, 2015). The aquaculture of abalone is also affected by the ocean acidification, and some abalones grown in captive conditions show some resistance to the ocean acidification, and some are highly vulnerable to mortality (Swezey et al., 2020).

CONCLUSION

Climate change has a huge impact on both marine and freshwater ecosystems. Ocean acidification, salinity changes in the water, temperature fluctuations, and sea-level rise all have an impact on the physiology and behavior of species in the ecosystem. These environmental changes cause mollusc species to lose their habitats. The commercial output of shellfish, including molluscs, is being diminished. To mitigate the effects of climate change on molluscs, we must minimize greenhouse gas emissions, coastal pollution, and the usage of fossil fuels. Although we cannot

completely undo the consequences of climate change on molluscs, we may prevent them from occurring. The protection of mollusc habitat is critical. More research should be done to assess the mollusk's vulnerability to various effects of climate change. The mollusk's shell growth, habitat alteration, and species-specific susceptibility should all be investigated. We must raise public awareness about the need to restore mollusc habitat and develop conservation plans. To boost the country's economy, aquaculture should be conducted more frequently in order to raise yearly mollusc production. Molluscan populations must be protected for community and economic reasons. To protect the marine ecology, the effects of climate change on molluscs should be mitigated.

ACKNOWLEDGMENTS

The authors would like to express our sincere thanks to PG and Research Department of Zoology, Ethiraj College for Women (Autonomous), Chennai, for their constant encouragement.

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Table 1 Stressors and their Impact on Mollusc Species.

Stressor	mollusc	Impacts	Reference
Ocean acidification	*H. coccoradiata*	Causes adverse effects on this larva.	Parker et al., 2010
	M. angulata	The hardness and the rigidity of the cell are decreased.	Meng et al., 2018
	C. gigas	Shell growth is inhibited and shows morphological abnormalities.	Barros et al., 2013
	M. edulis	The fracture toughness of the mussel is reduced, and the formed shell is fragile.	Fitzer et al., 2015
Salinity	*D. trunculus*	At 16.7 psu the juveniles show higher resistance to low salinity with higher survival rates.	Reyes- Mart*ínez et al., 2020*
	P. canaliculata	When this species is exposed to 0-6 psu for 30 days, the survival rate is more than 72%, and they can tolerate salinity.	Qin et al., 2020
Salinity and Temperature	*C. plana*	At lower salinity the larvae were intolerant, but the survival rate is higher at 20-29°C.	Zimmerman and Pechenik, 1991
	M. leucophaeata	A 4 hour old embryo has more impact when compared to a 2 day old embryo.	Verween et al., 2007
Temperature	*O.bimaculoides*	Shows increased growth rate due to elevated temperature during their developmental phase.	Forsythe and Hanlon, 1988
	A. maculata	The spawning of the adults and the survival rate of the embryos are higher at 22°C.	Pires, 2012
Temperature and Photoperiod	*C. aspersum*	Lay eggs in long days at a temperature of 15 °C, and the activity ceases in a short day environment.	Enée et al., 1982
	A. californica	Lay more eggs in short days in warm water than in long days in warm water.	Wayne and Block, 1992

Low pH	*C. gigas*	The rate of D-hinge oyster is diminished.	Venkataraman et al., 2019
	C. virginica	Larval survival increased, more abnormal development occurred, and shell development was reduced.	Clements et al., 2021