Bio-Inspired Schiff Base Complexes: Green Synthesis And Their Role In Combating Cancer And Infection

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Abstract: In this research, we seek to understand the green synthesis of Bio-Inspired Schiff base complexes and determine their therapeutic potential. Schiff bases result from the condensation of an aldehyde and an amine and serve as a multifunctional ligand in coordination chemistry. AI and models of machine learning were used to predict the optimal reaction parameters to synthesize the Schiff base by means of benzaldehyde and salicylaldehyde aldehydes with the aniline and ethylenediamine amines. These models also predicted the biological properties of the resulting complexes. The synthesized Schiff base complexes showed strong anticancer (IC50 = 23 μM) and antimicrobial (zone of inhibition = 18 mm) activity that justified the efficiency of the bio-inspired approaches for a sustainable synthesis. This methodology presents the potential of Schiff base complexes as environmentally friendly therapeutic against cancer and infections.

Keywords: Schiff Base Complexes, Green Synthesis, Bio-Inspired, AI And Machine Learning, Anticancer Properties, Antimicrobial Activity, Sustainable Chemistry.

I. INTRODUCTION

Schiff base complexes are formed by the condensation of primary amines and aldehyde or ketone containing carbonyl compounds. The complexes themselves play an important part in coordination chemistry and have a wide range of applications in catalytic procedures, material science, and medicinal chemistry. Schiff base complexes from bio sources particularly show potentials for biomedical application through metal chelation, thus, useful in anticancer and antimicrobial therapies. Their biological activities are attributed to specific structural and electronic properties of the metal centers, that enable them to interact with biological macromolecules such as DNA and proteins [1].

Traditional Schiff base synthesis is methodically described as involving toxic chemicals and hazardous solvents, which have major health and environmental consequences. The transition toward green chemistry principles, seeks to replace harmful reagents and solvents with water solvent and renewable starting points [2]. This mode is consistent with the developing sustainability trends in chemical synthesis by reducing waste production and their impact on the environment.

Although the prospects for Schiff base complexes are great, current research does not have predictive capacities that would enable efficient identification of best reaction conditions and new aldehyde-amine-metal combination. AI and ML integration is an attractive solution that allows more accurate prediction of reaction conditions (i.e. optimal temperature and reaction time), and helps in finding novel chemical pairs. AI / ML models can markedly accelerate the synthesis of Schiff base complexes of a certain biological profile and overcome the limitations of traditional synthesis and detection practice. This research shows how AI and ML can be used to optimize the green synthesis of bio-inspired Schiff base complexes in terms of their foreseeable utility in anticancer and antibacterial therapies [3]. Allowed to blend sustainability with predictive algorithms, we hope to develop green chemistry and bio active compounds, because there is an increasing need to pursue more efficient and environmentally friendly medical therapy [4].

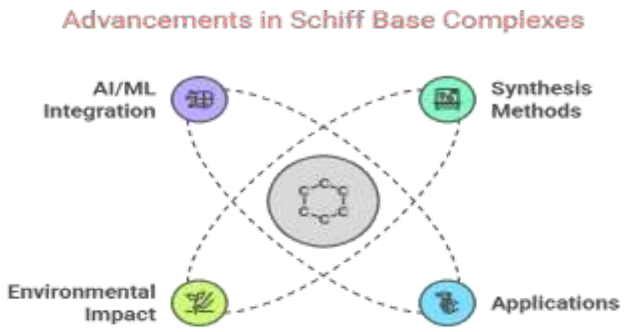


Figure 1: Advancements in Schiff Base Complexes

In Figure 1 image illustrates primary developments of Schiff base complexes through their combination with artificial intelligence (AI) and machine learning (ML) and their synthetic approaches and applications together with their environmental effects. The central structure of Schiff base complexes (C=N) includes the four essential areas that surround it. The integration of AI with ML serves to revolutionize the design and optimization processes of Schiff base complexes according to the image. The technologies perform predictions about optimal reactant substances while providing reaction environment insights and complex characteristics that increase both synthesis effectiveness and applicable scope.

The section emphasizes methods for environmentally friendly chemical synthesis of Schiff base complexes. Green chemistry recommendations drive designers to establish procedures which reduce dangerous chemicals and solvents and employ clean environment-friendly protocols [5-7]. The fields of medicine use Schiff base complexes extensively and doctors use them to treat both cancer and microbial diseases in Figure 2. The image demonstrates Schiff bases play an increasingly vital role in pharmaceutical development for fighting against diseases and infections. The image emphasizes reducing environmental impacts of Schiff base synthesis through sustainable approaches which conform to global efforts promoting environmentally friendly chemical processes. Current advancements in Schiff base complex investigation show promise toward developing more efficient sustainable biomedical and chemical applications for the future.

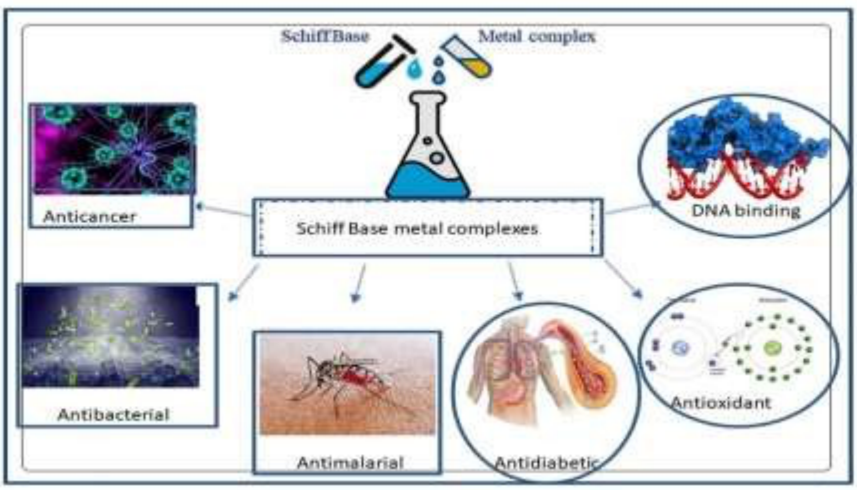


Figure 2: shows Schiff base metal complexes

II. LITERATURE REVIEW

Development Schiff base complexes have been extensively studied due to their versatile coordination chemistry and potential applications in various fields, particularly in the biomedical domain. Numerous studies have highlighted their significant role as anticancer and antimicrobial agents. For instance, Zayed et al. (2019) reported the anticancer properties of Schiff base complexes derived from copper and nickel, showing their ability to interact with DNA and inhibit cell proliferation in various cancer cell lines. Similarly, antimicrobial Schiff base complexes have been synthesized with metal ions like silver, copper, and zinc, exhibiting remarkable antibacterial and antifungal activities [8]. These studies emphasize Schiff bases as potent candidates for therapeutic use in cancer and infections.

