JOURNAL OF PHARMA INSIGHTS AND RESEARCH
ISSN NO. 3048-5428

REVIEW ARTICLE

Evaluating the Impact of AI and ML on Modern Drug Discovery

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Publication history: Received on 10th June; Revised on 20th June; Accepted on 2nd July 2024

Article DOI: 10.69613/8tckqp18

Abstract: Artificial intelligence has several effective applications, ranging from language modelling to pharmaceutical sector enhancement, and it speeds up and lowers the cost of medication research and development. As the amount of drug-related data increases, the deep-learning method has been applied at every stage of the drug development process. A broad overview of artificial intelligence (AI) and its use in medication research and discovery is discussed in this review. Drug metabolism, excretion, and recent advancements in colorectal cancer and tooth loss are discussed, along with the integration of plant-based traditional medicine and the use of computer-aided drug discovery and ligand-based quantitative structure activity and property (QSAR/QSPR) and De Novo drug design. The AI-assisted platform used to discover the serotonin 5-HT1A drug is demonstrated, and it reached the clinical trial in less than 12 months—a significantly shorter time than the conventional method, which requires four years to complete. The challenges, ethical considerations, and future perspectives of AI in drug discovery were also discussed in this review.

Keywords: Machine learning; Artificial intelligence; Computer-assisted drug research; Drug development; Drug discovery.

1. Introduction

Artificial intelligence (AI) has been increasingly employed in various domains of society, particularly in the pharmaceutical industry. The innovation of the AI approach has led to remarkable advancements in many fields, especially biological technology, to reduce the time, cost, and failure rate of drug discovery and development procedures [1]. Traditionally, the drug discovery process is known to be lengthy, taking around 12 years from preclinical research to final drug approval for human use. It is also an expensive endeavor, costing over 1.2 billion dollars, and is further complicated by the withdrawal of drugs from the market due to adverse side effects. However, complex systems like artificial intelligence (AI), including machine learning (ML) and deep learning (DL), have effectively expedited and reduced the cost of the drug development process [2,3].

AI, often referred to as machine intelligence, is the emulation of human intellect. It involves the use of software and systems that enable autonomous decision-making for specific goals by learning and interpreting from input data [4]. This allows a computer to simulate the cognitive processes associated with the human brain, such as learning and problem-solving [5]. AI leverages machine learning models, which are a subfield of computer science that combines engineering and statistics to create models or algorithms that accomplish tasks and provide behaviors like decision-making and prediction without explicit programming. Deep learning, a neural network approach, guides the machine's incoming data, increasing its accuracy and minimizing the system's bias [6]. These machine learning algorithms help predict the three-dimensional structure of the target protein, which is crucial in the search for new drugs [7]. Google's DeepMind (https://github.com/deepmind) recently developed AlphaFold, an AI-based tool that predicts 3D protein structure based on amino acid sequences, using PDB structural data as a training set [8,9]. Machine learning has been applied to various aspects of drug discovery and development, including small molecule design, target identification, and biomarker prediction, as demonstrated by Jessica Vamathevan et al. [10]. This review will briefly discuss the applications of AI, its limitations, and potential future uses, highlighting the value of AI in drug discovery.

2. AI role in drug discovery

AI offers several benefits in drug development, such as:

- Rapid screening of large chemical libraries: AI algorithms can quickly sort through millions of molecules to identify the most promising ones for further investigation [11].

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- Improved prediction accuracy for drug efficacy: AI algorithms can accurately predict the efficacy of potential compounds, allowing researchers to focus on the most promising candidates [12].
- Early detection of potential side effects: AI systems can predict the possible side effects of a compound before human testing, reducing the risk of adverse outcomes [13].
- Personalized medicine: AI can help researchers develop drugs tailored to specific individuals based on their genetic composition and other health information [14].
- Lower drug development costs: By optimizing the drug development process, AI drug discovery can significantly reduce the time and cost required to bring new drugs to market [15].
- AI is also being used to identify drug interactions, enhance drug efficacy, and optimize clinical trials. These applications of AI in drug development are opening up new avenues for research and have the potential to revolutionize the pharmaceutical industry [16].

