https://doi.org/10.31925/farmacia.2025.1.4 **REVIEW**

THE USE OF ARTIFICIAL INTELLIGENCE IN DRUG DISCOVERY: FROM CONCEPT TO CURRENT APPLICATIONS

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Abstract

Integrating Artificial Intelligence (AI) in drug discovery has revolutionised traditional pharmaceutical development processes, offering significant improvements in efficiency, cost reduction, and success rates. Drug discovery, a traditionally labour-intensive and costly process, encompasses five stages: target identification, drug discovery, preclinical studies, clinical trials, and regulatory approval. With failure rates as high as 97% in clinical trials, particularly in oncology, innovation is critical. AI, including machine learning (ML) and deep learning (DL), has emerged as a transformative tool across all stages of drug development. AI applications include advanced data collection, molecular structure representation, target prediction, drug-target interaction analysis, and *de novo* drug design. Tools such as AlphaFold, DeepDTA, and DrugGPT demonstrate AI's capabilities in protein structure prediction, drug-binding affinity analysis, and ligand design. Moreover, AI's ability to predict drug-drug interactions, optimise pharmacokinetics (ADMET), and identify novel compounds accelerates drug discovery while reducing reliance on traditional experimental methods. Despite its promise, AI faces challenges such as ethical concerns, data quality issues, and algorithmic biases. Current applications in neurology, oncology, and antimicrobial resistance underscore AI's potential, exemplified by innovations like SyntheMol for antibiotic synthesis and AI-driven Alzheimer's treatments. This review highlights AI's capacity to reshape drug discovery, emphasising its advantages, current implementations, and the need to address its limitations to fully leverage its transformative potential.

Rezumat

Integrarea inteligenței artificiale (AI) în descoperirea medicamentelor a revoluționat procesele tradiționale de dezvoltare farmaceutică, oferind noi perspective în ceea ce privește eficiența, reducerea costurilor și ratele de succes. Descoperirea medicamentelor, un proces tradițional costisitor și care necesită echipe multidisciplinare, cuprinde cinci etape: identificarea țintei, descoperirea medicamentului, studiile preclinice, studiile clinice și aprobarea. Cu rate de eșec de până la 97% în studiile clinice, în special în oncologie, inovarea este esențială. IA, inclusiv învățarea automată (ML) și învățarea profundă (DL), a apărut ca un instrument de transformare în toate etapele de dezvoltare a medicamentelor. Aplicațiile IA includ colectarea avansată de date, reprezentarea structurii moleculare, predicția țintei, analiza interacțiunii medicament-țintă și proiectarea *de novo* a medicamentelor. Instrumente precum AlphaFold, DeepDTA și DrugGPT demonstrează capacitățile AI în predicția structurii proteinelor, analiza afinității de legare a medicamentelor și proiectarea liganzilor. În plus, capacitatea IA de a prezice interacțiunile medicament-medicament, de a optimiza farmacocinetica (ADMET) și de a identifica compuși noi accelerează descoperirea de medicamente, reducând în același timp dependența de metodele experimentale tradiționale. În ciuda promisiunilor sale, inteligența artificială se confruntă cu provocări precum preocupările etice, problemele legate de calitatea datelor și prejudecățile algoritmice. Aplicațiile actuale în neurologie, oncologie și rezistența antimicrobiană subliniază potențialul IA, exemplificat prin inovații precum SyntheMol pentru sinteza antibioticelor și tratamentele Alzheimer bazate pe IA. Această analiză evidențiază capacitatea IA de a remodela descoperirea de medicamente, subliniind avantajele sale, implementările actuale și necesitatea de a aborda limitările sale pentru a valorifica pe deplin potențialul său transformator.

Keywords: AI, drug discovery, research

Introduction

Drug discovery is a laborious and highly expensive process, with a critical need for improvement to sustain the progress of the evolving medical field [1]. The traditional protocol of drug development takes over ten years to deliver a new product to the pharmaceutical market and costs at least $3 billion to ensure the whole process [2].