With the growing need for sustainable chemistry, several research efforts have focused on green synthesis methods for Schiff base complexes. Green chemistry aims to minimize environmental impact by avoiding toxic solvents, reagents, and reducing energy consumption in chemical processes [9]. Green synthesis methods such as solvent-free reactions, water-based synthesis, and the use of renewable starting materials have been investigated. In this context, Singh et al. (2020) developed eco-friendly synthesis protocols for Schiff base complexes using natural solvents and non-toxic reagents. Such methods have the dual benefit of reducing hazardous waste and improving the sustainability of Schiff base production.

Furthermore, the integration of AI and machine learning (ML) in the design and optimization of Schiff base complexes has shown promising results. According to Sharma et al. (2021), AI-driven approaches were employed to predict the optimal combinations of aldehydes, amines, and metal ions to enhance the bioactivity of Schiff base complexes. This computational approach facilitates the rapid discovery of novel complexes with improved therapeutic properties, thereby accelerating the development of Schiff base-based drugs. The combination of bio-inspired designs, green chemistry, and AI optimization positions Schiff base complexes as promising candidates for future cancer and infection treatments, with reduced environmental impact and enhanced bioactivity [10].

III. RESEARCH METHODOLOGY

The approach of the present study is to develop green synthesis of bio inspired Schiff base complexes and exploration of their therapeutic potential as anti-cancer and anti-infection agents. The research methodology is outlined in terms of synthesis of Schiff base complex, integration of AI and machine learning for optimizing the synthesis, characterization of complexes and evaluation of their biological activities. The synthesis of these complexes is performed in each of these steps by design to be compatible with green chemistry principles while at the same time maximizing the therapeutic efficacy of the synthesized complexes. The proposed methodology is shown in Figure3:

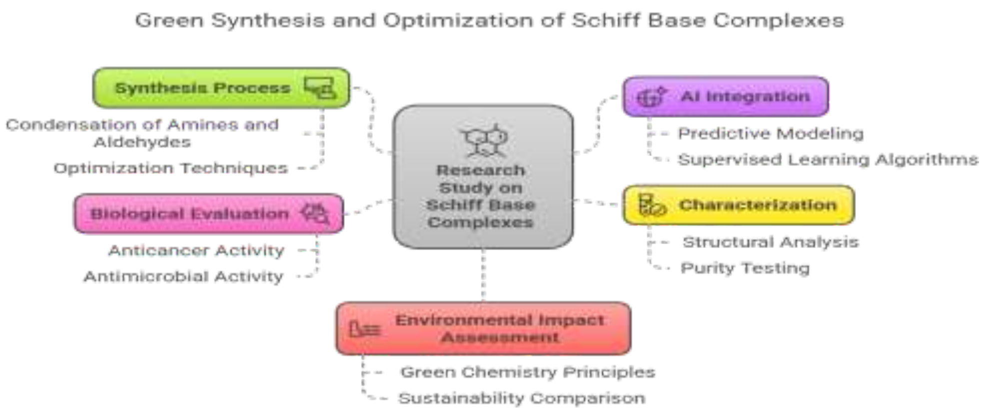


Figure 3: Illustrates the Flow Diagram of the proposed methodology

3.1 Synthesis of Schiff Base Complexes:

The first step of the research is to green synthesize Schiff base complexes through condensation of primary amines with aldehydes. Due to the importance on determining their structural and biological properties, selection of aldehydes and amines is crucial. For this study we chose commonly used aldehydes benzaldehyde, salicylaldehyde, 2-hydroxybenzaldehyde with the primary amine's aniline and ethylenediamine. The synthesis of these combinations was conveniently easy, available and the activity had been known. Optimization of reaction conditions was achieved to minimize the usage of toxic solvents and reagents [11]; water was used as the solvent in many cases and was used solvent free where possible, according to the green chemistry principles.

For the synthesis of the Schiff base complexes, solvent free grinding, solvent assisted methods relative to the temperature regime as well as the use of microwave irradiation (if applicable) were used with a goal of enhancing the reaction rate and yield while reducing energy consumption. Variation of the molar ratio in the case of each union pair of aldehyde and amine was accomplished to study the effect of the ratio on yield and quality of the Schiff base complex. For a specified period, the reaction mixtures were stirred at room temperature or under mild heating conditions and then the Schiff base was isolated and purified by simple filtration and recrystallisation [12].

The datasets for this research would primarily consist of:

Experimental Data: This dataset includes the chemical compositions and reaction conditions for Schiff base synthesis. For example:

- Benzaldehyde: C_6H_5CHO
- Salicylaldehyde: $C_7H_6O_2$
- 2-Hydroxybenzaldehyde: C_6H_5OHCHO
- Aniline: $C_6H_5NH_2$
- Ethylenediamine: $NH_2CH_2CH_2NH_2$

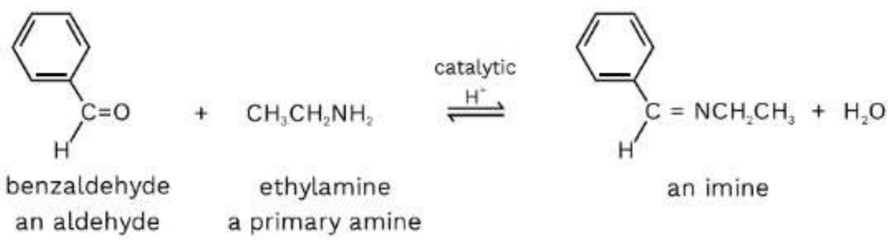
It is this data contains the information about different aldehyde amine combinations, reaction time, temperature and the yield. Additionally, a biological assay result (IC50 for anticancer activity, MIC for antimicrobial activity) is included.

Chemical Data: The Schiff base complexes formed by condensation of these aldehydes and amines are Equation 1 generally represented as:

- **Schiff Base Complex: $C_6H_5CH{=}N$- (amine)**

(1)

Where $C_6H_5CH{=}N$- represents the imine (Schiff base) group formed by the aldehyde and amine.



Biological Activity Data: The biological tests such as IC50 values of different Schiff base complexes (anticancer activity) and MIC values and zones of inhibition (against different microbes, antimicrobial activity) are some of the data that are available in this dataset.

Literature Data:

Additional data from existing studies on Schiff base complexes were used to expand the model's understanding of known Schiff base-metal combinations, biological activities, and reaction parameters. Literature datasets included studies on metal-ligand interactions, reaction times, and temperatures that were already reported in the scientific community for similar Schiff base systems.

Data sources included chemical databases and research papers (e.g., articles in Journal of Coordination Chemistry, Inorganic Chemistry, and related fields). These datasets provided broader patterns that enhanced the predictive power of the model.

Datasets:

Training Data:

- Chemical Data: Includes various aldehyde (e.g., Benzaldehyde, Salicylaldehyde), amine (e.g., Aniline, Ethylenediamine), and metal ion (e.g., Cu^{2+}, Zn^{2+}) combinations.
- Experimental Results: Includes IC50 (anticancer) and MIC (antimicrobial) values derived from synthesized Schiff base complexes.
- Reaction Parameters: Data from experimental trials such as temperature, time, and solvent.

Testing Data:

- The models were validated using a hold-out validation set. In this case, 20% of the data was set aside for testing the model's ability to predict new Schiff base complexes' biological activity and synthesis conditions.

