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Review article

An In-Depth Examination of Drug-Drug Interaction Databases: Enhancing Patient Safety through Advanced Predictive Models and Artificial Intelligence Techniques

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Abstract

Background: Drug-drug interactions (DDIs) pose a significant risk to patient safety, leading to adverse effects and increased hospitalizations. With the rise of polypharmacy, especially among elderly patients and those with chronic conditions, understanding and predicting DDIs has become imperative for effective clinical management. **Methods**: This review synthesizes current literature on drug-drug interaction databases and their role in predicting DDIs. A systematic search of relevant databases focused on studies utilizing artificial intelligence (AI) and machine learning techniques for DDI prediction. Key databases, such as DrugBank, PubChem, and the Pharmacogenomics Knowledgebase (PharmGKB), were analyzed for their contributions to DDI research. **Results**: The findings indicate that AI-driven methodologies significantly enhance the identification and prediction of DDIs. Various machine learning techniques, including conventional and unconventional methods, have been employed to assess drug interactions effectively. The review highlights real-world examples of critical DDIs, demonstrating the clinical implications of these interactions. Databases provide essential tools for healthcare providers to manage medications and prevent adverse events.

Conclusion: Integrating drug-drug interaction databases into clinical practice is crucial for improving patient safety and treatment efficacy. Future research should focus on enhancing the predictive capabilities of these models through continuous data integration and validation. By leveraging advanced computational techniques, healthcare systems can better anticipate and mitigate the risks associated with drug interactions.

Keywords: Drug-drug interactions, artificial intelligence, machine learning, patient safety, pharmacovigilance.

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1. Introduction

Medicine is essential for human advancement and growth. Pharmaceutical goods are the primary agents used for the prevention, treatment, and diagnosis of illnesses. The advancement of modern medical pharmacology, drug treatment, and pharmaceutical research has led to the discovery of different medication combinations that successfully treat patients with varied or complicated illnesses [1]. However, the primary issue with using many medicines concurrently is that patients face a significantly increased risk of unfavorable effects. Various adverse medication responses may arise from drug-drug interactions (DDI). This may result in either beneficial or detrimental alterations in the drug's efficacy when combined with another treatment. This alteration may result in diminished therapeutic efficacy and increased toxicity, jeopardizing patient safety and elevating disease prevalence, particularly in certain populations with preexisting conditions. In a hospital environment, drug-drug interactions (DDI) may lead to various problems, extend the duration of hospitalizations, and perhaps result in mortality [2,3].

Drug-drug interactions (DDIs) represent a substantial concern in the United States, resulting in more than 74,000 emergency division visits and 195,000 admissions per year. The CDC indicates that 10% of the US population uses five medications, while 36% of elderly Americans employ five simultaneously [4]. Fifteen percent of medication combinations among individuals aged 61 to 80 provide a risk of adverse drug interactions. Adverse pharmaceutical interactions occur in around 5% of cases, resulting in over 2.5 million hospitalizations because of drug addiction or serious drug reactions [5].

Among these cases, around 200,000 fatalities resulted from improper or erroneous medication use, representing 0.38% of overall hospitalizations as well as 7.9 percent of instances attributed to negative drug responses [6]. In a hospital case involving an 83-year-old female patient with pre-existing renal dysfunction, intravenous imipenem/cilastatin sodium was administered at a dosage of 0.5g three times daily over four days. Subsequently, the patient experienced seizures and severe epilepsy. A clear correlation was established between the administration of imipenem/cilastatin sodium and the onset of seizures, which resolved after discontinuing the medication. This case indicates that the seizures were likely linked to the imipenem/cilastatin sodium treatment. It underscores the critical need for precise drug-drug interaction (DDI) predictions to identify potential adverse events and mitigate risks in healthcare environments [7].

DDI denotes the concurrent or successive administration of several pharmaceuticals resulting from drug interactions, whereby the efficacy of one or more substances is diminished or altered to variable extents. Research indicates that drug-drug interactions (DDI) may elicit various reactions in pharmaceuticals, pharmacokinetics (PK), as well as pharmacodynamics (PD) [2,3]. The manifestation of pharmacy drug-drug interactions (DDIs) arises from physical or chemical incompatibility. Pharmacokinetic drug-drug interactions arise when medications influence one another during digestion, metabolism, absorption, and excretion. Conversely, PD DDI occurs when one medication elicits a pharmacological reaction to another drug at an equivalent dose. The deleterious effects of DDI have enhanced the knowledge of drug responses, hence improving the security and effectiveness of medication treatment and promoting secure and efficient drug combination options [8-10].