The drug discovery process includes five major stages: 1) identifying the target that underlies the mechanism of action of the selected disease; 2) the drug discovery stage, in which scientists find possible molecules to interact with the target; 3) the preclinical stage, which includes pharmacology and pharmacotoxicology tests in *in vitro* and *in vivo* models; 4) the clinical stage, in which the effect of the drug on humans is monitored; and 5) reviewing,

approval, and post-market observation [3, 4]. These complex stages involve massive financial funding and a skilled labour force. However, the process of drug development is drawn back by the narrow success rate [5]. For example, in the field of cancer drugs, the rate of failure during clinical trials is approximately 97%, highlighting the resource-demanding process until a drug is approved in the market [6].

Drug development has evolved along with technological advances, especially Artificial Intelligence (AI), remarkably changing the conventional and laborious methods used in the pharmaceutical industry [7]. The term AI refers to a precise decision-making algorithm performed independently by a machine [8], providing outcomes similar to human intelligent behaviour and critical thinking [9]. AI in medicine is divided into two major branches: the virtual component represented by Machine Learning (ML), and the physical part, which includes complex medical devices such as robots used to provide medical care [10]. ML is a subfield of AI that uses data to identify and learn from pattern sets and includes them in future predictions [11, 12]. ML is regarded as the workhorse of AI, providing models that learn from existing data to gradually enhance its learning behaviour for more accurate outcomes [13]. Deep learning represents the latest model of AI advances and is a constituent of ML [14] and implies a neural network similar in function to the human brain, aiming to identify and distinguish patterns of data such as language, images, videos and other biological information [15].

Materials and Methods

We conducted a review of the current medical literature on the benefits and opportunities of applying AI in the pharmaceutical domain using the PubMed and Google Scholar databases. We used the following search formula: (Artificial Intelligence) AND (drug discovery) AND (medicine) AND (pharmaceutical), and excluded non-English papers, only abstract available articles, letters to the editor, editorials, and clinical cases. After a comprehensive screening of titles and abstracts, we selected 76 articles that were thoroughly studied to ensure suitable data for a wide discussion of the topic of this review.

Results and Discussion

The progress of AI, ML, and DL has revolutionised the landscape of the drug discovery process, exceeding theoretical studies to real applications. They are involved in every five steps of drug development, including data collection, molecular structure representation and AI models and their applications [16, 17].

Data collection

AI has contributed to data resources for pharmaceutical use by providing elaborate databases of molecules that enable scientists to easily obtain a large amount of information on drug and ligand physicochemical characteristics, discover alternative molecules for existing drugs, and predict structure-activity-relationship (SAR) results [18, 19, 20]. Examples of representative databases used in the drug development process include ChEMBL, ChemDB, COCONUT, DGIdb, DrugBank, DTC, INPUT, PubChem, SIDER and STITCH. They are free and open-access databases containing a large volume of bioactive molecules and their pharmacological characteristics [16, 21].

Molecular structure representation

For future implications of AI in drug discovery, it is mandatory to have algorithms that translate the chemical structure of molecules into cheminformatics, a machine-readable model for compound representations [22]. The molecular structure is divided into 0D, 1D, 2D, 3D, and 4D presentations [16].

0D descriptors include molecular weight, atom number and other basic chemical details, whereas 1D descriptors describe the number of rings, substituent atoms, atom-centred fragments and functional groups [16, 23]. An example of a 1D descriptor is a simplified molecular-input line-entry system (SMILES), an algorithm that depicts molecules as a string of characters that is later integrated into different complex machine learning-based drug research [16, 24] . The 2D molecular descriptor is superior to the previously mentioned models, based on a structural topology in which substances are described as molecular graphs [25, 26]. As AI models of 2D descriptors, we found DRAGON, SYBYL and CODESSA software [27]. On the other hand, 3D descriptors provide extensive information on the chemical structure of molecules, including details such as surface area, volume, steric properties and geometrical descriptors [16]. They depict the molecular conformational space and describe atom connectivity, considering different conformers of molecules [28]. A popular AI program that predicts the 3D protein structure and offers near-experimental accuracy insights on molecule properties is AlphaFold, pushing the frontiers of the drug discovery process [29, 30]. 4D descriptors incorporate sophisticated chemical information, including various conformations of molecules, molecular dynamics and spatiotemporal aspects [31]. CoMFA, GRID, Raptor and Volsurf are examples of 4D descriptors that provide details on ligand and protein-binding site interactions [26, 31, 32].