Table 1. Comparison of Traditional and AI-Assisted Drug Discovery Approaches

Aspect	**Traditional Approach**	**AI-Assisted Approach**
Time	12-15 years [1]	Potentially reduced to 1-2 years [2]
Cost	$1.2-2.6 billion [3]	Potentially reduced by 30-50% [4]
Hit Identification	High-throughput screening (HTS) [5]	Virtual screening and AI-driven compound generation [6]
Lead Optimization	Iterative synthesis and testing [7]	AI-guided optimization and property prediction [8]
Preclinical Studies	Animal models and in vitro assays [9]	AI-driven toxicity prediction and biomarker analysis [10]
Clinical Trials	Phased human trials (I, II, III) [11]	AI-optimized patient selection and trial design [12]
Drug Repurposing	Serendipitous discovery [13]	AI-driven prediction of new indications [14]
Personalized Medicine	Limited by data availability [15]	AI-enabled tailoring of treatments to individuals [16]

3. Applications

One of the most significant AI breakthroughs was IBM Watson, whose development led to the creation of DeepQA software, a computer system that emulates competitive success on Jeopardy compared to elite players at the Jeopardy! Quiz show (www.jeopardy.com). DeepQA uses structured and unstructured data to logically answer questions through natural language processing, employing various models that are scored based on a training set through a testing set and screening with multilayer logistic regression [17]. Pfizer has extensively utilized this IBM Watson system to accelerate the search for drugs for immuno-oncology conditions.

Table 2. Examples of AI Applications in Drug Discovery and Development

Application	**AI Technique**	**Example**
Target Identification	Machine learning, deep learning	Identification of novel drug targets for COVID-19 [17]
Compound Screening	Convolutional neural networks (CNNs)	Screening of large chemical libraries for hits [18]
De Novo Drug Design	Generative adversarial networks (GANs)	Design of novel compounds with desired properties [19]
ADME/Tox Prediction	Random forests, support vector machines	Prediction of drug absorption, distribution, metabolism, excretion, and toxicity [20]
Biomarker Discovery	Deep learning, natural language processing	Identification of novel biomarkers for disease diagnosis and treatment response [21]
Drug-Drug Interactions	Graph neural networks (GNNs)	Prediction of potential adverse drug-drug interactions [22]
Clinical Trial Design	Bayesian optimization, reinforcement learning	Optimization of patient recruitment and dosing strategies [23]
Drug Repurposing	Knowledge graphs, network analysis	Identification of existing drugs for new therapeutic indications [24]

José Jiménez-Luna et al. investigated the use of AI-assisted computational models in drug discovery, specifically in ligand-based quantitative structure-activity and property (QSAR/QSPR) and De Novo drug design. Successful progress has been made in predicting pharmacokinetic parameters and biological activity using QSAR/QSPR. Molecular descriptors are used to provide machine-readable numbers representing the structural characteristics of molecules, including functional groups, pharmacophore distribution, and physicochemical properties [18]. Although ligand and/or structure-based approaches are the most well-known methods for creating unique molecular profiles with efficient pharmacological potency and characteristics, computer-assisted de novo drug creation remains a challenging task [19,20].

AI can assist in predicting the 3D structure of a targeted protein and discovering hit and lead compounds with faster confirmation of the therapeutic target [21]. PDBbind is a database that describes the protein-ligand structural complex [22]. HiFiBiO Therapeutics has established a novel translational platform of Drug Intelligence Science (DIS) that integrates AI/ML with single-cell technology to improve biomarker prediction and the discovery of high-quality, disease-associated drug targets [23]. This process yields high-resolution outcomes related to drugs, targets, and patients.

AI in drug research and development can enhance therapeutic efficacy and safety by accelerating metabolism and excretion, which is crucial for avoiding the accumulation of toxic substances that cause organ damage and metabolic disorders. Predictions of drug metabolism and excretion help in the development of new drugs with improved efficacy and reduced toxicity [24,25]. Numerous studies have demonstrated the importance of AI in predicting drug metabolism and excretion. For example, Khan addressed the integration of traditional medicine with AI in drug development, providing a framework for plant-based traditional medicine [26], while Ryza Rynazal employed a local explanatory technique to tailor bacteria strains as biomarkers for colon and rectal cancer [27]. Sumitomo Dainippon Pharma developed DSP-1181, the first AI-drug molecule and a serotonin 5-HT1A receptor agonist, which entered human testing in less than a year, in contrast to traditional medication [28]. Chen-Chang-Chen also developed an AI-based detection model for dentistry practitioners [29]

4. Limitations

Despite the significant advancements in drug development and innovation, the lack of accountability may hinder the adoption of AI [30]. AI is reported to generate harmful content, raising concerns about safety and misinformation. Moreover, the automation of specialized tasks may lead to job displacement; however, enhanced human skills may create new job opportunities and increase productivity. AI implications may also lead to ethical dilemmas regarding bias and data privacy. Although the data used to train the model should be handled carefully, AI/ML does not pose inherent ethical issues for the discovery of new drugs [31].

