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A Comprehensive Review on Artificial Intelligence in Drug Discovery

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ABSTRACT

Artificial intelligence (AI) is a key component in the development of novel medications, and artificial neural networks, including deep neural networks and recurrent neural networks, are the main driving force behind this research. In recent years, applications for predicting molecular properties or activities, such as physicochemical features and ADMET traits, have increased substantially. These applications rely on quantitative structure–property relationships (QSPR) and quantitative structure–activity relationships (QSAR), which further strengthen the versatility of this technology. In de novo drug design, artificial intelligence guides the synthesis of novel, physiologically active, and functional molecules toward specific desired properties. Several examples have demonstrated the success of artificial intelligence in this field. Through synthesis planning and improved ease of synthesis, AI enables the integration of synthesis with drug discovery, and consequently, computer-assisted drug development is expected to expand in the near future. However, the pharmaceutical industry is currently facing challenges in sustaining drug development efforts due to reduced productivity and increasing research and development expenditures. Therefore, this article examines the main factors influencing attrition rates in new drug approval, explores possible solutions, reviews different types of AI-based software aimed at enhancing the effectiveness of the drug research process, and discusses partnerships between AI-driven pharmaceutical companies and major pharmaceutical industry leaders.

***Keywords:** Artificial intelligence, AI-powered drug development companies, quantitative structure-property correlations, AI-based software*

Introduction

Artificial intelligence (AI) is the science and technology involved in designing machines, particularly intelligent computer programs capable of performing tasks that typically require human intelligence. Although AI is conceptually similar to using computers to analyze human intelligence, it is not limited to processes observable through biological means [1,2]. The first AI program, Logic Theorist, developed in 1956 by Allen Newell and associates, marked a foundational milestone in the field [3]. Despite not fully achieving its initial goals, AI has found widespread applications across industries due to its ability to perform complex computational tasks. Modern AI techniques, including image analysis, voice translation, and robotics, have expanded beyond computer science into diverse scientific domains such as biology, chemistry, and pharmaceuticals. In pharmaceutical research, AI has enabled novel methods for organic synthesis, improved understanding of complex biological systems, and facilitated the creation of new active pharmaceutical ingredients (APIs). It also supports advanced analytical and diagnostic tool development and is applied in metabolic prediction, drug development, drug repurposing, and drug discovery [4]. The increasing availability of multiomics data and advances in high-performance computing have made real-world AI applications feasible, allowing efficient processing of large-scale biological datasets. AI-driven approaches have been integrated into drug discovery pipelines, including de novo design, bioavailability prediction, and drug target identification [5]. Collaborations between major pharmaceutical companies, such as Pfizer, Roche, and Bayer, and IT firms highlight the growing adoption of AI for drug development and manufacturing, with examples like Insili-

co Medicine's AI-discovered treatment for idiopathic pulmonary fibrosis showing promising outcomes. These advances have collectively transformed pharmaceutical research, giving rise to Artificial Intelligence in Drug Discovery (AIDD). While still in early stages compared with ligand-based or structure-based drug design, AIDD and machine learning–driven drug discovery (MLDD) are increasingly applied to complex challenges. Techniques such as ANN (Artificial Neural Network), DNN (Deep Neural Network), RNN (Recurrent Neural Network), CNN (Convolutional Neural Network), GA (Genetic Algorithm), SVM (Support Vector Machine), Bayesian networks (Bayesian Networks), decision trees (Decision Trees), logistic regression (Logistic Regression), Naïve Bayes (Naïve Bayes Classifier), and k-NN (k-Nearest Neighbors) are widely used in computational drug design [6-10].

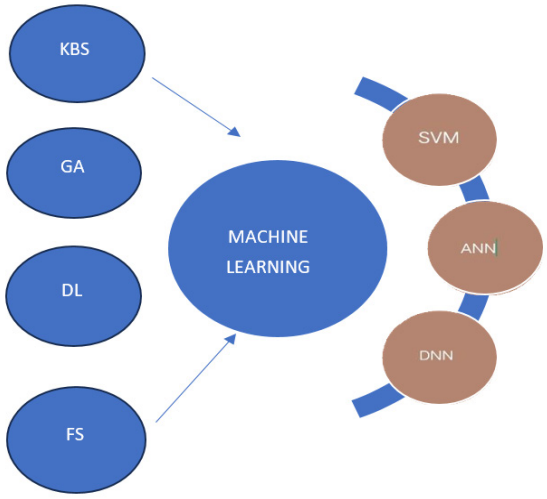

Figure 1. Artificial Intelligence in Drug discovery (AIDD).