Experimental evaluation of medicines in both human as well as laboratory environments may aid scientists and pharmaceutical companies in precisely detecting detrimental drug-drug interactions. This may also facilitate the advancement of modeling

methodologies to better identify possible drug-drug interactions (DDIs). Nonetheless, laboratory research methodologies may be very costly and, in many instances, unfeasible to implement. Consequently, there is a notable trend in using computational and machine-learning methodologies to predict and accelerate the detection of drug-drug interactions (DDIs). This mitigates related social, economic, and wellness expenses [8].

AI Health has partnered with AstraZeneca to use artificial intelligence in developing pharmaceuticals and medical services for diverse communities. The partnership allows paramedics to analyze patients using AI algorithms, streamlining their transfers to suitable hospitals and enabling the availability of more patient-centric drugs. This significant advancement in healthcare decision-making is expected to improve patient outcomes [11].

As research into pharmaceutical interactions progresses, there has been a growing number of publications, alongside continuously evolving websites and databases that provide drug and disease information [12, 13]. This landscape offers researchers the chance to gather drug data from multiple sources, facilitating the advancement of computational modeling techniques for predicting drug-drug interactions. Recently, various review articles have been published focusing on different facets of identifying pharmaceutical interactions, including the development of knowledge graphs and the significance of understanding these interactions [14-16]. Most of these evaluations center on methods for predicting direct medication interactions.

2. Biomedical Databases

Biomedical databases have become valuable resources for AI, generating considerable interest in their data-driven applications. By analyzing vast amounts of drug-related data, AI can uncover emerging trends and extract meaningful insights. The rapid progress in computer science and genome sequencing over recent decades has led to an abundance of knowledge concerning pharmaceuticals, encompassing information about drugs, diseases, genes, and proteins. This wealth of data greatly enhances drug-related research, as it necessitates integrating various pharmacological characteristics and documented drug-drug interactions (DDIs) to anticipate potential interactions [16].

Frequently used resources involve DrugBank, which mostly contains drug characteristics. PubChem and ChEMBL primarily provide information on chemicals, including their roles and advantages for living organisms [17-19]. Data on more than 12,000 medicines and 200,000 interactions are available in the Kyoto Encyclopedia of Genomes and Genes (DDI), which is based on prescription medication packaging from Japan [20, 21]. The Pharmacogenomics Library (PharmGKB) offers gene-drug interaction information and is among the first pharmaceutical knowledge bases. The Therapeutic Target Database (TTD) offers data on drug-target interactions and pharmaceutical combinations. These datasets are derived from sources such as books, journal papers, the FDA drug database, drug manufacturer statements, and the US patent database [22].

DailyMed, SIDER, TWOSIDES, DDInter, pharmaceuticals.com, and MecDDI are libraries that offer data on diverse drugs, side effects, and drug-drug interactions [23]. DailyMed includes information on 96,955 different drugs, while SIDER compiles data on 1,430 drugs, 5,868 adverse reactions, and 139,756 drug adverse event combinations. TWOSIDES features 59,220 drug pairings and 868,221 significant connections linked to 1,301 adverse events [24, 25]. DDInter contains 240,000 documents related to drug-drug interactions (DDIs), encompassing details about 1,833 drugs [26, 27]. Pharmaceuticals.com provides educational information on more than 24,000 prescription medications, over-the-counter treatments, and natural products. Additionally, MecDDI offers a comprehensive analysis of drug-drug interaction

processes and supplies valuable data for researchers looking to predict new DDIs.

3. Prediction of Undirected Drug-Drug Interactions

Undirected drug reactions occur when two drugs are taken together or in sequence, resulting in one drug affecting the properties of the other, regardless of the order in which they are administered. This type of drug interaction focuses solely on the combination of medications used, without considering the specific effects of the drug-drug interaction (DDI). For example, it does not take into account whether the effect of a single drug is enhanced or diminished, whether the effects of multiple drugs are increased or decreased simultaneously, or whether the interaction results in a beneficial or antagonistic outcome. These nuances are overlooked in cases of undirected drug interactions.

