

Artificial Intelligence and Machine Learning Approaches for Predicting Drug–Drug Interactions in Clinical Practice

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Abstract: Drug–drug interactions (DDIs) represent a major challenge in clinical medicine and pharmacotherapy, often leading to adverse drug reactions, therapeutic failure, hospitalisation, and increased healthcare costs. Traditional methods of detecting DDIs rely heavily on clinical trials, post-marketing surveillance, and spontaneous reporting systems, which are often time-consuming and limited in predictive capability. Recent advancements in Artificial Intelligence (AI) and Machine Learning (ML) have transformed the field of drug safety by enabling accurate prediction, early detection, and risk assessment of DDIs. This article reviews the role of AI and ML techniques in predicting DDIs, including deep learning, natural language processing, neural networks, and data mining approaches. The study further discusses data sources, predictive models, clinical applications, advantages, limitations, and future directions of AI-driven DDI prediction systems. The integration of AI technologies into healthcare systems can significantly improve patient safety, optimise therapeutic outcomes, and support precision medicine.

Keywords: Artificial Intelligence, Machine Learning, Drug–Drug Interactions, Clinical Pharmacology, Deep Learning, Pharmacovigilance, Precision Medicine

I. INTRODUCTION

Drug–drug interactions occur when one drug affects the pharmacological activity, metabolism, absorption, or elimination of another drug. DDIs are particularly common among elderly patients, critically ill individuals, and patients receiving polypharmacy treatment. Clinically significant DDIs may result in toxicity, reduced therapeutic efficacy, or life-threatening adverse events.

Conventional methods for identifying DDIs mainly include laboratory experiments, clinical trials, and pharmacovigilance reporting systems. However, these approaches are expensive, labour-intensive, and incapable of rapidly handling the growing number of available drugs. The emergence of AI and ML technologies offers new opportunities for predicting unknown DDIs efficiently and accurately.

Artificial Intelligence refers to computer systems designed to simulate human intelligence, while Machine Learning is a subset of AI that allows systems to learn patterns from data and improve performance without explicit programming. AI and ML algorithms can analyse large biomedical datasets, identify hidden relationships among drugs, and predict potential interactions before clinical occurrence.

II. CONCEPT OF DRUG–DRUG INTERACTIONS

2.1 Pharmacokinetic Interactions

Pharmacokinetic drug–drug interactions occur when one drug alters the absorption, distribution, metabolism, or excretion (ADME) of another drug, thereby affecting its concentration in the body. These interactions can significantly influence the therapeutic effectiveness and safety of medications. Pharmacokinetic interactions are among the most common causes of adverse drug reactions in clinical practice.

Drug Absorption

Drug absorption interactions occur when one medication affects the rate or extent to which another drug enters the bloodstream. Such interactions may result from changes in gastric pH, gastrointestinal motility, or drug-binding mechanisms. For example, antacids containing calcium or magnesium may reduce the absorption of certain antibiotics such as tetracycline and ciprofloxacin by forming insoluble complexes.

Drug Distribution

Distribution interactions occur when one drug displaces another from plasma protein-binding sites, especially albumin. This displacement increases the free or active concentration of the affected drug in circulation, potentially leading to toxicity. Drugs such as warfarin and phenytoin are highly protein-bound and are particularly susceptible to such interactions.

Drug Metabolism

Drug metabolism interactions mainly occur in the liver and are commonly mediated by the cytochrome P450 (CYP450) enzyme system. Certain drugs may inhibit or induce these enzymes, thereby altering the metabolism of co-administered medications. Enzyme inhibition can increase drug concentration and toxicity, whereas enzyme induction can reduce therapeutic effectiveness. For instance, erythromycin inhibits CYP3A4 activity, while rifampicin acts as a potent enzyme inducer.

Drug Excretion

Excretion interactions involve changes in renal elimination or biliary clearance of drugs. Some medications compete for renal tubular secretion or alter urine pH, affecting drug elimination. Reduced drug excretion may increase plasma drug levels and toxicity risk.

Among these mechanisms, cytochrome P450 enzymes play a particularly important role in pharmacokinetic drug–drug interactions. AI and machine learning models are increasingly being used to predict CYP450-mediated interactions and improve medication safety in clinical practice.