Introduction to AI and Its Potential use in Drug Discovery

The application of artificial intelligence (AI) in medicinal chemistry has increasingly garnered attention in recent years, emerging as a potential game-changer for the pharmaceutical industry [11]. The process of discovering and developing new drugs, traditionally known as drug discovery, is inherently challenging and time-consuming, relying heavily on labor-intensive methods such as high-throughput screening and trial-and-error experimentation. In contrast, AI methodologies, including machine learning (ML) and natural language processing (NLP), offer the potential to enhance and accelerate this process by enabling the precise analysis of vast datasets, thereby improving decision-making and predictive accuracy [12]. Recent studies have demonstrated the successful implementation of deep learning (DL) to accurately evaluate drug efficacy [13], while AI-based approaches have also been applied to predict potential toxicity of drug candidates [14]. Collectively, these advances indicate that AI can substantially improve the effectiveness and efficiency of the drug discovery process. Nonetheless, the application of AI for designing novel bioactive compounds presents both technical challenges and ethical considerations, necessitating further investigation to fully delineate its advantages and limitations [15].

The Impact of AI on the Drug Discovery Process and Potential Cost Saving

One of the most impactful applications of AI in drug discovery is the rapid generation of novel compounds with specific desired properties. Unlike traditional methods, which depend on laborious processes to discover and modify existing molecules, AI-based techniques facilitate the efficient design of molecules with predefined structural and functional characteristics [16]. For instance, DL systems trained on datasets of known medicinal molecules and their properties, including solubility and bioactivity, have successfully generated new drug candidates. Notably, DeepMind's AlphaFold platform represents a groundbreaking development in structural biology, accurately predicting the three-dimensional structures of proteins from sequence data [17]. Such advancements are anticipated to revolutionize drug discovery and personalized medicine. Furthermore, the integration of molecular dynamics (MD) simulations with machine learning techniques has improved the efficiency and accuracy of de novo drug discovery, leveraging synergistic effects between computational methods [18]. Deep learning and interpretable machine learning (IML) approaches are increasingly applied in this context, combining with MD simulations to optimize drug development processes.

Roles of AI in Drug Discovery [11]

AI in Drug design

Drug design has been revolutionized by artificial intelligence (AI), which makes it possible to identify and optimize novel chemical entities using data. From molecular representations like SMILES strings, molecular graphs, and protein structures, artificial intelligence (AI) models such as deep learning (DL), support vector machines (SVMs), and generative frameworks may directly predict molecular characteristics, binding affinity, and biological activity [19]. These techniques frequently outperform conventional rule-based methods in facilitating de novo chemical design, scaffold hopping, and quantitative structure–activity relationship (QSAR) modeling [20]. AI can rank drugs with advantageous interactions and pharmacokinetic features by integrating with molecular docking and scoring mechanisms [21]. AI-driven drug design increases the likelihood of success in early-stage drug discovery, lowers trial costs, and speeds up lead identification and optimization [22].

AI in poly pharmacology

The study of pharmacological interactions with numerous targets, or polypharmacology, is essential for multi-target drug design and complicated disorders. Predicting off-target effects, drug–target interactions, and side-effect profiles is becoming more and more common with AI techniques such deep neural networks (DNNs), graph neural networks (GNNs), and multi-task learning models [23]. AI can find possible multi-target modulators, maximize selectivity, and reduce side effects by examining chemical, genomic, and proteomic datasets [24]. AI-guided polypharmacology improves efficacy and safety by enabling logical multi-target drug creation, repurposing of current medications, and customized medicine techniques [25].

AI in chemical synthesis

By forecasting reaction results, retrosynthetic paths, and ideal reaction circumstances, AI is also transforming chemical synthesis [26]. Automated synthesis planning is made possible by machine learning and deep learning models that have been trained on reaction databases. These models are able to prioritize reagents, estimate yields, and recommend synthetic paths [27]. AI-based retrosynthetic analysis helps find different synthetic approaches for complicated molecules while cutting down on the time and expense of chemical experiments [28]. AI can carry out and improve synthetic processes iteratively through integration with robots and automated laboratory platforms, speeding up the conversion of computer designs into physical substances [29].

AI in Drug screening

High-throughput drug screening creates extensive datasets that are perfectly suited for analysis using AI. AI models such as DNNs, SVMs, and ensemble learning techniques are utilized for virtual screening, hit identification, and the prioritization of potential molecules [30]. These models utilize molecular descriptors, fingerprints, and structural characteristics to forecast activity, selectivity, and toxicity, enhancing the effectiveness of both ligand- and structure-based screening efforts [31]. AI speeds up the drug discovery process by minimizing the number of experimental assays needed, enhancing hit rates, and facilitating the early identification of possible failures [32].