The method for predicting undirected drug interactions aims to identify unanticipated drug association labels by utilizing drug information with established classifications. The interaction labeling indicates the likelihood of drug interactions, with label 0 representing no interaction and label 1 indicating an interaction. Estimating undirected drug-drug interactions can be categorized into traditional machine-learning techniques, alternative machine-learning methods, and deep-learning approaches [29].

4. Conventional Machine Learning Techniques

Comparison evaluations focus on aligning processes induced by drugs, protein structures, molecular designs, and their functions. Vilar et al. [30] identified novel drug-drug interactions (DDIs) through an analysis of molecular structural analogies, utilizing the chemical structure features of drugs found in reported DDI data for predictive modeling. Gottlieb et al. [31] developed a computational framework for predicting drug interactions called INDI, which evaluates the similarity of chemical compositions and adverse reactions of drugs concurrently. This framework calculates seven categories of drug similarity and combines these attributes to create a feature that reflects the highest resemblance among drug pairs.

Logistic regression is an analytical framework used in machine learning and data analysis to assess the probability of binary outcomes. It serves as a regression model when the dependent variable is binary (0 or 1) and aims to find the best-fit line that defines the relationship between the dependent variable and independent variables. Ferdousi et al. [32] utilized the Russell-Rao method, incorporating key biological factors like transporters, proteins, and targets, to assess the compatibility of drug pairs using 12 binary vectors. This approach can predict over 250,000 potential unknown DDIs.

Documented drug-drug interactions (DDIs) are utilized as input for binary classification to predict additional potential interactions between medication combinations [33, 34]. Li et al. [35] introduced Probability Ensemble Approaches (PEA) that predict DDIs by leveraging molecular and pharmacological features through Bayesian network simulations and similarity methods. Kim et al. [36] enhanced the linear kernel concept by incorporating medical terminology and grammatical features, developing five distinct feature types to capture complex data.

Cheng et al. [37] created a methodology for modeling systems on a heterogeneous graph that combines phenotypic, therapeutic, pharmacological, and genetic characteristics of drugs. Yan et al. [38] provided a model that integrates multiple pharmacological features, calculating the cosine similarity among these variables as input for their classifier, ultimately employing a Recursive Least Squares (RLS) predictor to assess the likelihood of DDIs. Hung et al. [39] focused on forecasting potential adverse drug-drug interactions related to osteoporosis and Paget's disease, demonstrating the effectiveness of machine-learning techniques in predicting harmful drug-drug interactions specific to certain conditions.

Conventional machine learning methods predict unstructured drug impacts by employing similarity assumptions and classification techniques. Unconventional machine learning methodologies use a wider array of approaches and models to generate forecasts using conventional procedures and methodologies.

5. Prediction of drug-target associations

Drug-target interfaces (DTIs) are the specific interactions between an active drug ingredient and a protein or enzyme within human tissue cells, leading to therapeutic effects. Advancements in drug target association technology have significantly accelerated the study of drug interactions, allowing researchers to more accurately predict the interactions between drug molecules and specific target proteins or enzymes in human cells. This method enhances the efficiency of discovering potential therapeutic targets, speeding up the drug discovery process and facilitating the development of safer and more effective pharmaceuticals [40].

Machine learning techniques have become a preferred tool for data analysis to predict treatment targets due to their effectiveness and cost-efficiency. However, predicting drug-target relationships using machine learning is subjective and cannot precisely explain the specific mode of action of a drug receptor [41]. Zhang et al. [42] proposed a system for predicting drug-target interactions by combining the chemical structural properties of the drug with the amino acid composition and spatial information of the protein. Chen et al. [43] introduced DNN-DTIs, a technology for predicting drug-target interactions, which achieved an impressive 98.78 percent reliability on Kuang's dataset.

Artificial intelligence techniques have significantly improved the efficiency of identifying drug-target interactions. Current research focuses on developing a comprehensive and systematic approach for accurately identifying DTIs across diverse datasets. These technologies have the potential to greatly accelerate the drug discovery process and lead to the development of more effective and safer pharmaceuticals [44].

6. The forecasting of drug-to-drug interaction occurrences

Many machine learning algorithms have been developed to predict drug-drug interactions (DDIs); however, most of these algorithms are intended to ascertain if two drugs would interact. DDI prediction approaches generally include two scenarios: one involves predicting the existence of an interaction between two medications, while the other entails predicting the nature of the interaction, event, or impact that occurs between the drugs. The latter is a binary classification problem, while the former is a multi-classification task.