2.2 Pharmacodynamic Interactions

Pharmacodynamic drug–drug interactions occur when two or more drugs influence the same receptor, biological pathway, or physiological system without necessarily altering each other's concentration in the body. These interactions affect the pharmacological response of drugs and may either enhance or reduce therapeutic outcomes. Pharmacodynamic interactions are particularly important in patients receiving multiple medications for chronic diseases.

Synergistic Effects

Synergistic interactions occur when the combined effect of two drugs is greater than the sum of their individual effects. Such interactions may be therapeutically beneficial or potentially harmful. For example, the combined use of opioids and benzodiazepines can produce excessive central nervous system depression, leading to respiratory failure.

Additive Effects

Additive interactions arise when two drugs with similar pharmacological actions produce a cumulative effect equal to the sum of their individual effects. For instance, concurrent administration of antihypertensive drugs may result in an excessive reduction in blood pressure.

Antagonistic Effects

Antagonistic interactions occur when one drug reduces or blocks the effect of another drug. This may decrease therapeutic efficacy and compromise patient treatment outcomes. An example includes the use of nonsteroidal anti-inflammatory drugs (NSAIDs), which may reduce the antihypertensive effect of certain blood pressure medications. Pharmacodynamic interactions are often difficult to predict because they depend on complex physiological and receptor-mediated mechanisms. Artificial intelligence and machine learning techniques are increasingly being explored to identify such interactions by analysing large-scale clinical and pharmacological datasets.

2.3 Clinical Importance of Drug–Drug Interactions (DDIs)

Drug–drug interactions represent a major concern in modern healthcare because of their significant impact on patient safety, therapeutic effectiveness, and healthcare costs. DDIs are particularly common among elderly patients, critically ill individuals, and patients receiving polypharmacy treatment for chronic diseases.

Adverse Drug Reactions

DDIs are a leading cause of adverse drug reactions, which may range from mild side effects to severe life-threatening complications. Many preventable medication-related hospital admissions are associated with drug interactions.

Organ Toxicity

Certain interactions may increase drug concentrations to toxic levels, resulting in damage to vital organs such as the liver, kidneys, heart, or nervous system. For example, interactions involving nephrotoxic drugs may significantly impair renal function.

Increased Hospitalisation

Serious drug interactions often require emergency medical attention and hospitalisation. Patients experiencing severe DDIs may need prolonged treatment and intensive monitoring.

Mortality

Life-threatening interactions can contribute to increased mortality, especially in vulnerable populations such as elderly patients or individuals with multiple comorbidities. Fatal arrhythmias, respiratory depression, and severe bleeding are common examples.

Therapeutic Failure

Some DDIs reduce the effectiveness of medications by decreasing their absorption or increasing their metabolism. This may lead to treatment failure, disease progression, or drug resistance.

Economic Burden on Healthcare Systems

DDIs contribute significantly to healthcare expenditures through increased hospital admissions, additional diagnostic testing, prolonged treatment, and higher medication costs. Preventing DDIs can reduce both clinical complications and economic burden.

The growing complexity of pharmacotherapy highlights the importance of advanced predictive technologies such as artificial intelligence and machine learning to improve early detection and prevention of clinically significant drug interactions.

III. ARTIFICIAL INTELLIGENCE IN HEALTHCARE

Artificial Intelligence (AI) has emerged as one of the most transformative technologies in modern healthcare. AI refers to computer systems and algorithms capable of performing tasks that normally require human intelligence, including learning, reasoning, problem-solving, pattern recognition, and decision-making. In healthcare, AI technologies are increasingly being integrated into clinical practice to improve diagnostic accuracy, treatment planning, patient monitoring, and overall healthcare efficiency.

The rapid growth of electronic health records, biomedical databases, genomic information, and medical imaging data has created opportunities for AI systems to analyze vast amounts of clinical and pharmacological information. By processing complex datasets, AI can assist healthcare professionals in making evidence-based medical decisions and improving patient outcomes.

Disease Diagnosis

AI algorithms are widely used for early and accurate disease diagnosis. Machine learning models can identify patterns in patient symptoms, laboratory reports, and clinical histories to support diagnosis of diseases such as cancer, diabetes, cardiovascular disorders, and neurological conditions. AI-assisted diagnostic systems often improve clinical accuracy while reducing diagnostic errors.