Knowledge Based System (KBS) In Drug Discovery

Encompass multiple domains, including drug design, poly-pharmacology, chemical synthesis, and high-throughput drug screening. A particularly important AI tool in this space is the knowledge-based system (KBS), a computational method that integrates and applies knowledge from multiple sources [33]. KBS frameworks, including knowledge bases (KB), fact bases (FB), and rule bases (RB), are often combined with inference engines to form expert systems (ES) capable of supporting complex decision-making. Various drug-related KBS have been developed, such as PharmGKB, which focuses on drug-gene interactions [34,35]; DailyMed, which catalogs drug-disease information [36]; SuperTarget, covering drug-target interactions; and merged-PDDI, addressing drug-drug interactions [37]. These systems support applications such as drug repositioning, predicting beneficial drug combinations, and facilitating the integration of multi-omics data. Nevertheless, challenges remain regarding KBS integration, implementation, predictive accuracy, and the elimination of negative samples [38]. Knowledge-based scoring functions, frequently applied in computational drug design, leverage statistical observations of intermolecular interactions from extensive 3D structural databases. Prominent scoring functions, including Smog, ASP, DSX, IT-Score, and Drug Score, utilize this approach to guide molecular docking and structure-activity relationship (SAR) analyses [39-41].

Genetic Algorithms (GA) In Drug Discovery

Genetic algorithms (GA) represent another powerful AI technique in drug discovery. These algorithms emulate natural selection to iteratively evolve optimal solutions to constrained and unconstrained optimization problems. Across successive generations, data are modified through fitness-based selection, crossover, and mutation, gradually refining solutions [42-45]. GA methods are widely applied in QSAR modeling, molecular docking, and descriptor selection [46]. For example, Sun et al. employed GA combined with QSAR to identify methyl transferase inhibitors, applying multilevel regression for statistical validation [47]. In molecular docking, GA evaluates multiple conformers per generation, refining selections based on docking scores derived from knowledge-based energy functions. Tools such as AutoDock (Lamarckian GA), Glide, AutoGrow, and MoleGear implement GA for lead optimization, including de novo ligand design [48-50]. The GANDI framework further extends GA to parallel processing, enhancing efficiency in lead optimization [51].

Machine Learning (ML) In Drug Discovery

Machine learning (ML) is extensively utilized in drug discovery to identify patterns and generate predictive models from large datasets. Unlike traditional methods, ML algorithms learn from data rather than manually encoding relationships, with commonly used approaches including artificial neural networks (ANN), support vector machines (SVM), random forests (RF), logistic regression (LR), and naïve Bayes (NB) [52,53]. Deep neural networks (DNN) are increasingly applied to characterize nonlinear relationships between molecular descriptors and therapeutic outcomes, often surpassing traditional QSAR models in predictive performance. Tools such as Chemception exemplify DNN applications for drug discovery [54-56]. Moreover, explainable artificial intelligence (XAI) methods enhance interpretability, offering transparency, justification, and uncertainty estimation for ML-driven predictions [57]. Recent investigations have explored the application of recurrent neural networks (RNN), convolutional neural networks (CNN), and DNNs in drug design, further expanding the capabilities of AI in pharmaceutical research [58].

Deep Learning (DL) in Drug Discovery

A key artificial intelligence paradigm in drug development is deep learning (DL), which makes it possible to automatically understand intricate, nonlinear correlations from sizable chemical and biological datasets [59,19]. DL models reduce reliance on manually designed descriptors by using multilayer neural networks to directly extract hierarchical representations from molecular graphs, SMILES strings, protein sequences, and omics data [60]. In QSAR modeling, virtual screening, molecular property prediction, and drug–target interaction analysis, architectures like convolutional neural networks (CNNs), graph neural networks (GNNs), recurrent neural networks (RNNs), and transformer-based models are frequently used, frequently outperforming conventional machine learning techniques in predictive accuracy and scalability [61]. DL techniques enhance molecular docking and binding affinity prediction in structure-based drug design by capturing complex ligand–protein interaction patterns that go beyond traditional scoring functions [62]. Additionally, generative DL frameworks, such as diffusion-based models, variational autoencoders (VAEs), and generative adversarial networks (GANs), allow for de novo mo-

lecular design tuned for many goals, including potency, selectivity, and ADMET characteristics [63]. Recently, DL has been combined with multi-objective optimization techniques and reinforcement learning to further speed up lead discovery and optimization, providing effective and affordable early-stage drug development options [64].

