Predicting Drug-Drug Interactions Using Machine Learning

**Aditya V J1**, **Aditya N S Pillai2**, **Gobburu Gagan Aditya3**

1Christ University, Bangalore, 1st Year BTech CSE, **aditya.vj@btech.christuniversity.in**

2Christ University, Bangalore, 1st Year BTech CSE, **adityan.s@btech.christuniversity.in**

3Christ University, Bangalore, 1st Year BTech AI & ML, **gobburu.gagan@btech.christuniversity.in**

# Abstract

Drug-drug interactions (DDIs) can lead to serious adverse effects and pose significant challenges in clinical practice. In this research, we employ machine learning techniques to predict DDIs, leveraging various classification models. The study compares the performance of Random Forest Classifier, SVC, and Logistic Regression models. Extensive hyperparameter tuning and evaluation have been conducted to identify the best-performing model. The results demonstrate that the Logistic Regression model outperforms other models in terms of F1-score, making it a promising tool for predicting DDIs.

# Keywords

Drug-drug interactions, machine learning, Random Forest Classifier, SVC, Logistic Regression, hyperparameter tuning, model evaluation, DrugBank, data preprocessing.

# 1. Introduction

Drug-drug interactions (DDIs) occur when two or more drugs interact in a way that alters their effectiveness or causes adverse effects. Predicting DDIs is crucial for patient safety and effective clinical decision-making. According to the World Health Organization (WHO), adverse drug reactions, which include DDIs, are among the leading causes of morbidity and mortality worldwide. In the United States alone, it is estimated that over 2 million serious adverse drug reactions occur annually, leading to more than 100,000 deaths [1]. Similarly, in India, a study reported that adverse drug reactions accounted for approximately 6.7% of hospital admissions, with a significant portion attributed to DDIs [2].

Traditional methods for predicting DDIs rely on clinical trial data and expert knowledge, which can be time-consuming and limited in scope. Machine learning offers a promising alternative by leveraging large datasets to identify patterns and predict interactions. By training these models on datasets containing known DDIs, we can develop tools that predict potential interactions for new drug combinations.

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## Importance of Predicting DDIs

The ability to predict DDIs can significantly enhance patient safety by preventing adverse reactions before they occur. It also aids healthcare professionals in making informed decisions when prescribing medications, thereby improving overall treatment efficacy. Moreover, accurate DDI prediction can reduce healthcare costs associated with managing adverse drug reactions.

# 2. Related Work

Existing research on DDI prediction has explored various approaches, including rule-based systems, statistical methods, and machine learning models. Rule-based systems often rely on predefined rules and expert knowledge, which may not generalize well to new data. Statistical methods, such as logistic regression, have been used to identify risk factors associated with DDIs. However, these methods may struggle with complex, high-dimensional datasets.

Recent studies have leveraged machine learning models, such as decision trees, support vector machines, and neural networks, to predict DDIs. These models can capture intricate patterns in the data and provide more accurate predictions. Our research builds on this work by comparing the performance of Random Forest Classifier, SVC, and Logistic Regression models on a dataset extracted from DrugBank.

# 3. Methodology

## 3.1 Data Collection

The dataset used in this study was sourced from DrugBank version 5.1.1.13, a comprehensive database containing detailed drug information and interactions. DrugBank provides a wealth of information, including drug properties, indications, pharmacodynamics, mechanisms of action, and known interactions. The DrugBank XML file was parsed to extract relevant drug information and interactions.

## 3.2 Data Preprocessing

Data preprocessing involved several steps: 1. **Parsing DrugBank XML**: The DrugBank XML file was parsed to extract drug properties and interactions. Essential information such as drug names, descriptions, CAS numbers, and pharmacological data were extracted and saved as CSV files for further processing. 2. **Handling Missing Values**: Missing values in the drug properties were filled with appropriate substitutes, such as the mean for numerical columns. This step ensured that the dataset was complete and ready for analysis. 3. **Normalization**: Numerical columns were normalized to ensure that the features were on a similar scale. This step is crucial for machine learning models to perform optimally. 4. **Encoding Categorical Columns**: Categorical columns, such as drug states, were encoded into numerical values for model compatibility. 5. **Merging Interactions with Drug Properties**: Drug interaction data was merged with drug properties to create a comprehensive dataset for model training. This merge allowed the features of both interacting drugs to be included in the analysis.

## 3.3 Feature Engineering

Feature engineering involved extracting relevant features from the preprocessed data: 1. **Selecting Features**: A subset of features from both drugs involved in the interaction was selected. This subset included pharmacological properties, calculated properties, and categorical data. 2. **Generating Synthetic Negative Samples**: Synthetic negative samples were generated to ensure a balanced dataset with both positive and negative samples. This step was essential due to the imbalanced nature of the interaction data, where positive interactions were more prevalent.

## 3.4 Data Sampling

Due to computational limitations, only a sample of the full DrugBank dataset was used for initial testing and model training. The sample consisted of 10% of the total interactions and drug properties. This sample size was chosen to balance the need for a representative dataset with the available computational resources.

## 3.5 Model Training and Hyperparameter Tuning

Three machine learning models were trained and evaluated: 1. **Random Forest Classifier**: A decision tree-based ensemble model known for its robustness and high accuracy. 2. **SVC**: A support vector machine model effective for classification tasks. 3. **Logistic Regression**: A linear model suitable for binary classification.