Medical Imaging

Artificial intelligence plays a significant role in medical imaging and radiology. Deep learning techniques, particularly convolutional neural networks (CNNs), are capable of analyzing X-rays, CT scans, MRI images, and ultrasound reports with high precision. AI-based imaging systems help detect abnormalities such as tumors, fractures, and organ damage at early stages, thereby improving treatment outcomes.

Drug Discovery

AI has accelerated the process of drug discovery and pharmaceutical research by identifying potential drug candidates, predicting molecular interactions, and optimizing drug design. Traditional drug development is time-consuming and expensive; however, AI-driven computational models can rapidly screen thousands of compounds and predict their biological activity. This significantly reduces the cost and duration of pharmaceutical development.

Personalized Medicine

Personalized medicine aims to provide individualized treatment based on a patient's genetic profile, lifestyle, and disease characteristics. AI systems analyze genomic, proteomic, and clinical data to recommend personalized therapeutic strategies. Such approaches improve treatment effectiveness while minimizing adverse drug reactions and drug-drug interactions.

Clinical Decision Support Systems

AI-powered Clinical Decision Support Systems (CDSS) assist physicians, pharmacists, and healthcare professionals in making informed clinical decisions. These systems provide real-time alerts regarding medication errors, allergies, contraindications, and potential drug-drug interactions. AI-based CDSS improves patient safety and enhances the quality of healthcare delivery.

Predictive Analytics

Predictive analytics uses AI and machine learning algorithms to forecast clinical outcomes, disease progression, and patient risk factors. Hospitals and healthcare organizations use predictive models to identify high-risk patients, prevent complications, and optimise healthcare resource allocation.

Overall, artificial intelligence has become an essential component of modern healthcare systems. AI technologies improve diagnostic accuracy, support clinical decision-making, enhance patient safety, and contribute to more efficient healthcare management. In the context of drug-drug interactions, AI systems can analyse large pharmacological datasets and predict potentially harmful interactions before they occur in clinical practice.

IV. MACHINE LEARNING TECHNIQUES FOR PREDICTING DDIs

Machine learning techniques have become highly valuable in predicting drug-drug interactions (DDIs) because of their ability to analyse large biomedical datasets and identify hidden relationships among drugs. These computational approaches improve the accuracy and efficiency of DDI prediction and support safer clinical decision-making. Different machine learning models are applied depending on the type of available data and the complexity of interaction patterns.

4.1 Supervised Machine Learning

Supervised machine learning involves training algorithms using labelled datasets containing known drug-drug interactions. In this approach, the model learns from previously identified interaction patterns and predicts whether new drug combinations are likely to interact. Supervised learning is one of the most commonly used approaches in DDI prediction because of its high predictive performance and interpretability.

Common Supervised Learning Algorithms**Decision Trees**

Decision tree algorithms classify drug interactions based on a series of decision rules derived from training data. These models are easy to interpret and help identify important pharmacological variables associated with DDIs.

Random Forest

Random Forest is an ensemble learning method that combines multiple decision trees to improve prediction accuracy and reduce overfitting. It is widely used in biomedical data analysis because of its robustness and ability to handle large datasets.

Support Vector Machine (SVM)

Support Vector Machine algorithms classify interacting and non-interacting drug pairs by identifying optimal boundaries between data categories. SVM models are particularly effective for high-dimensional pharmacological data.

Logistic Regression

Logistic regression predicts the probability of drug interactions using statistical relationships between variables. This method is commonly applied for binary classification of interacting versus non-interacting drug pairs.

These supervised learning methods help classify whether two drugs are likely to interact and are increasingly integrated into clinical decision support systems.

4.2 Unsupervised Machine Learning

Unsupervised machine learning identifies hidden structures and patterns in unlabeled datasets without prior knowledge of interaction outcomes. These methods are valuable for discovering previously unknown DDIs and understanding complex pharmacological relationships.

Clustering Algorithms

Clustering techniques group drugs based on similarities in chemical structure, therapeutic action, side effects, or molecular targets. Drugs within the same cluster may exhibit similar interaction profiles.

Association Rule Mining

Association rule mining identifies frequent co-occurrence patterns among drugs in clinical databases and electronic health records. This method helps detect potential interaction patterns and adverse drug events that may not have been previously recognized.