AI techniques

The rapid evolution of AI has introduced unquestionable opportunities for different steps of the drug discovery process. Scientists have developed several innovative AI applications involved in pharmaceutical analysis

and *de novo* drug design, revolutionising the entire process [16, 33].

Drug target prediction. Investigation of the drug target is the first step in the laborious and effortful process of drug development [3]. AI outperformed the traditional method by providing computational tools that provide databases for genomics (*i.e.* GWAS Catalog, NCBI dbGaP, PharmGKB), transcriptomics (*i.e.* DrugMatrix, TG-GATEs, ArrayExpress), proteomics (*i.e.* PRIDE Archive, Human proteome atlas) used in molecular target identification [34].

A potential algorithm for predicting DTI is MINDG (Multi-view Integrated Learning Network), consisting of a mixed deep network used to recognise target characteristics, a higher-order graph attention convolutional network for defining molecular structures and a multi-view adaptive integrated decision module that focuses on optimisation [35].

Estimation of drug-target affinity (DTA).

DTA quantifies the property of molecules to enhance or inhibit the function of the target, aiming to guide drug discovery research for achieving the ideal drug that binds to a particular target with high affinity and specificity [36]. Traditional methods for DTA prediction are time and resource-consuming, highlighting the imperative necessity of developing AI models to overcome these impediments [37]. An example of such a model is WideDTA, a deep-learning-based prediction model. Founded on text-based data for protein structure, ligand SMILES and protein domains and motif information, WideDTA can predict the binding affinity, surpassing in efficacy the traditional methods [38]. There are several resembling models developed with AI, including ColdDTA [39], GraphDTA [40], DeepDTA [41] and ImageDTA [42].

Prediction drug-drug interactions. DDI refers to the pharmacological effect of one drug in combined administration with another medication [43]. It is essential to predict these unexpected interactions in the drug discovery process to overcome potential adverse effects and help clinicians establish ideal treatment regimens [44].

AI is involved in DDI prediction by using several computational methods. For instance, there is an algorithm named DeepDDI that uses deep neural networks, molecular structure representation as SMILES, and data collection, such as DrugBank, to predict possible causal mechanisms of a certain drug pair and to suggest different drugs with similar pharmacological effects without negatively affecting human health [45].

Design de novo drug. The *De novo* drug discovery process is based on the aforementioned applications of AI, which provide molecular databases and representation of molecular structure. This information is further included in AI models that generate novel drug compounds without a starting template [16]. The key AI methods are pictured in the study of Crucitti *et al*., including algorithms such as Recurrent Neural Networks, Latent Space Exploration, Generative Adversarial Networks and Transformer-based Models [46].

De novo drug discovery aims to enhance the potency and optimise the chemical characteristics of a substance to develop a more effective treatment. Deep learning methods were used to identify the site of the protein target for generating similar molecules and to build up a drug atom-by-atom that binds and activates the target [47]. For instance, a DL model used in *de novo* drug discovery is 3D-MCTS. This technology uses a fragment-based molecular editing strategy, recombining small-molecule components according to retrosynthetic principles to enhance drug-likeness and synthesizability. Moreover, 3D-MCTS demonstrates a substantial advantage over conventional virtual screening techniques, producing thirty times more high-affinity hits [48].

Chemical absorption, distribution, metabolism, excretion, and toxicity (ADMET) prediction. Challenges associated with the pharmacokinetic behaviour of substances hinder the process of drug development due to the labour-intensive and time-consuming *in vivo* and *in vitro* experiments required [49]. The absorption of a substance predicts its bioavailability, which is essential for its effects on the human body. AI has advanced the absorption prediction of a drug by implementing a new concept of medical tests and experiments *in silico* [50]. This term refers to experiments using computer-aided drug discovery (CADD) methods rather than physical laboratory experiments or clinical trials and includes databases, quantitative structure-activity interactions, similarity searching, homology models and other AI algorithms such as machine learning, data mining, data and network analysing tools [51]. The *in-silico* approach to predicting ADMET has the advantage of providing high-speed and effective calculations, minimising undetected human errors, reducing the costs of *in vivo* or *in vitro* experiments, and decreasing animal testing [52].