5. Opportunities of AI in drug discovery

Traditional drug discovery methods have historically been expensive, time-consuming, and error-prone. However, the emergence of machine learning drug discovery is transforming the industry [32]. Researchers can analyze vast amounts of data and identify potential chemical compounds with medicinal properties by using machine learning and big data analytics.

5.1. Target Identification

AI systems can rapidly analyze large databases of chemical and biological data to identify potential targets for drug intervention. By drawing insights from massive amounts of readily available data, researchers are better equipped to find potential therapeutic targets that were previously undetected [33,34].

5.2. Molecular Simulations

Molecular simulations help researchers understand how drug candidates interact with their molecular targets. AI models can predict the behavior of molecules in various scenarios, significantly reducing the time and cost of experimentation [35]. This means that researchers can screen a large number of molecules in a matter of days and identify the most promising ones for further investigation and development.

5.3. Prediction of Drug Properties

AI models can simulate the interactions that drug candidates will have with the human body based on chemical and biological data. By analyzing this data, AI can predict drug properties such as bioavailability, toxicity, and efficacy, providing crucial information about the therapeutic potential of drug candidates [36,37]. This knowledge enables scientists to make more informed decisions about which drug candidates to pursue and focus their efforts on areas with the highest likelihood of success.

5.4. Candidate Drug Prioritization

Once researchers have identified viable candidates, AI algorithms can rank potential therapeutic candidates by predicting their properties and comparing them with existing approved drugs. This can help researchers prioritize the most promising compounds, reducing the time and cost of bringing drugs to market [38].

5.5. Synthesis Pathway Generation

AI algorithms can predict the most efficient way to synthesize therapeutic candidates. By considering the properties of drug candidates and available resources, AI can generate synthetic routes that minimize the number of steps and reagents required while optimizing yields. This results in a more efficient and environmentally friendly drug production process [39].

5.6. Drug Repurposing

Drug repurposing involves using an already-approved drug for a new therapeutic purpose. AI models can identify the potential for therapeutic repurposing by analyzing existing drug data and identifying putative off-targets. Repurposing has significant advantages because existing drugs have known safety profiles, and the development of new drugs takes less time [40].

5.7. Drug Adherence and Dosage

AI algorithms that incorporate patients' genetic, physiological, and lifestyle data can help personalize drug adherence and dosage. AI can monitor a patient's response to treatment and adjust the dosage as needed to ensure the best possible therapeutic outcomes [41-43].