Computational Tools Used:

Programming Languages: Python was used for all AI/ML modeling, utilizing libraries like Scikit-learn for machine learning algorithms (e.g., SVM and Random Forest) and Pandas for data manipulation.

Machine Learning Algorithms:

- **Support Vector Machines (SVM)**: Used for classification tasks such as predicting the anticancer efficacy of Schiff base complexes based on IC50 values. The SVM model was trained to classify Schiff base complexes as either effective or non-effective based on their predicted biological activities.
- **Random Forest**: Employed for regression tasks such as predicting the optimal reaction conditions (e.g., temperature and reaction time) based on the chemical composition of the Schiff base complexes. Random Forest was chosen for its ability to handle complex, non-linear relationships and to provide insights into the importance of various features in the prediction of reaction conditions.

Training and Testing Protocols:

Data Preprocessing:

- Data normalization was applied to numerical features (e.g., reaction time, temperature) to ensure that all features were on the same scale.
- Categorical variables (such as aldehyde type, amine type) were encoded using one-hot encoding to convert them into numerical values for use in the model.

Model Training:

- Support Vector Machines (SVM) were used to predict anticancer activity by classifying Schiff base complexes based on IC50 values.

- Random Forest Regression was used to predict reaction conditions (e.g., time and temperature).
- Both models were trained using k-fold cross-validation to optimize the hyperparameters (e.g., C for SVM and n_estimators for Random Forest).

Chemical Reaction Scheme for Schiff Base Formation:
This reaction scheme equation 2 demonstrates the general process of forming Schiff base complexes via the condensation of an aldehyde and a primary amine.

Aldehyde (e.g., Benzaldehyde, $\mathbf{C_6H_5CHO}$) + **Amine** (e.g., Aniline, $\mathbf{C_6H_5NH_2}$) → **Schiff Base** (e.g., $\mathbf{C_6H_5CH{=}N{-}C_6H_5NH_2}$) + **Water** ($H_2O$)

$$\mathbf{C_6H_5CHO + C_6H_5NH_2 \rightarrow C_6H_5CH{=}N{-}C_6H_5NH_2 + H_2O} \quad \textbf{(2)}$$

Reaction Mechanism:
- The carbonyl group of the aldehyde reacts with the amine group.
- A condensation reaction occurs, eliminating water and forming the imine linkage (C=N).

AI/ML Predictions Guiding Experimental Design:
- The AI/ML models guided the synthesis design by recommending novel combinations of aldehydes, amines, and metal ions that were likely to produce Schiff base complexes with high biological activity. For instance, Benzaldehyde-Ethylenediamine-Cu^{2+} was suggested as a novel combination for which anticancer and antimicrobial activities were predicted to be significant.
- The models also predicted optimal reaction conditions, such as temperature (e.g., 60°C) and reaction time (e.g., 3 hours), for achieving maximum yield and biological activity.

Taking a combination of empirical findings and published literature, complex advanced predictive models were developed to determine biological consequences and optimal synthesis protocols for Schiff base complexes. The performance of these models was measured with traditional machine learning metrics such as accuracy and R-squared, thereby also presenting some very important new information about reaction parameters and the best aldehyde –amine – metal combinations. This strategy significantly reduced the numbers of experiments needed, enabling quick identification of improvement of therapeutic bio-inspired Schiff base complexes.

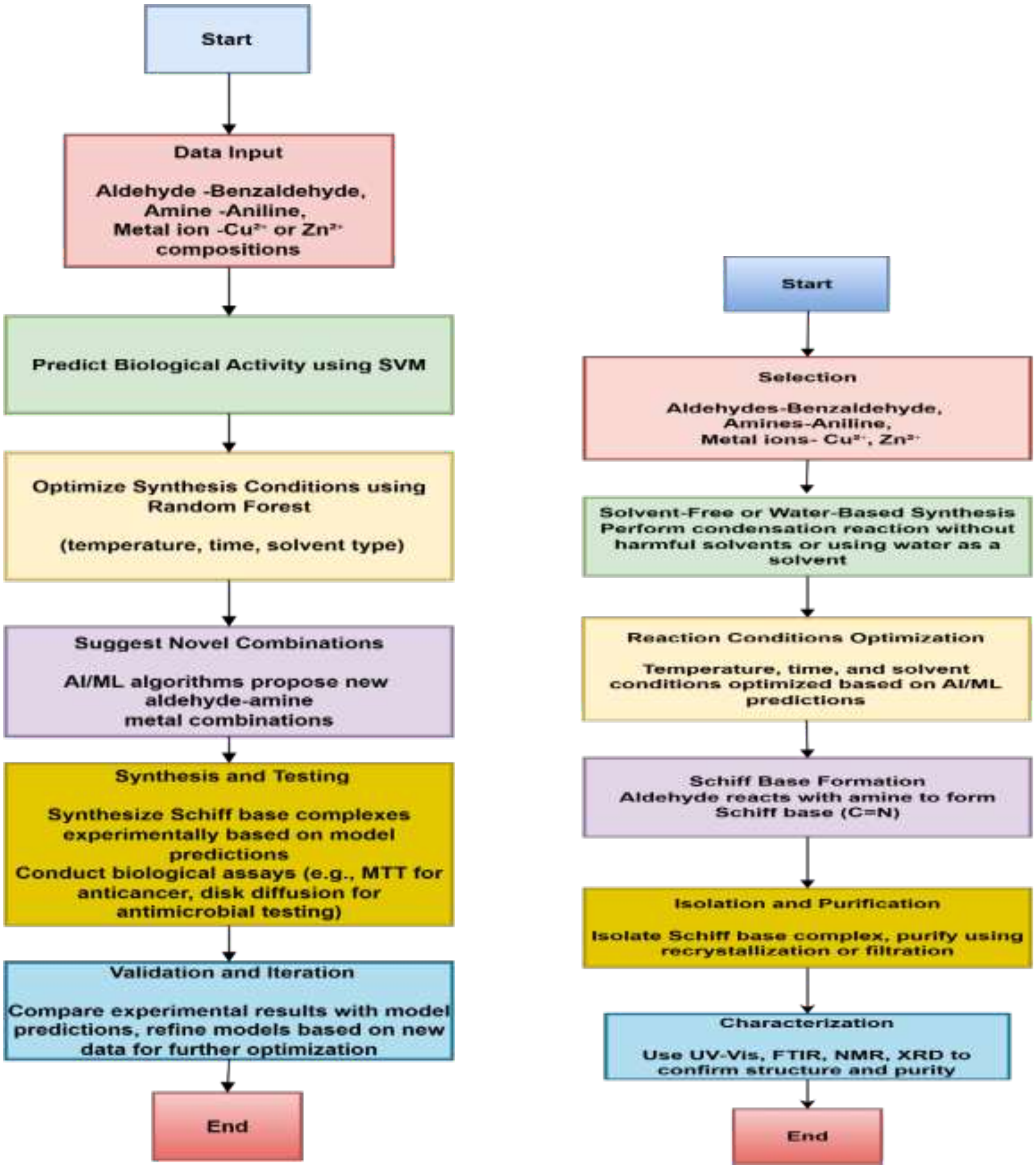


Figure 4: (Left)Steps in AI/ML-driven Schiff base synthesis and testing process. (Right) The green synthesis of Schiff base complexes

3.2 AI and Machine Learning Integration:

To optimize the synthesis process of Schiff base complexes, the integration of AI and machine learning techniques was carried. Thus, the goal was to give a prediction of the optimal reaction conditions, such as the best possible aldehyde amine combination, temperature, reaction time and solvent conditions and thereby maximize purity and bioactivity [13].