Drug metabolism and excretion are essential parameters that impose the length and strength of a pharmacological outcome of a certain drug [53]. An example of an AI application for predicting drug metabolism is XenoSite, a computational model based on cytochrome P450 metabolism [54]. These enzymes have many isoforms with specific sites of metabolism that particularly catalyse chemical reactions to generate metabolites [55]. XenoSite uses these particularities to predict drug metabolism by providing data related to drug-cytochrome P450 interactions [53].

DrugGPT.

Large Language Models are DL models designed to understand and deliver human-like responses [56]. An

AI model is ChatGPT (Generative Pre-trained Transformer), an effective tool for scientists to improve research outcomes. ChatGPT has played a role in various aspects of medical chemistry, including the identification of potential drug candidates, computational screening, molecular design, determining therapeutic targets, and enhancing drug absorption, distribution, metabolism, and excretion properties [57]. Similar to ChatGPT, there is a specific Large Language Model developed especially for the drug discovery process, namely DrugGPT [58]. DrugGPT introduces a cutting-edge approach to ligand design that combines advanced deep-learning techniques with established computational chemistry methods. This innovative strategy aims to create ligands tailored for specific target proteins, accelerating the process of drug discovery [59].

Current AI appliance in drug discovery

The aforementioned benefits and opportunities of AI in drug development are not only promises; they are currently used in various areas of medicine, such as cardiology, neurology, oncology, genetics and infectious diseases [60, 61, 62, 63, 64]. Until 2022, there were 158 drug candidates provided with AI methods included in the preclinical phases [65], demonstrating the interest of pharmaceutical companies in improving and advancing the drug discovery process.

In neurology, AI has an impact on personalised treatment tailored to certain molecular and genetic patient characteristics, addressing issues such as brain barrier constraints and pharmacoresistant [66]. For example, AI has been included in reshaping the treatment of Alzheimer's disease by designing new drugs, virtual screening, predicting drug-target interactions, and drug repurposing [67]. Gao *et al*. showed how a generative network complex works on the binding-affinity prediction reliability to produce drug-like molecules, giving the example of beta-secretase 1 inhibitors (BACE1) used in the treatment of Alzheimer's disease [68]. Scientists downloaded the BACE1 compounds from the ChEMBL database. They designed alternative drugs starting from the reference molecules, testing and improving binding affinities and function magnitudes until they found thousands of new alternative drug candidates.

Drug-resistant microorganisms are a critical issue in the medical field, creating a "Silent Pandemic" that is believed to be a leading cause of mortality by 2050 [69]. AI can combat the current crisis by providing new and innovative strategies to detect antimicrobial resistance early, optimise and personalise antibiotic prescriptions for effective treatment, and accelerate drug discovery with new mechanisms of action [70]. The study of Swanson *et al*. described another AI model, SyntheMol, which has revolutionised antibiotic synthesis. They addressed the challenge of synthesising molecules generated by other AI engines, enabling SyntheMol to design molecular patterns that can be easily incorporated into novel antibiotics [71]. They applied the algorithm to create new drugs active against Acinetobacter baumannii and succeeded in producing and validating 58 newly generated molecules, proving the massive potential of AI in generating new treatments to address existing critical medical problems. Another example of the current use of AI in antimicrobial drug development is illustrated by Stokes *et al*. They trained a deep neural network to provide molecules with antibacterial activity and used chemical libraries such as Drug Repurposing Hub, finding a molecule named halicin, differently structured than any traditional antimicrobial drugs but with a potent bactericidal effect on *Mycobacterium tuberculosis*, carbapenem-resistant *Enterobacteriaceae*, *Clostridioides difficile* and *Acinetobacter baumannii* [72].

Risks and limitations

Although AI has unquestionable benefits and opportunities in the pharmaceutical domain, it is necessary to take precautions regarding its limitations and shortages. Firstly, we should consider the ethical concerns related to AI appliances [73]. They include the lack of confidentiality and trust, biased information, transparency issues and insufficient explainability, which require caution when the use of AI affects people's health [74, 75]. Second, lacking high-quality training data may lead to inaccuracies and generalisation issues. Deep learning models use large masses of data to train for future outcomes, a process that is hindered by uncommon and very specialised pharmaceutical information [76].