Feature Selection (FS) in AI-Based Drug Development

Finding the most informative molecular, biological, or clinical descriptors from high-dimensional datasets is the goal of feature selection (FS), a crucial preprocessing stage in AI-driven drug discovery [65]. FS enhances model robustness, predictive accuracy, and interpretability by removing redundant or noisy variables and minimizing redundancy, especially in QSAR modeling, ADMET prediction, and biomarker identification [61]. FS approaches are frequently divided into three categories: filter, wrapper, and embedding methods. Each of these approaches offers unique trade-offs between predictive effectiveness and computing economy [66]. While wrapper approaches assess subsets of features based on model performance, frequently employing optimization techniques like genetic algorithms, filter methods use statistical criteria to rank features independently of the learning algorithm [67]. Regularized regression and tree-based algorithms are examples of embedded techniques that incorporate feature selection directly into model training [68]. Effective FS supports dependable and comprehensible AI models for early-stage drug development by reducing overfitting in short or unbalanced datasets and promoting mechanistic insight by identifying important physicochemical or biological determinants of activity [63].

Support vector machines (SVMs)

Support vector machines (SVMs) are supervised machine-learning algorithms that are used for both regression and classification tasks. They work especially well with high-dimensional, nonlinear datasets that are frequently employed in drug development. In order to improve model generalization, SVMs compute an ideal separating hyperplane that optimizes the margin between data points of various classes [69]. Kernels like linear, polynomial, radial basis function (RBF), and sigmoid kernels are used to transfer input data into higher-dimensional feature spaces for nonlinear situations such that linear separation is possible. In order to minimize overfitting in small and noisy datasets, regularization parameters that balance model complexity and prediction error regulate the performance of SVM models [70]. SVMs are widely used in virtual screening, ADMET property prediction, and quantitative structure–activity relationship (QSAR) modeling.SVMs frequently outperform conventional regression-based techniques in QSAR research by establishing strong connections between chemical structure and biological activity using molecular descriptors, fingerprints, and physicochemical attributes [71]. To differentiate between active and inactive drugs across a variety of therapeutic targets, SVM-based descriptor selection and classification has proven to be effective [72]. For example, research has shown that SVM models are useful for predicting receptor ligands and enzyme inhibitors using optimal molecular feature sets that have been verified by cross-validation and external test datasets [73]. SVMs have been incorporated with molecular docking procedures in structure-based drug development to enhance scoring and post-docking analysis. In contrast to traditional scoring functions, SVM-based scoring functions trained on known protein–ligand complexes are used to analyze docked conformations, enabling better discriminating between real binders and false positives [74]. Additionally, SVM classifiers are frequently employed in ADMET and toxicity screening, where they use chemical and biological descriptors to predict features including blood-brain barrier permeability, cardiotoxicity, and hepatotoxicity [75]. SVMs continue to be a crucial machine-learning technique in AI-assisted drug discovery because of their resilience, scalability, and solid theoretical underpinnings, especially in situations with little experimental data and high descriptor dimensionality [76].

Artificial neural networks (ANNs)

In artificial intelligence-based drug development, artificial neural networks (ANNs), which are computational models inspired by the structure and operation of the human brain, are frequently used to solve challenging nonlinear classification and regression issues [77]. ANNs are made up of interconnected processing units (neurons) arranged into input, hidden, and output layers. Activation functions are used to alter and convey information through weighted connections [78,79]. In order to reduce prediction error, model training entails iteratively adjusting these weights using learning methods like backpropagation [80]. ANNs are ideal for modeling complex interactions between chemical structure and biological activity in high-dimensional datasets due to their capacity to approximate nonlinear functions [81]. ANNs are extensively utilized in virtual screening, QSAR modeling, and pharmacokinetic and toxicological property prediction. They frequently outperform traditional machine-learning techniques in predicting bioactivity by utilizing physicochemical characteristics, fingerprints, and molecular descriptors [82]. Enzyme inhibitors and receptor ligands can be successfully identified thanks to descriptor optimization over training generations, which increases model accuracy and resilience [61]. By learning intricate ligand-protein interactions, ANN-based scoring functions improve binding affinity predictions in structure-based drug design, surpassing conventional scoring techniques [83]. In order to decrease late-stage drug attrition, ANNs are also used in ADMET and toxicity prediction [84]. ANNs continue to be a crucial tool in AI-driven lead optimization and drug development due to expanding biological datasets and processing power [85].