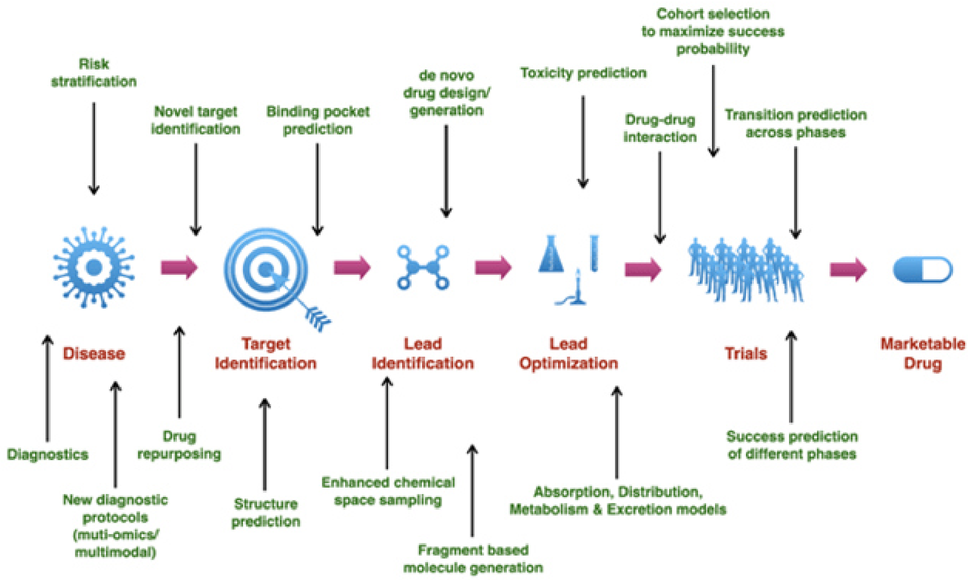

Figure 1. AI role in various phases of drug discovery

6. Conclusion

The practical application of Artificial Intelligence (AI) and Machine Learning (ML) in pharmaceutical settings is proving to be a crucial step in enhancing the reliability and efficiency of human decision-making processes. These technologies are not just supplementing but revolutionizing the entire drug research and development pipeline. Deep learning, a subset of AI, has been particularly impactful in accelerating the identification of promising drug candidates through Computer-Aided Drug Design (CADD) techniques.

References

[1] Vamathevan J, Clark D, Czodrowski P, et al. Applications of machine learning in drug discovery and development. Nat Rev Drug Discov. 2019;18(6):463-477.

[2] Chen H, Engkvist O, Wang Y, Olivecrona M, Blaschke T. The rise of deep learning in drug discovery. Drug Discov Today. 2018;23(6):1241-1250.

[3] Schneider G. Automating drug discovery. Nat Rev Drug Discov. 2018;17(2):97-113.

[4] Zhavoronkov A, Ivanenkov YA, Aliper A, et al. Deep learning enables rapid identification of potent DDR1 kinase inhibitors. Nat Biotechnol. 2019;37(9):1038-1040.

[5] Yang X, Wang Y, Byrne R, Schneider G, Yang S. Concepts of artificial intelligence for computer-assisted drug discovery. Chem Rev. 2019;119(18):10520-10594.

[6] Popova M, Isayev O, Tropsha A. Deep reinforcement learning for de novo drug design. Sci Adv. 2018;4(7):eaap7885.

[7] Segler MHS, Preuss M, Waller MP. Planning chemical syntheses with deep neural networks and symbolic AI. Nature. 2018;555(7698):604-610.

[8] Stokes JM, Yang K, Swanson K, et al. A deep learning approach to antibiotic discovery. Cell. 2020;180(4):688-702.e13.

[9] Mak KK, Pichika MR. Artificial intelligence in drug development: present status and future prospects. Drug Discov Today. 2019;24(3):773-780.

[10] Schneider P, Walters WP, Plowright AT, et al. Rethinking drug design in the artificial intelligence era. Nat Rev Drug Discov. 2020;19(5):353-364.

[11] Duan Y, Edwards JS, Dwivedi YK. Artificial intelligence for decision making in the era of Big Data – evolution, challenges and research agenda. Int J Inf Manage. 2019;48:63-71.

[12] Paul D, Sanap G, Shenoy S, Kalyane D, Kalia K, Tekade RK. Artificial intelligence in drug discovery and development. Drug Discov Today. 2021;26(1):80-93.

[13] Jiang S, Hu Y, Wang Z, et al. Artificial intelligence in healthcare: past, present and future. Stroke Vasc Neurol. 2017;2(4):230-243.

[14] Ekins S, Puhl AC, Zorn KM, et al. Exploiting machine learning for end-to-end drug discovery and development. Nat Mater. 2019;18(5):435-441.

[15] Rifaioglu AS, Atas H, Martin MJ, Cetin-Atalay R, Atalay V, Doğan T. Recent applications of deep learning and machine intelligence on in silico drug discovery: methods, tools and databases. Brief Bioinform. 2019;20(5):1878-1912.

[16] Kumari P, Nath A, Chaube R. Identification of human drug targets using machine-learning algorithms. Comput Biol Med. 2015;56:175-181.

[17] Deng J, Yang Z, Ojima I, Samaras D, Du W. Generative adversarial networks for de novo molecular design. Mol Inform. 2020;39(1-2):1900124.

[18] Lim J, Ryu S, Kim JW, Kim WY. Molecular generative model based on conditional variational autoencoder for de novo molecular design. J Cheminform. 2018;10(1):31.

[19] Sarella PN, Vipparthi AK, Valluri S, Vegi S, Vendi VK. Nanorobotics: Pioneering Drug Delivery and Development in Pharmaceuticals. Research Journal of Pharmaceutical Dosage Forms and Technology. 2024 Feb 22;16(1):81-90.