DDI response patterns may generally be classified into three categories: synergy, antagonism, and no reaction. The optimal outcome is the occurrence of a synergistic response; in other words, these procedures are often used to ascertain if the combined impacts of medications A and B surpass the effects of each drug administered separately. The most detrimental result of combination therapy is an antagonistic reaction, resulting in diminished therapeutic effect; when drugs A and B are administered concurrently, their collective effectiveness is inferior to the sum of their separate efficacies [45].

Moreover, antagonistic responses may induce additional adverse effects, perhaps proving lethal to the patient. When administered concurrently, Drugs A and B exhibit no effects beyond those seen with each drug individually, indicating a lack of interaction between the two treatments. Antagonistic medication-drug interactions constituted 30% of all known adverse drug events [46-49]. Clinical trials may identify the nature of medication interactions; however, in vitro approaches are generally time-consuming, labor-intensive, and often lack repeatability [50-53]. Consequently, it is essential to use computational approaches to identify the kind of drug-drug interactions (DDI) in pharmacological

research, which may aid in developing secure and more effective prescriptions for medication combinations and may facilitate the understanding of the underlying causes of adverse drug responses [54].

7. Prediction of asymmetric medication interactions

Drug-drug interactions (DDIs) encompass various types, including asymmetric drug relationships. Experimental tests have demonstrated discrepancies in DDIs. Wicha et al. [55] found that most pharmacological arrangements involving antifungal and non-antifungal agents resulted in unidirectional interactions. Terbinafine could facilitate unidirectional opposition through its effect on ergosterol, while Amphotericin B significantly increased its INT value, although its EC50 remained relatively stable. Noguchi et al. [56] introduced mining association rules as an innovative method for predicting asymmetric drug-drug interactions (DDIs), using the connection rule B→A∩C. The asymmetric relationship is characterized by the impact of the perpetrator's drug on the unidirectional activity of the target drug.

In polypharmacy, asymmetric interactions influence the sequence of drug administration. An assessment of the optimal temporal sequence for intravenous administration of vincristine and cyclophosphamide showed no synergistic benefit when given concurrently, but an incremental effect was observed with prolonged administration. Developing innovative deep-learning techniques for predicting asymmetric DDIs is essential [57].

DGAT-DDI is the first approach for forecasting asymmetric DDI, employing a graph attention network (GAT) on a targeted drug interactions map to encode the drug's attributes [29]. The method considers factors of aggressiveness and susceptibility, evaluating the influence of the number of pharmaceutical interactions on their interaction tendencies. The DGAT-DDI prediction module identifies asymmetric interactions between drugs using two proximity measurements and role-specificity components [58].

8. Improving Care for Complex Patients:

Enhancing the management of difficult patients, especially the elderly and those with chronic illnesses, presents a multidimensional issue in healthcare. Older persons, often managing several health conditions, typically engage in polypharmacy, the concurrent use of many drugs [59]. Polypharmacy markedly elevates the likelihood of medication interactions, potentially resulting in severe effects and problems [60]. Patients with chronic diseases, including diabetes and heart disease, may need many drugs for successful health management [61,62]. These individuals have comparable risks of medication interactions, requiring meticulous treatment and oversight by healthcare professionals.

A primary strategy to mitigate these concerns is the use of drug databases and electronic health records (EHRs). These technologies assist healthcare practitioners in monitoring all drugs a patient is taking, therefore decreasing the chance of dangerous drug interactions. EHRs provide a detailed account of a patient's medication history, allowing doctors to make educated judgments about the prescription of new drugs or modifications to current ones. The incorporation of decision support systems into electronic health records might improve this process by notifying doctors of possible medication interactions and contraindications in real time [63].

9. Building Trust in the Healthcare System:

The significance of establishing trust within the healthcare system is paramount. Minimizing medical mistakes is an essential component of this initiative. The use of EHRs with pharmaceutical databases has shown an enhancement in healthcare quality by reducing mistakes associated with drug prescription and administration. These technologies guarantee that healthcare personnel possess precise and current information, therefore improving patient safety and results [64].