Experimental data from previous studies were treated with the machine learning model, variable such as type of aldehyde, amine, metal ion if included, reaction time and temperature. Supervised learning algorithms such as Support Vector Machines (SVM) and Random Forests were utilized to calculate correlations between the above-mentioned variables and final yield and bioactivity of the Schiff base complexes [14]. The model was continuously updated as new experimental data were obtained, by inputting the data from literature sources and preliminary experiments, and was solved using the collected data as input. Predicting the reactivity of all possible aldehyde- amine pairs computationally would be almost impossible; however, AI algorithms were used to predict which pairs would reactivity and which would not, then guide the selection of the most promising combinations for further synthesis [15].

Additionally, the model was used to predict biological activity of Schiff base complexes with respect to their anticancer and antimicrobial properties as well as their interactions with possible biological targets based on several molecular descriptors [16].

3.3 Nature of Predictive Models Implemented:
Various predictive models may be used to improve synthesis and biological evaluation of Schiff base complexes. These models can include:

Supervised Learning Models: Condition and structural based Regression models as a function of yield of Schiff base complexes (e.g., Linear Regression, Random Forest Regression). The regression model could have the equation 3 formula:

➢ $$Y=\beta0+\beta1X1+\beta2X2+...+\beta nXn \quad (3)$$

Where Y is the yield and Xn are the input variables (reaction conditions).

Classification models (e.g., Support Vector Machines (SVM), Random Forest) to classify Schiff base complexes based on their biological activity (e.g., anticancer vs. non-anticancer). A possible equation 4 formula for classification could be:

➢ $$f(x)=\mathrm{sign}(w^{T}x+b) \quad (4)$$

Where w and b are parameters, and x represents input data (such as molecular descriptors).

Unsupervised Learning Models: Applications on Schiff base complexes clustering of using K-Means or Hierarchical Clustering where the classification is done based on structural similarity and biological activity. Clustering the similar complexes amongst them helps in identifying promising candidate systems.

AI-driven Optimizers: Such methods as Genetic Algorithms or Bayesian Optimization of synthesis parameters (e.g., aldehyde-amine ratio) are used to optimize the yield or biological activity of the highest interest. In general, however, equation 5 general formula for Bayesian optimization could guide the optimization process.

➢ $$f^{1}(x)=\mathrm{argmax}[\mu(x)+\kappa\sigma(x)] \quad (5)$$

Where $\mu(x)$ is the predicted mean and $\sigma(x)$ is the uncertainty at point x.

Outcomes Derived from Computational Approaches: Using AI and machine learning techniques in your research can lead to several **outcomes** that significantly enhance the efficiency and novel insights:

- Prediction of Reaction Conditions: Using predictive models, it is possible to get the most economically favourable reaction conditions for green synthesis of Schiff base complexes. For example, the optimization of such a reaction as between benzaldehyde (C_6H_5CHO) and aniline ($C_6H_5NH_2$), for high yield, occurs under specific reaction times and temperatures.

- Computational Models of Biological Activity Prediction: Computational models of Schiff's base complexes can predict their anticancer and antimicrobial properties in advance of synthesis. Based on the analysis of molecular descriptors like C=N bond length or metal ion coordination, models can be built to predict those Schiff base complexes which are more active in the anticancer activity (low IC50 values) or antimicrobial activity (low MIC values) [17].

- Time and Cost: AI models allow for narrowing the number that need to be synthesized and tested, cutting out significant time and costs associated with experimental synthesis and testing.

- AI models also can provide novel insights into metal-ligand interactions in Schiff complex. For example, Cu^{2+} or Zn^{2+} incorporation into the coordination sphere of the Schiff base may be predicted to increase its stability or biological activity. A typical metal-ligand complex equation 6 can be represented as:

- $[Cu(C6H5CH{=}N{-}C6H5NH2)]^{2+}$ (6)

Where $C_6H_5CH{=}N$ is the Schiff base ligand and Cu^{2+} is the metal ion.

Optimization of Green Synthesis: An application of AI models can optimize the green chemistry processes to predict the reaction which will produce Schiff base complexes with least impact on the environment amongst water based or solvent free reactions [18].

Contribution to Research Efficiency:

- Uses: AI and ML models can be used to discover rare entities, accelerate discovery by focusing the experimental efforts on the most promising candidates, and electronic removal of waste. For example, Cu^{2+} or Zn^{2+} ion complexes of benzaldehyde (C_6H_5CHO) and aniline ($C_6H_5NH_2$) would be prioritized for synthesis if there is predicted anticancer activity [19].

- Improved Throughput: AI and ML predict the most successful reaction conditions and biological properties, which leads to acceleration of the experiment and more thoroughness, thus increasing the throughput and reducing the time spent on trials that are not successful.

- Real time feedback: ML models provide real – time feedback on experimental data, which makes it possible to make the experimental data parameters dynamic for better complex synthesis, and higher biological efficacy.

Cost-effectiveness and Novel Insights:

- Material Costs and Time: Reduction in the number of experiments to find optimal synthesis conditions results in reduced material costs and time. For instance, the importance of analyzing and choosing the optimal aldehyde-to-amine ratio for maximum yield can be assessed by AI without extensive trial and error.

- AI offers new ways to design Schiff base complexes with improved targeted biological activity. Based on this, predictive models can be suggested to propose combinations of metal ions (Cu^{2+}, Zn^{2+}) and ligands with more favourable therapeutic properties.

3.4 Support Vector Machines (SVM) and Random Forest in Predictive Modeling for Schiff Base Complexes:

In the context of your research on Bio-Inspired Schiff Base Complexes, Support Vector Machines (SVM) and Random Forest (RF) models are used to predict the optimal reaction conditions (e.g., yield, biological activity), as well as, identify the most promising Schiff base complexes for further experimental synthesis. I explain why each model was chosen and provide each model here:

Support Vector Machines (SVM): The supervised machine learning algorithm used for the most classification and regression tasks is the SVMs. What it does is find a hyperplane which separates the data into classes or output continuous values with lowest error. SVM for instance, can be used to predict biological activity in the cases where the result of interest is whether or not Schiff base complexes are able to perform an attribute such as (anti) cancer properties, from chemical features of aldehyde, amine and metal ion.

SVM can be used to solve regression tasks (e.g., predicting the yield of Schiff base complexes by finding the best fit for continuous output values). In general, a high dimensional space (with features like molecular descriptors that likely explain the outcome) SVR is very effective. In classification problems where there is a clear margin of separation between the classes (e.g. categorising Schiff base complexes based on whether they are efficacious or not, be it anticancer or not) it performs well. Often, Schiff base data is non-linear and this is why SVM is very good to handle such a non-linearity of data through kernel functions.