Unsupervised learning approaches are particularly useful in exploratory pharmacovigilance and large-scale biomedical data analysis.

4.3 Deep Learning Approaches

Deep learning is an advanced subset of machine learning that utilizes artificial neural networks with multiple hidden layers to analyze highly complex biomedical relationships. Deep learning models can automatically extract meaningful features from large datasets and achieve superior predictive performance in DDI prediction.

Convolutional Neural Networks (CNN)

CNN models are commonly used for analyzing structured biomedical and molecular data. They can identify interaction-related patterns in drug chemical structures and biological pathways.

Recurrent Neural Networks (RNN)

RNN models process sequential and time-dependent data, making them useful for analyzing longitudinal patient records, medication histories, and temporal clinical information.

Graph Neural Networks (GNN)

Graph Neural Networks represent drugs and their relationships as interconnected networks or graphs. GNNs are particularly effective in modeling molecular interactions, protein-drug relationships, and complex pharmacological networks.

Deep learning approaches provide high predictive accuracy for large-scale DDI datasets and are increasingly applied in precision medicine and computational pharmacology.

4.4 Natural Language Processing (NLP)

Natural Language Processing (NLP) is a branch of artificial intelligence that enables computers to understand, interpret, and process human language. In healthcare and pharmacology, NLP techniques are widely used to extract DDI-related information from unstructured textual data sources.

- Sources of NLP-Based DDI Information
- Biomedical literature
- Electronic health records (EHRs)
- Clinical notes
- Drug databases
- Adverse event reports
- Pharmacovigilance records

NLP systems can automatically identify drug names, adverse reactions, interaction mechanisms, and clinical outcomes from large volumes of medical text. This reduces manual effort and improves the efficiency of pharmacovigilance activities.

NLP-based methods also support real-time monitoring of adverse drug events and contribute to early detection of potentially harmful drug interactions in clinical practice.

V. DATA SOURCES FOR AI-BASED DRUG-DRUG INTERACTION PREDICTION

Artificial Intelligence (AI) and Machine Learning (ML) models rely heavily on large, accurate, and diverse datasets for effective prediction of drug-drug interactions (DDIs). The quality, quantity, and reliability of input data significantly influence the predictive performance of computational models. Modern AI-based DDI prediction systems integrate information from multiple biomedical and clinical data sources to identify complex pharmacological relationships and improve medication safety.

Electronic Health Records (EHRs)

Electronic Health Records are one of the most valuable sources of real-world clinical data for DDI prediction. EHRs contain detailed patient information, including:

- Medication history
- Diagnoses
- Laboratory reports
- Clinical notes
- Treatment outcomes
- Adverse drug reactions

Machine learning models analyze EHR data to identify patterns of co-prescribed medications and detect clinically significant interactions. Real-time analysis of EHRs also supports clinical decision support systems that alert healthcare professionals about potential DDIs during prescription.

DrugBank Databases

DrugBank is a comprehensive bioinformatics and pharmacological database containing detailed information about drugs and their interactions. It includes:

- Chemical structures
- Drug targets
- Metabolic pathways
- Mechanisms of action
- Pharmacokinetic properties
- Known drug interactions

AI systems frequently use DrugBank datasets for training predictive models because of their structured and validated pharmacological information.

FDA Adverse Event Reporting System (FAERS)

The FDA Adverse Event Reporting System (FAERS) is a large pharmacovigilance database maintained by the United States Food and Drug Administration. It collects reports of:

- Adverse drug reactions
- Medication errors
- Drug-related complications
- Patient safety events

Machine learning algorithms analyze FAERS data to identify potential DDIs associated with adverse clinical outcomes. This database plays an important role in post-marketing surveillance and early detection of harmful interactions.

Biomedical Literature

Scientific journals, research articles, conference papers, and medical publications provide extensive information regarding drug interactions, pharmacological mechanisms, and adverse effects. Natural Language Processing (NLP) techniques are commonly used to extract DDI-related knowledge from biomedical literature automatically.

Text mining approaches help identify newly reported interactions and support continuous updating of AI prediction models.

Genomic and Proteomic Databases

Genomic and proteomic databases contain information related to genes, proteins, enzymes, and molecular pathways involved in drug metabolism and therapeutic response. These datasets are essential for understanding:

- Genetic variability
- Enzyme activity
- Drug metabolism pathways
- Personalized medicine approaches

AI models integrate genomic and proteomic data to predict individual susceptibility to DDIs and optimize personalized treatment strategies.