Transparency in healthcare is an essential element in fostering trust. Medication databases and electronic health records provide dependable information that is available to both healthcare providers and patients. This accessibility fosters an open and transparent healthcare environment, enabling patients to engage more actively in their treatment choices. Research indicates that patients with access to their health data and comprehension of their prescription regimens are more inclined to comply with their treatment programs. Furthermore, this openness cultivates a collaborative connection between patients and healthcare professionals, enhancing trust and elevating overall treatment quality [65].

Practical examples demonstrate the significance of these technologies. A significant instance is the interaction between warfarin, a frequently given anticoagulant, and some antibiotics. Certain antibiotics may enhance the efficacy of warfarin, resulting in a heightened risk of hemorrhage [66]. Utilizing pharmaceutical databases enables healthcare practitioners to detect interactions before providing antibiotics to patients on warfarin, thereby averting adverse effects.

Likewise, statins, often used to reduce cholesterol levels, may interact with other pharmaceuticals, increasing the chance of muscular injury [67]. Statins are processed by hepatic enzymes, and some medications may obstruct these enzymes, resulting in elevated statin concentrations in the bloodstream. Utilizing medication databases, doctors may ascertain individuals at risk and implement suitable interventions, such as modifying the statin dosage or selecting an alternate medicine [68].

Consequently, enhancing the management of difficult patients, especially senior citizens and those with chronic ailments, needs a holistic strategy that incorporates prescription databases and electronic health records (EHRs). These instruments not only mitigate the likelihood of medication interactions and medical blunders but also augment transparency and foster confidence in the healthcare system. By providing precise and current information, they allow healthcare practitioners to make educated choices and facilitate more patient involvement in their treatment. Practical instances, such as the interactions between warfarin and antibiotics or statins and other pharmaceuticals, highlight the essential function of these technologies in safeguarding patient safety and enhancing health results [69]. The ongoing evolution of healthcare necessitates the integration of modern information systems to effectively handle the intricate demands of patients and provide high-quality treatment.

10. Obstacles and Future Direction

The occurrence of adverse drug-drug interactions (DDIs) poses a significant threat to patient safety and the efficacy of medication delivery. In recent years, machine learning has gained prominence in bioinformatics, proving effective in predicting DDIs and mitigating the risks associated with such interactions. Consequently, there is a pressing need to develop more advanced machine-learning techniques for predictive modeling. This research systematically classifies AI methodologies for DDI prediction based on various types of drug interactions and addresses the challenges associated with future DDI prediction tasks.

One of the persistent challenges is enhancing the interpretability of existing models. It is essential to understand the roles of different factors in predicting effectiveness and the fundamental principles of model design to improve interpretability. Biomedical elements, including medication interactions and properties, involve complex linkages and hidden structural information, necessitating the integration of diverse data to build reliable models. As a result, the successful amalgamation of information from multiple sources and the development of strategies for its effective use in training models has become a critical research focus. The quality of data is essential for ascertaining the correctness and reliability of analytical results. Obtaining accurate information from diverse sources and developing strategies for its

effective incorporation into learning models provide significant issues requiring future investigation.

Numerous research studies lack evidence-based backing for anticipated results, and reliance simply on model assessment criteria is inadequate. Thorough clinical validation is required to verify the accuracy of forecasts. Current research evaluates models from several perspectives; nevertheless, a common standard for model assessment is absent owing to the varying focal points of the models. Consequently, it is essential to assess and contrast various models from different viewpoints. Researchers are pursuing a comprehensive, conclusive highest-quality dataset for evaluating and assessing objectives.

The investigation of drug interaction events is increasingly prominent and merits additional research; however, no models have been established to predict in vivo drug interactions in humans, remaining confined to in vitro experiments. Advancing the ability to hypothesize potential in vivo drug interactions post-administration in specific populations would significantly alleviate the burden on clinical practitioners and expedite the drug development process, representing a pivotal avenue for the advancement of drug repurposing initiatives. Moreover, asymmetric drug interaction investigations show significant potential, with just one existing prediction framework, DGATDDI. We assert that pioneering research may be undertaken in the future based on DGATDDI.