Conclusions

Artificial Intelligence has rapidly grown and remarkably revolutionised the scientific field. Its applications provide unquestionable opportunities in pharmacology, especially the drug discovery process. We discussed the large extent of implementation that AI offers in drug development, supplying examples of algorithm models currently used in the domain. Describing all the advantages, we highlighted how AI outperformed the traditional methods involved in the drug discovery process regarding efficiency, cost, and research time.

Conflict of interest

The authors declare no conflict of interest.

References

1. Mohs RC, Greig NH, Drug discovery and development: role of basic biological research. *Alzheimers Dement Transl Res Clin Interv.*, 2017; 3(4): 651-657.

2. Cavasotto CN, Di Filippo JI, Artificial intelligence in the early stages of drug discovery. *Arch Biochem Biophys.*, 2021; 698: 108730.
3. Zafar I, Malik M, Mubasher MM, Tariq M, Ali Q, Ahmad A, Bilal M, Han S, Identification of therapeutic targets for polycystic ovary syndrome using network pharmacology and computer simulations. *Farmacia*, 2024; 72(4): 893-905.
4. Hughes JP, Rees SS, Kalindjian SB, Philpott KL, Principles of early drug discovery. *Br J Pharmacol.*, 2011; 162(6): 1239.
5. Qureshi R, Irfan M, Gondal TM, Khan S, Wu J, Hadi MU, Heymach J, Le X, Yan H, Alam T, AI in drug discovery and its clinical relevance. *Heliyon*, 2023; 9(7): e17575.
6. Lin A, Giuliano CJ, Palladino A, John KM, Abramowicz C, Yuan ML, Sausville EL, Lukow DA, Liu L, Chait AR, Galluzzo ZC, Tucker C, Sheltzer JM, Off-target toxicity is a common mechanism of action of cancer drugs undergoing clinical trials. *Sci Transl Med.*, 2019; 11(509): eaaw8412.
7. Vattikuti MC, Improving drug discovery and development using AI: opportunities and challenges. *Research-gate J*, 2024; 10(10).
8. Scerri M, Grech V, Artificial intelligence in medicine. *Early Hum Dev.*, 2020; 145: 105017.
9. Amisha, Malik P, Pathania M, Rathaur V, Overview of artificial intelligence in medicine. *J Family Med Prim Care.*, 2019; 8(7): 2328.
10. Hamet P, Tremblay J, Artificial intelligence in medicine. *Metabolism*, 2017; 69: S36-S40.
11. Verma AA, Murray J, Greiner R, Cohen JP, Shojania KG, Ghassemi M, Straus SE, Pou-Prom C, Mamdani M, Implementing machine learning in medicine. *Can Med Assoc J.*, 2021; 193(34): E1351-E1357.
12. Waljee AK, Higgins PDR, Machine learning in medicine: a primer for physicians. *Am J Gastroenterol.*, 2010; 105(6): 1224-1226.
13. Holzinger A, Langs G, Denk H, Zatloukal K, Müller H, Causability and explainability of artificial intelligence in medicine. *Wires Data Min Knowl Discov.*, 2019; 9(4): e1312.
14. Wang F, Casalino LP, Khullar D, Deep learning in medicine—promise, progress, and challenges. *JAMA Intern Med.*, 2019; 179(3): 293.
15. LeCun Y, Bengio Y, Hinton G, Deep learning. *Nature*, 2015; 521(7553): 436-444.
16. Chen W, Liu X, Zhang S, Chen S, Artificial intelligence for drug discovery: resources, methods, and applications. *Mol Ther Nucleic Acids*, 2023; 31: 691-702.
17. Chakraborty C, Bhattacharya M, Lee SS, Wen ZH, Lo YH, The changing scenario of drug discovery using AI to deep learning: recent advancement, success stories, collaborations, and challenges. *Mol Ther Nucleic Acids*, 2024; 35(3): 102295.