Clinical Trial Repositories

Clinical trial repositories contain data from controlled experimental studies evaluating drug safety, efficacy, and interaction profiles. These repositories provide validated evidence regarding:

- Drug combinations
- Pharmacokinetic interactions
- Adverse effects
- Therapeutic outcomes

Machine learning systems use clinical trial data to improve prediction accuracy and validate computational models before clinical implementation.

High-quality datasets are essential for building reliable AI and ML models for DDI prediction. Accurate, diverse, and well-structured data improve model training, reduce prediction errors, and enhance the clinical applicability of AI-based pharmacovigilance systems. The integration of multiple biomedical data sources enables comprehensive analysis of drug interactions and contributes to safer and more effective healthcare delivery.

VI. CLINICAL APPLICATIONS OF AI-BASED DRUG-DRUG INTERACTION PREDICTION

Artificial Intelligence (AI) and Machine Learning (ML) technologies have significant clinical applications in predicting and managing drug-drug interactions (DDIs). These technologies improve medication safety, optimise therapeutic

outcomes, and support healthcare professionals in evidence-based clinical decision-making. AI-driven systems are increasingly being integrated into hospitals, pharmaceutical industries, and pharmacovigilance programs to reduce the risks associated with adverse drug interactions.

6.1 Clinical Decision Support Systems

Clinical Decision Support Systems (CDSS) are AI-integrated healthcare tools designed to assist physicians, pharmacists, and healthcare professionals during clinical practice. These systems analyse patient information, medication history, laboratory reports, and drug databases to identify potential DDIs in real time.

AI-powered CDSS can generate automatic alerts during prescription and medication review processes, thereby helping healthcare providers avoid harmful drug combinations. Such systems improve prescribing accuracy, reduce medication errors, and enhance patient safety. In hospital settings, AI-based DDI alert systems are particularly useful for managing patients receiving multiple medications, including elderly and critically ill individuals.

Modern CDSS platforms also prioritise clinically significant alerts to minimise alert fatigue among healthcare professionals. By integrating AI into hospital information systems and electronic health records, healthcare institutions can improve therapeutic decision-making and reduce adverse drug events.

6.2 Personalised Medicine

Personalised medicine refers to individualised treatment approaches based on a patient's unique biological and clinical characteristics. Artificial intelligence plays a crucial role in tailoring drug therapy according to:

- Patient genetics
- Disease conditions
- Drug metabolism profiles
- Lifestyle factors
- Medical history

AI systems analyse genomic, proteomic, and pharmacological data to predict how individual patients may respond to specific medications or drug combinations. Such analysis helps healthcare professionals select the most appropriate drug therapy while minimising the risk of adverse drug interactions.

For example, genetic variations affecting cytochrome P450 enzymes can alter drug metabolism and increase susceptibility to DDIs. AI-driven predictive models can identify these variations and support precision dosing strategies. Personalised medicine, therefore, contributes to safer, more effective, and patient-centred healthcare.

6.3 Pharmacovigilance

Pharmacovigilance involves the detection, assessment, monitoring, and prevention of adverse drug reactions and medication-related risks. Machine learning technologies have significantly enhanced pharmacovigilance activities by enabling continuous analysis of large-scale healthcare data.

AI systems monitor:

- Electronic health records
- Adverse event reporting systems
- Clinical notes
- Biomedical literature
- Social media and healthcare databases

Machine learning algorithms can identify previously unknown drug interactions and detect early warning signals associated with medication-related complications. Natural Language Processing (NLP) techniques further assist in extracting relevant DDI information from unstructured clinical text and scientific publications.

AI-driven pharmacovigilance improves the speed, accuracy, and efficiency of adverse event detection, thereby enhancing patient safety and regulatory surveillance.

6.4 Drug Development

Artificial intelligence has become increasingly important in pharmaceutical research and drug development. Pharmaceutical companies use AI models to evaluate potential DDI risks during the early stages of drug discovery and clinical development.