Currently, it is essential to tackle the issue of the imbalance in drug interaction samples. Initially, the quantity of drug-drug interactions (DDIs) identified from the medical database is markedly lower than the amount of drug combinations devoid of DDIs. Regrettably, an adequate resolution to address this data inconsistency has yet to be identified. Secondly, several objectively existing medication interactions remain undetected and aren't recorded in established databases. Consequently, in the validation of model effects or the assessment of metrics, possible false-negative data (drug combinations without interactions) may include unknown drug-drug interactions (DDIs). Exploring methods to detect these probable false-negative samples is advisable.

11. Conclusion

This study thoroughly examines AI-driven methodologies to forecast drug relationships, classified into three primary categories: estimate of unstructured drug relationships, incidence of interactions between drugs, and prediction of asymmetric drug relationships. Drug-drug interaction databases are essential for safeguarding patient safety, improving therapeutic efficacy, and facilitating clinical decision-making. Additionally, they help reduce healthcare costs, promote scientific research, and harness technological advancements in the healthcare sector.

In future model creation for DDI issue-solving, one may ascertain which problem categories are most effectively addressed using the three aforementioned methodologies. Additionally, the biological databases and datasets frequently utilized in drug interaction forecasting are presented. We delineate the attributes and impacts of classical models across three distinct study domains concerning medication interactions, while also addressing the obstacles and future possibilities in the identification of drug interactions. Ultimately, we anticipate that upon reviewing this study, researchers in the domains of AI as well as DDI estimation will choose a more suitable methodology that corresponds with their research competencies. For instance, they may concentrate on asymmetric drug relationships inside targeted graphs, drug interaction occurrences in multi-type forecasts, or unstructured drug connections in binary categorization. The initial efforts detailed in these three areas may inspire researchers for future enhancements and research trajectories.

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فحص معمق لقواعد بيانات التفاعلات الدوائية: تعزيز سلامة المرضى من خلال النماذج التنبؤية المتقدمة وتقنيات الذكاء الاصطناعي

الخلفية:

تشكل التفاعلات الدوائية (DDIs) خطرًا كبيرًا على سلامة المرضى، مما يؤدي إلى آثار جانبية وزيادة في حالات دخول المستشفى. مع تزايد استخدام الأدوية المتعددة، خاصة بين كبار السن والمرضى الذين يعانون من أمراض مزمنة، أصبح فهم التفاعلات الدوائية والتنبؤ بها أمرًا ضروريًا للإدارة السريرية الفعالة.

المنهجية:

تقوم هذه المراجعة بتجميع الأدبيات الحالية حول قواعد بيانات التفاعلات الدوائية ودورها في التنبؤ بـ .DDIs تم إجراء بحث منهجي في قواعد البيانات ذات الصلة، مع التركيز على الدراسات التي تستخدم تقنيات الذكاء الاصطناعي (AI) والتعلم الآلي للتنبؤ بالتفاعلات الدوائية. تم تحليل قواعد بيانات رئيسية مثل DrugBankو PubChemو PharmGKBلدراسة مساهماتها في أبحاث التفاعلات الدوائية.

النتائج:

تشير النتائج إلى أن الأساليب المدعومة بالذكاء الاصطناعي تعزز بشكل كبير من تحديد التفاعلات الدوائية والتنبؤ بها. تم توظيف العديد من تقنيات التعلم الآلي، التقليدية وغير التقليدية، لتقييم التفاعلات الدوائية بفعالية. تسلط المراجعة الضوء على أمثلة حقيقية للتفاعلات الدوائية الحرجة، مما يوضح الآثار السريرية لهذه التفاعلات. توفر قواعد البيانات أدوات أساسية لمقدمي الرعاية الصحية لإدارة الأدوية ومنع الأحداث الضارة.

الاستنتاج:

يعد دمج قواعد بيانات التفاعلات الدوائية في الممارسات السريرية أمرًا ضروريًا لتحسين سلامة المرضى وفعالية العلاج. ينبغي أن تركز الأبحاث المستقبلية على تعزيز القدرات التنبؤية لهذه النماذج من خلال التكامل المستمر للبيانات والتحقق من صحتها. من خلال الاستفادة من التقنيات الحسابية المتقدمة، يمكن لأنظمة الرعاية الصحية التنبؤ بالمخاطر المرتبطة بالتفاعلات الدوائية والتخفيف من حدتها بشكل أفضل.

الكلمات المفتاحية:

التفاعلات الدوائية، الذكاء الاصطناعي، التعلم الآلي، سلامة المرضى، اليقظة الدوائية.