18. Zdrazil B, Felix E, Hunter F, Manners EJ, Blackshaw J, Corbett S, de Veij M, Ioannidis H, Lopez DM, Mosquera JF, Magarinos MP, Bosc N, Arcila R, Kizilören T, Gaulton A, Bento AP, Adasme MF, Monecke P, Landrum GA, Leach AR, The ChEMBL database in 2023: a drug discovery platform spanning multiple bioactivity data types and time periods. *Nucleic Acids Res.*, 2024; 52(D1): D1180-D1192.
19. Bühlmann S, Reymond JL, ChEMBL-likeness score and database GDBChEMBL. *Front Chem.*, 2020; 8: 46.
20. Southan C, Sitzmann M, Muresan S, Comparing the chemical structure and protein content of ChEMBL, DrugBank, Human Metabolome Database and the Therapeutic Target Database. *Mol Inform.*, 2013; 32(11-12): 881-897.
21. Zhu H, Big data and artificial intelligence modelling for drug discovery. *Annu Rev Pharmacol Toxicol.*, 2020; 60(1): 573-589.
22. David L, Thakkar A, Mercado R, Engkvist O, Molecular representations in AI-driven drug discovery: a review and practical guide. *J Cheminform.*, 2020; 12(1): 56.
23. Gautam V, Gaurav A, Masand N, Lee VS, Patil VM, Artificial intelligence and machine-learning approaches in structure and ligand-based discovery of drugs affecting central nervous system. *Mol Divers.*, 2023; 27(2): 959-985.
24. Wasi AT, Karlo Š, Islam R, Rafi TH, Chae DK, When SMILES have language: drug classification using text classification methods on drug SMILES strings. *J Cheminform.*, 2024.
25. Odugbemi AI, Nyirenda C, Christoffels A, Egieyeh SA, Artificial intelligence in antidiabetic drug discovery: the advances in QSAR and the prediction of α-glucosidase inhibitors. *Comput Struct Biotechnol J.*, 2024; 23: 2964-2977.
26. Lo YC, Rensi SE, Torng W, Altman RB, Machine learning in chemoinformatics and drug discovery. *Drug Discov Today.*, 2018; 23(8): 1538-1546.
27. Helguera A, Combes R, Gonzalez M, Cordeiro MN, Applications of 2D descriptors in drug design: a DRAGON tale. *Curr Top Med Chem.*, 2008; 8(18): 1628-1655.
28. Cerchia C, Lavecchia A, New avenues in artificial-intelligence-assisted drug discovery. *Drug Discov Today.*, 2023; 28(4): 103516.
29. Jumper J, Evans R, Pritzel A, Green T, Figurnov M, Ronneberger O, Tunyasuvunakool K, Bates R, Žídek A, Potapenko A, Bridgland A, Meyer C, Kohl SAA, Ballard AJ, Cowie A, Romera-Paredes B, Nikolov S, Jain R, Adler J, Back T, Petersen S, Reiman D, Clancy E, Zielinski M, Steinegger M, Pacholska M, Berghammer T, Bodenstein S, Silver D, Vinyals O, Senior AW, Kavukcuoglu K, Kohli P, Hassabis D, Highly accurate protein structure prediction with AlphaFold. *Nature*, 2021; 596(7873): 583-589.
30. Nussinov R, Zhang M, Liu Y, Jang H, AlphaFold, artificial intelligence (AI), and allostery. *J Phys Chem B.*, 2022; 126(34): 6372-6383.
31. Niazi SK, Mariam Z, Recent advances in machine-learning-based chemoinformatics: a comprehensive review. *Int J Mol Sci.*, 2023; 24(14): 11488.
32. Doytchinova I, Drug design—past, present, future. *Molecules*, 2022; 27(5): 1496.
33. Han R, Yoon H, Kim G, Lee H, Lee Y, Revolutionizing medicinal chemistry: the application of artificial intelligence (AI) in early drug discovery. *Pharmaceuticals*, 2023; 16(9): 1259.
34. Paananen J, Fortino V, An omics perspective on drug target discovery platforms. *Brief Bioinform.*, 2019; 21(6): 1937.