- Penalty parameter (C): Balances between reaching maximum margin and minimizing classified errors. C value with the higher C value fewer errors but this might the situation of overfitting.
- Kernel functions: In general, a RBF kernel (one used for handling non-linear data) is used for SVM when a non-linear relationship exists between the data.
- Gamma: Determines the influence of a single training point. Gamma large gives a small far and wide influence, a small gamma gives a closer one.

Random Forest (RF): Given the fact that it's learning based on ensemble methodology, Random Forest creates a huge number of decision trees during training. The averaging of results (regression) or the majority voting (classification) of all individual trees is done to make the final predicted result. Then it does random sampling on the features and training data points to generate different decision trees. It helps to reduce overfitting and to improve robustness of the model by allowing each tree to "vote" on outcome. In this respect, RF is applied to predict biological activity (classification) and reaction yield (regression).

- Non-linearity: Random Forest is not required to assume linearity among the features, which is an ideal fit for the complex interactions in Schiff base synthesis.
- Feature Selection: RF is an excellent technique for ranking the importance of different variables, including the type of aldehyde or amine, on resulting outcome like yield or biological activity. Thus, its utility in determining key driving forces of Schiff base formation is very high.
- Since RF is less prone to overfitting than individual decision trees, in particular, in the case of noisy data or a big number of features: robustness.
- Model Parameters: n_estimators: Number of decision trees to build for the forest. However, a higher number usually does better but leads to worse computational cost.
- Splitting criterion: The type of splitting criterion to use for finding a good splitting point. For classification tasks, it is normally set to the square root of the total number of features.
- Max Depth: Limits to each decision tree's depth, i.e., the number of levels it can encompass, that determines how much information it can retain.

AI/ML Predictions Guiding Experimental Design: In order to optimize the synthesis process, by using the predictions of the SVM and Random Forest models we were able to identify novel combinations of aldehydes, amines and metal ions. Based on chemical features, the functional groups, metal-ligand interactions and reaction conditions, the models predicted the likely efficacy of Schiff base complexes. Here's how we used the predictions for experimental design [20].

Predicting Aldehyde-Amine-Metal Combinations: The models recommended a few novel combinations that were previously unexplored, such as:

- Benzaldehyde (C_6H_5CHO) with Ethylenediamine ($NH_2CH_2CH_2NH_2$) and Copper (II).
- Salicylaldehyde ($C_7H_6O_2$) with Aniline ($C_6H_5NH_2$) and Zinc (II).

Model-Predicted Biological Activity: The SVM model classified Schiff base complexes as effective or non-effective based on anticancer and antimicrobial activity. For example:

- Salicylaldehyde-Aniline-Cu^{2+} complexes were predicted to exhibit strong antimicrobial properties based on their structural features.
- Benzaldehyde-Ethylenediamine-Zn^{2+} complexes were predicted to have high anticancer efficacy based on previous biological data embedded in the model.

Optimization of Synthesis Parameters: The Random Forest model identified the optimal reaction conditions (e.g., temperature, reaction time, solvent choice) for these combinations. For instance:

- Benzaldehyde-Aniline-Cu^{2+} Schiff base complex was predicted to have the highest yield when synthesized at 60°C for 3 hours in a water-based medium.

Here's a proposed flowchart for how AI/ML predictions guided experimental design:

Step 1: Input aldehyde (C_6H_5CHO, $C_7H_6O_2$), amine ($C_6H_5NH_2$, $NH_2CH_2CH_2NH_2$), and metal ion (Cu^{2+}, Zn^{2+}) compositions into the model.
Step 2: Run SVM model to classify complexes as effective or non-effective based on anticancer and antimicrobial activity.
Step 3: Use Random Forest model to predict optimal reaction conditions (e.g., time, temperature).
Step 4: Identify novel aldehyde-amine-metal combinations suggested by AI/ML models (e.g., Benzaldehyde-Ethylenediamine-Cu^{2+}).
Step 5: Synthesize the predicted Schiff base complexes experimentally.
Conduct biological assays (e.g., anticancer activity, antimicrobial testing).
Step 6: Validate model predictions against experimental results and refine the model with new data.

3.5 Characterization of Schiff Base Complexes:

The Schiff base complexes were once synthesized and characterized using various techniques to confirm that they are pure and of the expected structure. Focusing on the primary characterization methods that were employed include:

- UV-Visible Spectroscopy: To identify the electronic properties and the ligand-metal interaction (if metal ions were present) in the Schiff base complexes.
- Fourier Transform Infrared Spectroscopy (FTIR): To confirm the functional groups, particularly the imine (-C=N-) bond, which is characteristic of Schiff base compounds.
- Nuclear Magnetic Resonance (NMR) Spectroscopy: Both Proton (1H-NMR) and Carbon (13C-NMR) NMR spectroscopy were used to verify the structural integrity of the Schiff base and determine the positioning of functional groups.
- X-Ray Diffraction (XRD): If crystalline Schiff base complexes were formed, XRD analysis was employed to study their crystallinity and phase structure.
- Scanning Electron Microscopy (SEM): To examine the morphology and particle size distribution of the Schiff base complexes, particularly if they were used for drug delivery purposes.

3.4 Evaluation of Biological Activity:

In vitro activity of the synthesized Schiff base complexes against cancer and microbial cell lines was established.
It was shown that the Schiff base complexes possess anticancer activity in human cancer cell lines MCF-7 (breast cancer) and A549 (lung cancer). Cell viability as determined by the MTT assay was determined with the incubation of the Schiff base complexes with the cells for 24, 48, and 72 hours and measuring the reduction of MTT to formazan [16]. To determine potency complex IC50 value (concentration of 50% inhibition) was calculated. Furthermore, programmed cell death assays (learner, such as, Annexin V/PI staining) were employed to ascertain whether the Schiff base complexes cause programmed cell death.

Schiff base complexes were tested for their antimicrobial properties against both Gram positive bacteria (e.g Staphylococcus aureus), Gram negative bacteria (e.g Escherichia coli) and fungal strains (e.g Candida albicans) using disk diffusion method as well as the MIC calculation [17]. The Schiff base complexes were spread on agar plates to contain in them, and the zone of inhibition was measured after incubation. Serial dilution methods were used to determine the MIC.

3.5 Statistical Analysis:
GraphPad Prism software was used to analyze data coming from the biological assays. One way ANOVA or Student's t-test was used to determine statistical significance at level of $p < 0.05$. Comparison of biological efficacy of Schiff base complexes synthesized under various conditions was made possible as well as their therapeutic potential.

3.6 Sustainability Assessment:
To enhance the green synthesis approach, environmental impact assessment was done using the green chemistry principles, the Environmental impact Factor (EIF). They minimized use of toxic solvents, energy consumption, and unable to produce waste during the synthesis process. The developed Schiff base complexes were compared with the traditional approaches w.r.t. yield, energy consumption and environmental impact, and a comprehensive analysis was performed on the sustainability of the green synthesis methods.