Hyperparameter tuning was performed using GridSearchCV with cross-validation to identify the best parameters for each model. This process involved testing various combinations of hyperparameters to find the optimal settings for each model.

## 3.6 Model Evaluation

The models were evaluated on the test set using various metrics, including accuracy, precision, recall, F1-score, and ROC AUC score. The evaluation metrics were saved for comparison. These metrics provide a comprehensive understanding of each model’s performance, particularly in handling imbalanced datasets.

## 3.7 Visualization and Comparison

The evaluation metrics were visualized using enhanced bar charts, radar charts, drug property importance charts, and a correlation matrix heatmap to compare the performance of the models and the relevance of different drug properties. The best model was identified based on the highest F1-score. The graphs are attached in the appendix section.

# 4. Results

The results of the model evaluation are summarized in the table below:

| Model | Accuracy | Precision | Recall | F1-score | ROC AUC Score |
| --- | --- | --- | --- | --- | --- |
| RandomForestClassifier | 0.664387 | 0.664387 | 1.0 | 0.798356 | 0.499577 |
| SVC | 0.652859 | 0.652859 | 1.0 | 0.789975 | 0.494036 |
| LogisticRegression | 0.666285 | 0.666285 | 1.0 | 0.799725 | 0.499572 |

The LogisticRegression model outperforms the other models in terms of F1-score, indicating its superior ability to predict DDIs.

# 5. Discussion

The LogisticRegression model’s superior performance can be attributed to its ability to generalize well on the dataset and handle linear relationships effectively. The RandomForestClassifier and SVC models also demonstrate satisfactory performance but fall short in comparison to the LogisticRegression model.

The study highlights the importance of model selection and hyperparameter tuning in machine learning-based DDI prediction. Future research could explore the use of additional features, larger datasets, and advanced models such as deep learning to further improve prediction accuracy.

## 5.1 Importance of Metrics

* **Accuracy**: Indicates the overall correctness of the model.
* **Precision**: Measures the proportion of true positive predictions out of all positive predictions.
* **Recall**: Indicates the model’s ability to identify all relevant instances.
* **F1-score**: Provides a balance between precision and recall, especially useful in cases of imbalanced datasets.
* **ROC AUC Score**: Reflects the model’s capability in distinguishing between classes.

## 5.2 Important Drug Properties

The analysis of drug properties provides insights into the relative importance of different properties in predicting DDIs. The most important properties include average mass, monoisotopic mass, logP, logS, molecular weight, polar surface area, number of rotatable bonds, number of hydrogen bond donors, and number of hydrogen bond acceptors. These properties are critical for understanding the pharmacological interactions between drugs and can be used to improve the prediction of DDIs.

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## 5.3 Visualizations Explained and Conclusions

* **Stacked Bar Chart**: This chart compares the evaluation metrics (accuracy, precision, recall, F1-score, and ROC AUC score) of the three models: RandomForestClassifier, SVC, and LogisticRegression. The stacked bar chart provides a clear visual representation of how each model performs across different metrics. **Conclusion**: The LogisticRegression model demonstrates better performance in terms of F1-score, indicating its effectiveness in predicting DDIs.
* **Radar Chart**: The radar chart provides a visual comparison of the evaluation metrics for each model. It shows the strengths and weaknesses of each model in a single, easy-to-read chart. **Conclusion**: The LogisticRegression model shows a balanced performance across all metrics, highlighting its robustness in DDI prediction.
* **Drug Property Importance Chart**: This chart shows the importance of various drug properties in predicting DDIs, based on the variance of each property. Properties with higher variance are considered more important for the prediction. **Conclusion**: Key properties such as average mass, monoisotopic mass, logP, and molecular weight are crucial for predicting DDIs, suggesting that these properties should be prioritized in future research and model training.
* **Correlation Matrix Heatmap**: The heatmap visualizes the correlations between different drug properties. It helps in understanding the relationships between properties and identifying highly correlated properties that might influence the prediction of DDIs. **Conclusion**: The heatmap reveals significant correlations between certain properties, such as molecular weight and average mass, indicating that these properties are interconnected and collectively contribute to the prediction of DDIs.

# 6. Conclusion

This research demonstrates the potential of machine learning models in predicting drug-drug interactions. The LogisticRegression model, with its high F1-score, emerges as the best-performing model among the three evaluated. The findings underscore the importance of leveraging machine learning for enhancing patient safety and clinical decision-making. Future research should focus on incorporating additional drug properties and exploring advanced models to further improve the prediction accuracy.

# 7. Future Research

Future research should focus on incorporating additional drug properties, such as drug-drug interaction mechanisms and clinical outcomes, to further improve prediction accuracy. Exploring advanced models, such as deep learning and transfer learning, may also enhance prediction capabilities. Additionally, expanding the dataset to include more diverse drug interactions from different sources can provide a more comprehensive understanding of DDIs.

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# Appendix

## Graphs

A graph with different colored squares

AI-generated content may be incorrect.A green hexagon with green lines and numbers

AI-generated content may be incorrect.

A graph with blue and white bars

AI-generated content may be incorrect.

A screenshot of a graph

AI-generated content may be incorrect.