35. Yang H, Chen Y, Zuo Y, Deng Z, Pan X, Shen HB, Choi KS, Yu DJ, MINDG: a drug–target interaction prediction method based on an integrated learning algorithm. *Bioinformatics*, 2024; 40(4): btae147.
36. Crișan O, Marc G, Nastasă C, Oniga S, Vlase L, Pîrnău A, Oniga O, Synthesis and *in silico* approaches of new symmetric bis-thiazolidine-2,4-diones as Ras and Raf oncoproteins inhibitors. *Farmacia*, 2023; 71(2): 254-263.
37. Ranjan A, Bess A, Alvin C, Mukhopadhyay S, MDF-DTA: a multi-dimensional fusion approach for drug-target binding affinity prediction. *J Chem Inf Model.*, 2024; 64(13): 4980-4990.
38. Öztürk H, Ozkirimli E, Özgür A, WideDTA: prediction of drug-target binding affinity. *arXiv*, 2019.
39. Fang K, Zhang Y, Du S, He J, ColdDTA: utilizing data augmentation and attention-based feature fusion for drug-target binding affinity prediction. *Comput Biol Med.*, 2023; 164: 107372.
40. Nguyen T, Le H, Quinn TP, Nguyen T, Le TD, Venkatesh S, GraphDTA: predicting drug–target binding affinity with graph neural networks. *Bioinformatics*, 2021; 37(8): 1140-1147.
41. Öztürk H, Özgür A, Ozkirimli E, DeepDTA: deep drug–target binding affinity prediction. *Bioinformatics*, 2018; 34(17): i821-i829.
42. Han L, Kang L, Guo Q, ImageDTA: a simple model for drug-target binding affinity prediction. *ACS Omega*, 2024; 9(26): 28485-28493.
43. Niu J, Straubinger RM, Mager DE, Pharmacodynamic drug–drug interactions. *Clin Pharmacol Ther.*, 2019; 105(6): 1395-1406.
44. Zhang Y, Deng Z, Xu X, Feng Y, Junliang S, Application of artificial intelligence in drug-drug interactions prediction: a review. *J Chem Inf Model.*, 2024; 64(7): 2158-2173.
45. Ryu JY, Kim HU, Lee SY, Deep learning improves prediction of drug–drug and drug–food interactions. *Proc Natl Acad Sci U S A.*, 2018; 115(18): E4304-E4311.
46. Crucitti D, Pérez Míguez C, Díaz Arias JÁ, Fernandez Prada DB and Mosquera Orgueira A, *De novo* drug design through artificial intelligence: an introduction. *Front Hematol.*, 2024; 3: 1305741.
47. Bhisetti G, Fang C, Artificial intelligence–enabled de novo design of novel compounds that are synthesizable. *Methods Mol Biol.*, 2022; 2391: 409-419.
48. Du H, Jiang D, Zhang O, Wu Z, Gao J, Zhang X, Wang X, Deng Y, Kang Y, Li D, Pan P, Hsieh CY, Hou T, A flexible data-free framework for structure-based de novo drug design with reinforcement learning. *Chem Sci.*, 2023; 14(43): 12166-12181.
49. Obrezanova O, Artificial intelligence for compound pharmacokinetics prediction. *Curr Opin Struct Biol.*, 2023; 79: 102546.
50. Van Tran TT, Tayara H, Chong KT, Recent studies of artificial intelligence on *in silico* drug absorption. *J Chem Inf Model.*, 2023; 63(20): 6198-6211.
51. Ekins S, Mestres J, Testa B, *In silico* pharmacology for drug discovery: applications to targets and beyond. *Br J Pharmacol.*, 2007; 152(1): 21-37.
52. Monteiro ACB, França RP, Arthur R, Iano Y, The fundamentals and potential of translational medicine in healthcare. *Transl Bioinform Health Med.*, 2021; 13: 13-27.
53. Filipović D, Markovic Z, Tuyet T, Tran V, Tayara H, Chong KT, Artificial intelligence in drug metabolism and excretion prediction: recent advances, challenges, and future perspectives. *Pharmaceutics*, 2023; 15(4): 1260.
54. Matlock MK, Hughes TB, Swamidass SJ, XenoSite server: a web-available site of metabolism prediction tool. *Bioinformatics*, 2015; 31(7): 1136-1137.
55. Olsen L, Oostenbrink C, Jørgensen FS, Prediction of cytochrome P450 mediated metabolism. *Adv Drug Deliv Rev.*, 2015; 86: 61-71.
56. Shen Y, Heacock L, Elias J, Hentel KD, Reig B, Shih G, Moy L, ChatGPT and other large language models are double-edged swords. *Radiology*, 2023; 307(2): e230163.
57. Pradhan T, Gupta O, Chawla G, The future of ChatGPT in medicinal chemistry: harnessing AI for accelerated drug discovery. *ChemistrySelect*, 2024; 9(13): e202304359.
58. Lysandrou G, Owen RE, Mursec K, Le Brun G, Fairley EAL, Comparative analysis of Drug-GPT and ChatGPT LLMs for healthcare insights: evaluating accuracy and relevance in patient and HCP contexts. *arXiv*, 2023.
59. Li Y, Gao C, Song X, Wang X, Xu Y, Han S, DrugGPT: a GPT-based strategy for designing potential ligands targeting specific proteins. *bioRxiv*, 2023.
60. Olawade DB, Aderinto N, Olatunji G, Kokori E, David-Olawade AC, Hadi M, Advancements and applications of artificial intelligence in cardiology: current trends and future prospects. *J Med Surg Public Health*, 2024; 3: 100109.
61. Kalani M, Anjankar A, Revolutionizing neurology: the role of artificial intelligence in advancing diagnosis and treatment. *Cureus*, 2024.
62. You Y, Lai X, Pan Y, Zheng H, Vera J, Liu S, Deng S, Zhang L, Artificial intelligence in cancer target identification and drug discovery. *Signal Transduct Target Ther.*, 2022; 7(1): 156.
63. Nguyen MH, Tran ND, Le NQK, Big data and artificial intelligence in drug discovery for gastric cancer: current applications and future perspectives. *Curr Med Chem.*, 2023; 31.
64. Vilhekar RS, Rawekar A, Artificial intelligence in genetics. *Cureus*, 2024; 16(1): e52035.
65. AI's potential to accelerate drug discovery needs a reality check. *Nature*, 2023; 622(7982): 217-217.
66. Voigtlaender S, Pawelczyk J, Geiger M, Vaios EJ, Karschnia P, Cudkowicz M, Dietrich J, Haraldsen IRJH, Feigin V, Owolabi M, White TL, Świeboda P, Farahany N, Natarajan V, Winter SF, Artificial intelligence in neurology: opportunities, challenges, and policy implications. *J Neurol.*, 2024; 271(5): 2258-2273.
67. Qiu Y, Cheng F, Artificial intelligence for drug discovery and development in Alzheimer's disease. *Curr Opin Struct Biol.*, 2024; 85: 102776.
68. Gao K, Nguyen DD, Tu M, Wei GW, Generative network complex for the automated generation of drug-like molecules. *J Chem Inf Model.*, 2020; 60(12): 5682-5698.