[20] Weininger D. SMILES, a chemical language and information system. 1. Introduction to methodology and encoding rules. J Chem Inf Comput Sci. 1988;28(1):31-36.

[21] Gómez-Bombarelli R, Wei JN, Duvenaud D, et al. Automatic chemical design using a data-driven continuous representation of molecules. ACS Cent Sci. 2018;4(2):268-276

[22] Sarella PN, Vegi S, Vendi VK, Vipparthi AK, Valluri S. Exploring Aquasomes: A Promising Frontier in Nanotechnology-based Drug Delivery. Asian Journal of Pharmaceutical Research. 2024 May 28;14(2):153-61.

[23] Schutt KT, Arbabzadah F, Chmiela S, Muller KR, Tkatchenko A. Quantum-chemical insights from deep tensor neural networks. Nat Commun. 2017;8:13890.

[24] Mayr A, Klambauer G, Unterthiner T, et al. Large-scale comparison of machine learning methods for drug target prediction on ChEMBL. Chem Sci. 2018;9(24):5441-5451.

[25] Olivecrona M, Blaschke T, Engkvist O, Chen H. Molecular de-novo design through deep reinforcement learning. J Cheminform. 2017;9(1):48.

[26] Putin E, Asadulaev A, Ivanenkov Y, et al. Reinforced adversarial neural computer for de novo molecular design. J Chem Inf Model. 2018;58(6):1194-1204.

[27] Duvenaud DK, Maclaurin D, Iparraguirre J, et al. Convolutional networks on graphs for learning molecular fingerprints. Adv Neural Inf Process Syst. 2015;28:2224-2232.

[28] Sarella PN, Mangam VT. AI-Driven Natural Language Processing in Healthcare: Transforming Patient-Provider Communication. Indian Journal of Pharmacy Practice. 2024;17(1).

[29] Gilmer J, Schoenholz SS, Riley PF, Vinyals O, Dahl GE. Neural message passing for quantum chemistry. In: Proceedings of the 34th International Conference on Machine Learning. 2017;70:1263-1272.

[30] Jiménez-Luna J, Grisoni F, Weskamp N, Schneider G. Artificial intelligence in drug discovery: recent advances and future perspectives. Expert Opin Drug Discov. 2021;16(9):949-959.

[31] Bender A, Cortés-Ciriano I. Artificial intelligence in drug discovery: what is realistic, what are illusions? Part 1: Ways to make an impact, and why we are not there yet. Drug Discov Today. 2021;26(2):511-524.

[32] Baskin II. The power of deep learning to ligand-based novel drug discovery. Expert Opin Drug Discov. 2020;15(7):755-764.

[33] Zhang L, Tan J, Han D, Zhu H. From machine learning to deep learning: progress in machine intelligence for rational drug discovery. Drug Discov Today. 2017;22(11):1680-1685.

[34] Lavecchia A. Deep learning in drug discovery: opportunities, challenges and future prospects. Drug Discov Today. 2019;24(10):2017-2032.

[35] Lo YC, Rensi SE, Torng W, Altman RB. Machine learning in chemoinformatics and drug discovery. Drug Discov Today. 2018;23(8):1538-1546.

[36] Gaulton A, Hersey A, Nowotka M, et al. The ChEMBL database in 2017. Nucleic Acids Res. 2017;45(D1):D945-D954.

[37] Kim S, Chen J, Cheng T, et al. PubChem 2019 update: improved access to chemical data. Nucleic Acids Res. 2019;47(D1):D1102-D1109.

[38] Goodfellow I, Pouget-Abadie J, Mirza M, et al. Generative adversarial nets. Adv Neural Inf Process Syst. 2014;27:2672-2680.

[39] Kingma DP, Welling M. Auto-encoding variational bayes. arXiv preprint arXiv:1312.6114. 2013.

[40] Hochreiter S, Schmidhuber J. Long short-term memory. Neural Comput. 1997;9(8):1735-1780.

[41] Vaswani A, Shazeer N, Parmar N, et al. Attention is all you need. Adv Neural Inf Process Syst. 2017;30:5998-6008.

[42] Senior AW, Evans R, Jumper J, et al. Improved protein structure prediction using potentials from deep learning. Nature. 2020;577(7792):706-710.

[43] Jumper J, Evans R, Pritzel A, et al. Highly accurate protein structure prediction with AlphaFold. Nature. 2021;596(7873):583-589

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