AI-based computational models analyze:

- Molecular structures
- Drug targets
- Metabolic pathways
- Enzyme interactions
- Toxicological profiles

These predictive systems help researchers identify potentially harmful interactions before clinical trials, thereby reducing development costs and improving drug safety. AI can also assist in selecting safer drug combinations and optimizing clinical trial design.

By predicting DDI risks early in the development process, pharmaceutical companies can improve regulatory compliance, reduce drug attrition rates, and accelerate the development of safer therapeutic agents.

Overall, the clinical applications of AI and ML in DDI prediction have transformed modern healthcare and pharmaceutical practice. These technologies support real-time clinical decision-making, enhance pharmacovigilance, facilitate personalised medicine, and improve the safety and efficiency of drug development processes.

7. Advantages of AI and Machine Learning in DDI Prediction

The major advantages include:

- Faster prediction of interactions
- Improved accuracy
- Reduction in adverse drug events
- Cost-effective analysis
- Handling of large biomedical datasets
- Support for precision medicine
- Continuous learning capability
- AI systems can identify complex nonlinear relationships that traditional statistical methods may overlook.

VIII. CHALLENGES AND LIMITATIONS

Despite promising results, several challenges remain:

8.1 Data Quality Issues

Incomplete or biased datasets can reduce predictive accuracy.

8.2 Interpretability Problems

Some deep learning models function as “black boxes,” making interpretation difficult.

8.3 Privacy and Ethical Concerns

Use of patient data raises concerns regarding:

Confidentiality

Data security

Ethical approval

8.4 Regulatory Challenges

AI-based clinical tools require validation and approval from healthcare regulatory agencies.

IX. FUTURE PERSPECTIVES

Future research should focus on:

- Explainable AI models
- Integration of genomic and real-world data
- Improved interoperability of healthcare systems
- Hybrid AI models combining pharmacological knowledge with machine learning
- Global pharmacovigilance networks

The advancement of AI-driven healthcare systems may significantly enhance medication safety and clinical decision-making.

X. CONCLUSION

Artificial Intelligence and Machine Learning have emerged as powerful tools for predicting drug–drug interactions in clinical practice. These technologies can process massive biomedical datasets, identify hidden interaction patterns, and support healthcare professionals in preventing adverse drug events. AI-based DDI prediction systems have important applications in pharmacovigilance, personalized medicine, and clinical decision support. Although challenges related to data quality, interpretability, and ethics remain, ongoing technological advancements are expected to improve the reliability and clinical implementation of AI-driven DDI prediction models. The integration of AI into modern healthcare systems has the potential to revolutionize drug safety and optimize patient care.

REFERENCES

1. Wishart DS, Feunang YD, Guo AC, et al. DrugBank 5.0: A major update to the DrugBank database for 2018. *Nucleic Acids Research*. 2018;46(D1):D1082.
2. Vilar S, Uriarte E, Santana L, et al. Detection of drug–drug interactions by modeling interaction profile fingerprints. *PLoS ONE*. 2013;8(3).
3. Ryu JY, Kim HU, Lee SY. Deep learning improves prediction of drug–drug and drug–food interactions. *Proceedings of the National Academy of Sciences*. 2018;115(18):E4311.
4. Tatonetti NP, Ye PP, Daneshjou R, Altman RB. Data-driven prediction of drug effects and interactions. *Science Translational Medicine*. 2012;4(125):125ra31.
5. Zhang W, Chen Y, Liu F, et al. Predicting potential drug–drug interactions by integrating chemical, biological, phenotypic and network data. *BMC Bioinformatics*. 2017;18:18.
6. Noor A, Assiri A, Ayyaz S, Clark C. Machine learning approaches for predicting drug interactions using electronic health records. *Journal of Biomedical Informatics*. 2016;60:15–23.
7. LeCun Y, Bengio Y, Hinton G. Deep learning. *Nature*. 2015;521(7553):436–444.
8. Chen X, Liu M, Yan G. Drug–target interaction prediction by random walk on the heterogeneous network. *Molecular BioSystems*. 2012;8(7):1970–1978.
9. Percha B, Altman RB. Informatics confronts drug–drug interactions. *Trends in Pharmacological Sciences*. 2013;34(3):178–184.
10. Zhao XM, Iskar M, Zeller G, et al. Prediction of drug combinations by integrating molecular and pharmacological data. *PLoS Computational Biology*. 2011;7(12).