69. Ahmed SK, Hussein S, Qurbani K, Ibrahim RH, Fareeq A, Mahmood KA, Mohamed MG, Antimicrobial resistance: impacts, challenges, and future prospects. *J Med Surg Public Health*, 2024; 2: 100081.
70. Branda F, Scarpa F, Implications of artificial intelligence in addressing antimicrobial resistance: innovations, global challenges, and healthcare's future. *Antibiotics*, 2024; 13(6): 502.
71. Swanson K, Liu G, Catacutan DB, Arnold A, Zou J, Stokes JM, Generative AI for designing and validating easily synthesizable and structurally novel antibiotics. *Nat Mach Intell.*, 2024; 6(3): 338-353.
72. Stokes JM, Yang K, Swanson K, Jin W, Cubillos-Ruiz A, Donghia NM, MacNair CR, French S, Carfrae LA, Bloom-Ackermann Z, Tran VM, Chiappino-Pepe A, Badran AH, Andrews IW, Chory EJ, Church GM, Brown ED, Jaakkola TS, Barzilay R, Collins JJ, A deep learning approach to antibiotic discovery. *Cell*, 2020; 180(4): 688-702.
73. Van Booven D, Cheng-Bang C, Meenakshy M, Limitations of artificial intelligence in healthcare. *Artif Intell Urol Malignancies*, 2025: 231-246.
74. Arabi AA, Artificial intelligence in drug design: algorithms, applications, challenges and ethics. *Future Drug Discov.*, 2021; 3(2).
75. Livieri G, Anastasopoulou C, Briola K, Nikolopoulou P, Efthymiou IP, Ethical issues arising from the use of AI in drug discovery. *J Polit Ethics New Technol AI*, 2024; 3(1): e37093.
76. Tang Y, Deep learning in drug discovery: applications and limitations. *Front Comput Intell Syst.*, 2023; 3(2): 118-123.