Deep Neural Networks (DNNs)

Drug development is increasingly using deep neural networks (DNNs), a sophisticated version of artificial neural networks (ANNs) with numerous hidden layers, to model intricate, nonlinear interactions in massive chemical and biological datasets [86]. They enhance predictive accuracy in QSAR modeling, virtual screening, and ADMET property prediction by automatically learning hierarchical features from molecular descriptors, SMILES strings, protein sequences, and omics data [82]. DNNs frequently outperform shallow neural networks and conventional machine-learning models in the identification of new enzyme inhibitors and recep-

tor ligands [87]. By capturing complex ligand-protein interactions beyond traditional techniques, DNN-based scoring functions improve binding affinity prediction in structure-based drug design [88]. DNNs also make pharmacokinetic and toxicity evaluations easier, which lowers late-stage failures. DNNs are essential to AI-assisted drug discovery and lead optimization due to the growing availability of data and computing capacity [89].

Limitation of AI in Drug Discovery

Even while AI-based drug discovery strategies are quite effective, their functionality and capacity are still limited. One important criticism many artificial intelligence (AI) methods, such as neural networks, are often thought of as little more than black boxes that attempt to connect input and output variables using training data. The tool's generalizability to situations that the data set did not sufficiently describe is thus immediately called into doubt by this. One of the disadvantages of the genetic algorithm approaches is that, despite the fact that the results are highly beneficial, there is no guarantee that the "optimal" choice will be reached. In terms of derivatization or heuristic reasoning, we cannot promise that the machine learning method will provide the same outcomes as the model. Some information is gleaned from the provided data by the model itself. Verifying which portion of the supplied data was used to train which machine learning component is difficult. Deep learning's poor performance with small to medium amounts of data is one of its well-known drawbacks [90].

Advantages of AI in drug discovery

1. **Improved Drug Stability and Formulation:** AI can forecast a wide range of environmental factors that may influence a drug's stability and shelf life, enabling the development of more robust and well-formulated pharmaceuticals.
2. **Cost and Time Efficiency:** Artificial intelligence reduces the time and financial resources required for research and development, making drug discovery processes more accessible and efficient.
3. **Error Minimization:** AI enhances accuracy and reduces human error in experimental and analytical procedures, improving the reliability of outcomes.
4. **Exploration of Complex Domains:** AI is applied in challenging fields such as mining, fuel exploration, and oceanography, where it can process vast datasets and correct human mistakes.
5. **Support for Daily and Digital Tasks:** AI assists with routine activities, such as navigation via GPS, predictive input on smartphones, and spelling correction, demonstrating its practical utility in daily operations.
6. **Digital Assistants:** AI-driven avatars and digital assistants in modern organizations optimize decision-making, reduce the need for human intervention, and provide objective, logic-based solutions, which may help counteract human emotional biases.
7. **Medical Applications:** AI enables physicians to assess patient conditions, predict adverse effects, and evaluate potential health risks associated with medications, supporting safer clinical decision-making.

Disadvantages of AI in drug discovery

1. **High Implementation Costs:** Establishing and maintaining AI systems requires substantial investment in advanced hardware, software, and ongoing maintenance, making it an expensive undertaking.
2. **Lack of Originality:** AI relies on pre-existing data and past experiences, limiting its capacity for creative or novel problem-solving. For example, the robot Quill can generate reports based on supplied data but cannot produce original insights.
3. **Potential for Unemployment:** Automation and AI-driven robotics can displace human labor in certain industries, raising concerns about workforce reduction.
4. **Cognitive Dependence:** Overreliance on AI for repetitive or monotonous tasks may reduce human engagement in problem-solving and memory retention, potentially fostering cognitive laziness in future generations.
5. **Emotionless Decision-Making:** AI systems lack emotions and interpersonal understanding, which are critical in collaborative and team-based research environments, limiting their ability to fully replace human interaction.

Conclusions

AI holds transformative potential in drug discovery, offering improvements in target identification, drug repurposing, and novel molecule design while reducing costs and development timelines. By uncovering hidden patterns in complex datasets, AI may accelerate the discovery of safer and more effective therapeutics. However, challenges remain, particularly regarding explainable AI, access to high-quality data, and integration into existing drug development workflows. Continued advances in AI technologies, coupled with collaborative efforts between developers and researchers, are expected to usher in a new era of innovation in pharmaceutical research, ultimately improving global health outcomes.

Conflicts of Interest

The authors declare no conflict of interest and received no specific funding for this work.

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