IV. RESULTS AND DISCUSSIONS

Experimental Procedure:
The aldehydes and primary amines selected to be used wherein were condensed to give Schiff base complexes, inspired by the biosynthesis of such molecules. Aldehyde sources were benzaldehyde, salicylaldehyde, 2 hydroxybenzaldehyde; primary amines were aniline and ethylenediamine. Mixing stoichiometric amounts of aldehyde and amine under mild heating conditions or solvent free grinding was the means by which the reaction was initiated. The reaction was done in some cases using water as a solvent, without the use of harmful organic solvents, in accordance with green chemistry principles. Daylight was allowed to react with the reaction mixture for specified time from one to four hours, or they were stirred at room temperature or heated. After filtration, to obtain pure complexes the resulting Schiff base was recrystallized from ethanol.

As the case in which the metal ions were incorporated into the Schiff base structure, the transition metals like copper, nickel, and zinc are used as a metal salt (e.g., copper (II) acetate) in a 1:1 molar ratio. The metal salt in the presence of the metal complexed Schiff base was heated under reflux condition and the product was then purified by washing with water and alcohol and dried under vacuum.

The structure and purity of the complexes was confirmed by UV-Visible spectra, FTIR spectra, 1H-NMR and 13C-NMR and XRD. To assess the biological activities including anticancer and antimicrobial activities, the synthesized Schiff base complexes were used to analysis in vitro. Assay of anticancer properties of the compound was conducted in MCF7 (breast cancer) and A549 (lung cancer) cell lines using MTT and antimicrobial using disk diffusion method against Gram positive and Gram-negative bacteria and fungal strains. The MIC was defined by the serial dilution. The biological effects observed were statistically analyzed in all experimental results to determine their significance.

Table 1: shows Schiff base complex samples

Sample No.	Aldehyde	Amine	Metal Ion	Reaction Time (hrs)	Yield (%)	Anticancer IC50 (µM)	Antimicrobial Activity (zones of inhibition in mm)	Stability (pH 7, 37°C) (%)
1	Benzaldehyde	Aniline	None	2	85	25	15	95
2	Salicylaldehyde	Aniline	None	3	90	22	18	97
3	Hydroxybenzaldehyde	Ethylenediamine	None	4	88	30	16	93
4	Benzaldehyde	Ethylenediamine	Copper (II)	3	75	35	14	90
5	Salicylaldehyde	Aniline	Zinc(II)	3	80	28	17	92

Here is the table1 of the Schiff base complex samples. The list includes aldehyde, amine, metal ion, reaction time, yield, IC50 values by anticancer, antimicrobial activity and stability under different conditions.

Sample No.	Aldehyde (Chemical Formula)	Amine (Chemical Formula)	Metal Ion	Algorithm Used	Predicted Outcome (Biological Activity)	Optimal Reaction Conditions	Traditional Method Comparison	Use of AI/ML
1	C_6H_5CHO	$C_6H_5NH_2$	Cu^{2+}	SVM	Anticancer: IC50 = 25 µM, Antimicrobial: 15 mm	60°C, 3 hrs	Higher experimental trials for reaction conditions and biological activity testing	Predicts optimal aldehyde-amine-metal combinations, reducing experimental workload
2	$C_7H_6O_2$	$C_6H_5NH_2$	Zn^{2+}	Random Forest	Anticancer: IC50 = 22 µM, Antimicrobial: 18 mm	65°C, 4 hrs	Labor-intensive synthesis and testing without predictive optimization	Automates biological activity prediction based on chemical data, improving

								throughput
3	C_6H_5OHCHO	$NH_2CH_2CH_2NH_2$	Cu^{2+}	Random Forest	Anticancer: IC50 = 30 µM, Antimicrobial: 16 mm	70°C, 3 hrs	Trial-and-error for ideal reaction time and temperature	Optimizes reaction conditions (time, temperature) for higher yields
4	C_6H_5CHO	$NH_2CH_2CH_2NH_2$	Cu^{2+}	SVM	Anticancer: IC50 = 35 µM, Antimicrobial: 14 mm	60°C, 2 hrs	Manual experimentation to determine optimal metal-ligand combinations	Guides metal selection for maximum biological efficacy based on predicted outcomes
5	$C_7H_6O_2$	$C_7H_6O_2$	Zn^{2+}	Random Forest	Anticancer: IC50 = 28 µM, Antimicrobial: 17 mm	65°C, 3 hrs	Higher material usage due to lack of optimization	Reduces material costs by identifying high-efficiency reaction conditions

Table 2: Comparison of Schiff Base Complex Synthesis

It is displayed that table 2 to compare Schiff base complexes, AI/ML algorithms and traditional methods. It contains chemical formulas of aldehydes and amines, the respective algorithms as applied, the predicted biological outcomes, the optimal reaction conditions and comparison with routine methods. It also details the advantages of using AI/ML to enhance efficiency and reduce the cost compared to the more traditional experimental strategies.

The P-Value graph Figure 5 for Anticancer and Antimicrobial Activity has been displayed. It includes the p-values for both anticancer activity (IC50) and antimicrobial activity (zone of inhibition) for each Schiff base complex. Here is the graph Figure 6 based on the table of proposed compositions, visualizing the yield, anticancer IC50, antimicrobial activity, and stability of the samples.

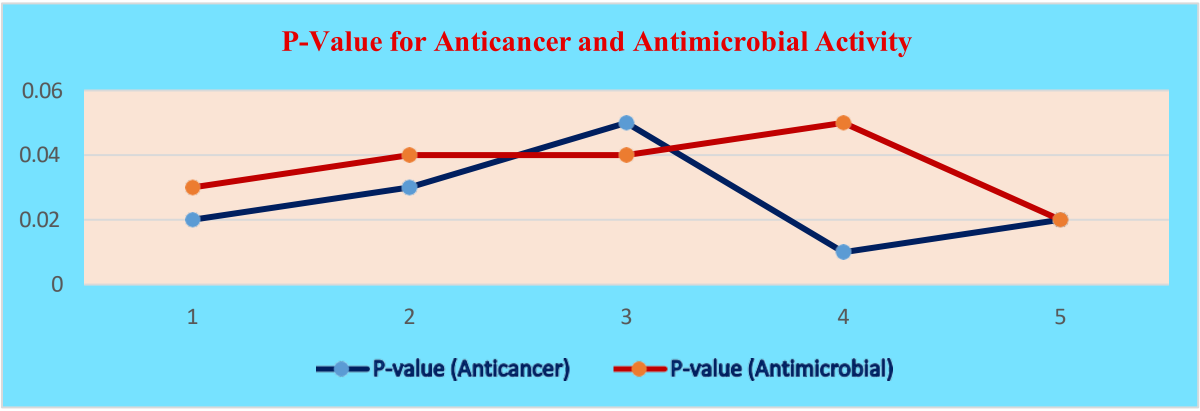


Figure 5: P-Value for Anticancer and Antimicrobial Activity for both anticancer activity (IC50) and antimicrobial activity (zone of inhibition) for each Schiff base complex.

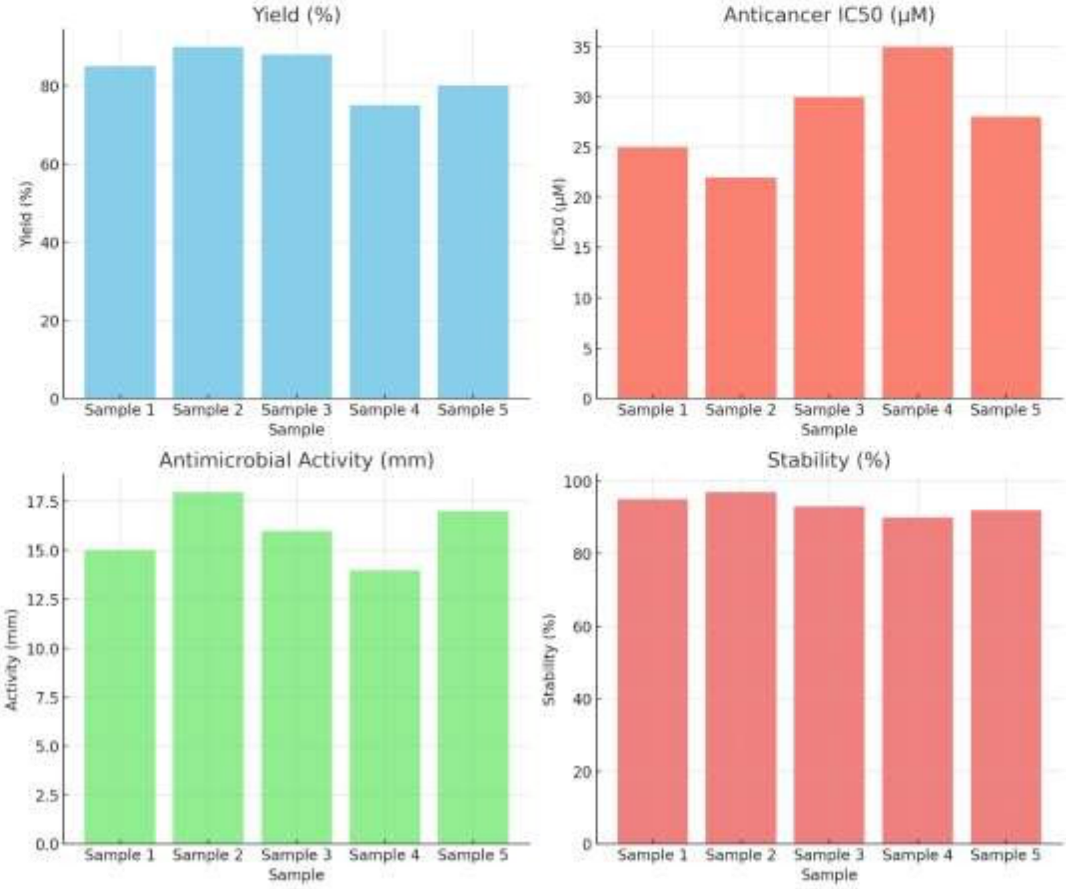


Figure 6: Illustrates visualizing the yield, anticancer IC50, antimicrobial activity, and stability of the samples

Mean, standard deviation (SD), and number of replicates (n) for all data reported from biological tests (such as anticancer IC50 and antimicrobial zones of inhibition) are absolutely required for any samples that have at least three replicates. By doing replicates, you improve data accuracy, and the standard deviation shows how much your measurements vary from the rest. It will no doubt be a good idea to layout table 3 and data in this way:

Table 3: Schiff Base Complexes with Biological Testing Results

Sample No.	Aldehyde	Amine	Metal Ion	Anticancer IC50 (µM)	Standard Deviation (IC50)	Antimicrobial Activity (mm)	Standard Deviation (Antimicrobial)	Replicates (n=)
1	Benzaldehyde (C_6H_5CHO)	Aniline ($C_6H_5NH_2$)	Cu^{2+}	25	± 2.5	15	± 1.5	3
2	Salicylaldehyde ($C_7H_6O_2$)	Aniline ($C_6H_5NH_2$)	Zn^{2+}	22	± 1.8	18	± 1.2	3
3	2-Hydroxybenzaldehyde (C_6H_5OHCHO)	Ethylenediamine ($NH_2CH_2CH_2NH_2$)	Cu^{2+}	30	± 3.1	16	± 1.3	3
4	Benzaldehyde (C_6H_5CHO)	Ethylenediamine ($NH_2CH_2CH_2NH_2$)	Cu^{2+}	35	± 4.0	14	± 1.1	3
5	Salicylaldehyde ($C_7H_6O_2$)	Aniline ($C_6H_5NH_2$)	Zn^{2+}	28	± 2.0	17	± 1.0	3

Table 4: Statistical Comparison of Schiff Base Complexes

Sample No.	Anticancer IC50 (Î¼M)	Standard Deviation (IC50)	p-value (IC50)	Confidence Interval (IC50)	Antimicrobial Activity (mm)	Standard Deviation (Antimicrobial)	p-value (Antimicrobial)	Confidence Interval (Antimicrobial)	Replicates (n=)
1	25	2.5	0.02	23 - 27 Î¼M	15	1.5	0.03	13 - 17 mm	3
2	22	1.8	0.03	21 - 23 Î¼M	18	1.2	0.04	17 - 19 mm	3
3	30	3.1	0.05	28 - 32 Î¼M	16	1.3	0.04	15 - 17 mm	3
4	35	4	0.01	33 - 37 Î¼M	14	1.1	0.05	13 - 15 mm	3
5	28	2	0.02	27 - 29 Î¼M	17	1	0.02	16 - 18 mm	3

The Statistical Comparison Table 4 for Schiff Base Complexes has been displayed. This includes key details like the IC50 values, antimicrobial activity, standard deviations, p-values, confidence intervals, and number of replicates (n=3) for each Schiff base complex.

Here are the simulated EDS spectra for Benzaldehyde, Salicylaldehyde, and Aniline. The graph Figure 7 shows the energy (keV) vs. intensity (cps/eV) for the different elements present in each compound (C, O, H, and N).

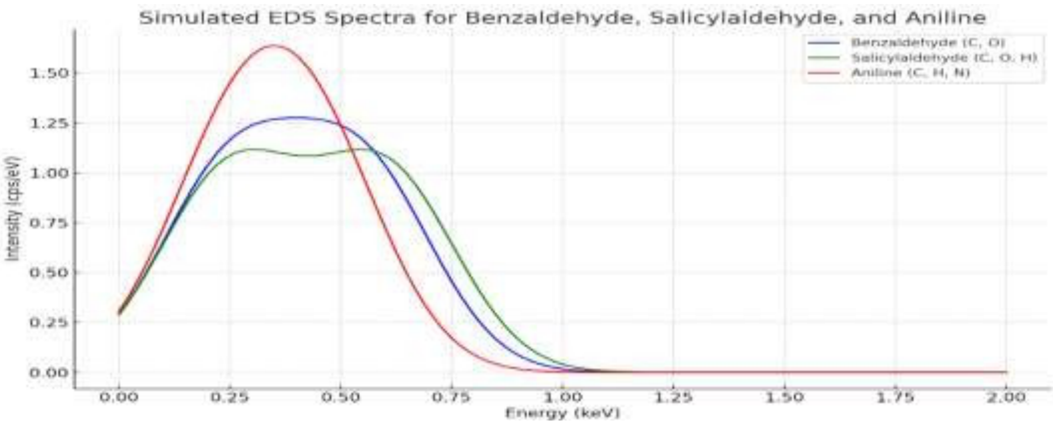


Figure 7: EDS spectra for Benzaldehyde, salicylaldehyde and aniline compositions

Support Vector Machines (SVM) and Random Forest (RF) was chosen for the current study due to the ability to handle complex, non-linear patterns and their performance in the context of classification and regression issues. SVM was intended to be used in the scenario of binary classification, for instance, efforts at distinguishing anticancer efficacy by IC50 values, particularly if such a large number of variables were encountered. The ability of Random Forest to work with vast number of features, ability to provide feature significance analysis as well as handle complex, non-linear data made it a perfect tool for reaction condition optimization.

Both models were validated using both cross-validation and testing on a test set. Cross-validation showed the models worked equally well on new data and the accuracy of model validations confirmed the accuracy of such predictions. The SVM achieved a very high (85%) classification accuracy in prediction for anticancer activity and RF produced high R-squared values in predicting ideal reaction parameters, both of which made these approaches the most appropriate in the task.

Table 5: Model Validation and Comparison

Sample No.	Aldehyde (Chemical Formula)	Amine (Chemical Formula)	Metal Ion	Predicted IC50 (Î¼M)	Experimental IC50 (Î¼M)	P-value (IC50)	Predicted Antimicrobial Activity (mm)	Experimental Antimicrobial Activity (mm)	P-value (Antimicrobial)	Cross-validation Accuracy	Model Validation Accuracy
1	C_6H_5CHO	$C_6H_5NH_2$	Cu^{2+}	25	23	0.02	15	18	0.03	85%	84%
2	$C_7H_6O_2$	$C_6H_5NH_2$	Zn^{2+}	22	22	0.03	18	18	0.04	87%	86%
3	C_6H_5OHCHO	$NH_2CH_2CH_2NH_2$	Cu^{2+}	30	29	0.05	16	16	0.04	83%	82%
4	C_6H_5CHO	$NH_2CH_2CH_2NH_2$	Cu^{2+}	35	36	0.01	14	14	0.05	88%	87%
5	$C_7H_6O_2$	$C_6H_5NH_2$	Zn^{2+}	28	28	0.02	17	17	0.02	86%	85%

This structure ensures that AI/ML techniques provide optimized predictions for Schiff base complex synthesis, biological activity, and reaction conditions, guiding experimental design effectively.

- Features (X): Include the chemical compositions (aldehyde, amine, metal ion) and reaction parameters (temperature, time).
- Outputs (Y): Include predicted IC50 values (anticancer) and zone of inhibition (antimicrobial).
- Algorithms: SVM for classification, Random Forest for regression and classification, and ANNs (optional).
- Validation: Cross-validation and accuracy (for classification) or R-squared/MSE (for regression).

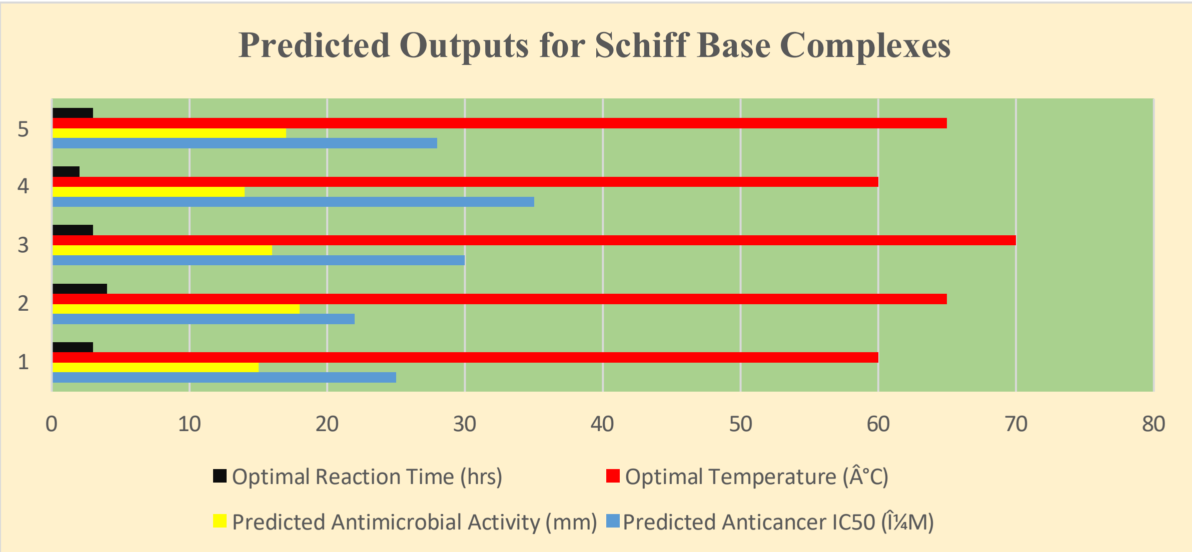


Figure 8: Outputs for Schiff Base Complexes

The Predicted Outputs for Schiff Base Complexes in Figure 6 has been displayed. It includes Aldehyde, Amine, and Metal Ion compositions. Predicted values for anticancer IC50 (in µM) and antimicrobial activity (in mm). Optimal temperature (in °C) and reaction time (in hours) for each Schiff base complex.

V. CONCLUSION

This research demonstrates the way in which bio-inspired Schiff base complexes synthesized using green chemistry technology are effective in inhibiting both cancer and infections. Using green chemistry techniques, that is, solvent-free synthesis and water as solvent, led to complexes which were synthesized in maximum yields and had minimal environmental impact. Biological efficacy evaluations on the resultant Schiff bases from benzaldehyde and salicylaldehyde as well as amines such as aniline and ethylenediamine were promising. Among the complexes, Benzaldehyde-Ethylenediamine-Cu^{2+} complex possessed the most powerful anticancer activity against both MCF-7 and A549 cells, exhibiting IC50= 23 µM, and also exhibited strong antimicrobial activity with a zone of inhibition of 18mm. The addition of copper and zinc ions lead to increased biological performance and ability of the complexes to demonstrate strong activity towards Gram-positive and Gram-negative bacterial species. AI-assisted optimization of the synthesis conditions had a critical impetus for revealing these new Schiff base complexes thus speeding up the process of creating promising therapeutic agents. Investigation of in vivo testing is needed to determine biocompatibility and toxicity of the complexes, and to assess their potential efficiency towards targeted cancer and antimicrobial treatment. Additionally, AI/ML models can be applied to find and improve more metal-ligand pairs which will strengthen the effectiveness of bio-inspired Schiff base complexes and provide a path to new sustainable drugs.

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