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Advances in drug design and discovery: A Comprehensive Review

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Abstract

The process of drug discovery and development is a complex, time-consuming, and costly endeavor. However, the integration of machine learning (ML) and Artificial Intelligence (AI) has revolutionized the pharmaceutical industry by providing innovative solutions to challenging problems. This review highlights the role of ML in drug discovery, including target identification, lead optimization, and drug design. ML-driven approaches, such as deep learning and neural networks, have accelerated the discovery process, reducing the time and expense involved in traditional drug development. Computational tools and software have made the drug research and development process more convenient, enabling the use of online screening, structure-based design, and lead optimization. The application of ML in drug discovery has the potential to transform the pharmaceutical industry, enabling the development of novel and effective therapies for various diseases. This review aims to provide an overview of the current state of ML in drug discovery, highlighting its applications, advantages, and future directions.

Keywords: Machine Learning; Drug Discovery; Drug Design; Target Identification; Computational Tools

1. Introduction

The process of developing new drugs is costly, time-consuming, and prone to failure. Machine learning (AI) has been a game-changing technology in the development of drugs in recent years, providing creative answers to challenging problems in the pharmaceutical sector. The many facets of AI's function in drug discovery are covered in this book, comprising AI-assisted drug administration design [1]. The introduction of numerous computational tools and software has made the drug research and development process extremely convenient. Computer programs for online screening by structure as well as ligand-based design along with lead optimization are typically used in drug design and discovery [2]. The structured creation of novel medications is a relatively young discipline, despite the fact that the usage of therapeutic herbs is documented in the oldest texts [3].

With its computational capacity and data-driven methodologies, machine learning has transformed drug research and development and completely changed the pharmaceutical industry. Target verification, lead optimization, and reusing drugs have been greatly accelerated by AI-driven approaches such as machine learning, deep learning, and neural networks, which have decreased the time and expense involved in conventional drug development [4]. In medicinal chemistry, drug discovery is essential since it forms the basis for creating novel therapies to treat a variety of illnesses. In order to improve the drug discovery process, this study highlights the importance of cutting-edge techniques including chemical sciences, targeted protein deposition (TPD), DNA-Encoded Laboratories (DELs) and Machine-learning Drug Design (CADD) [5].

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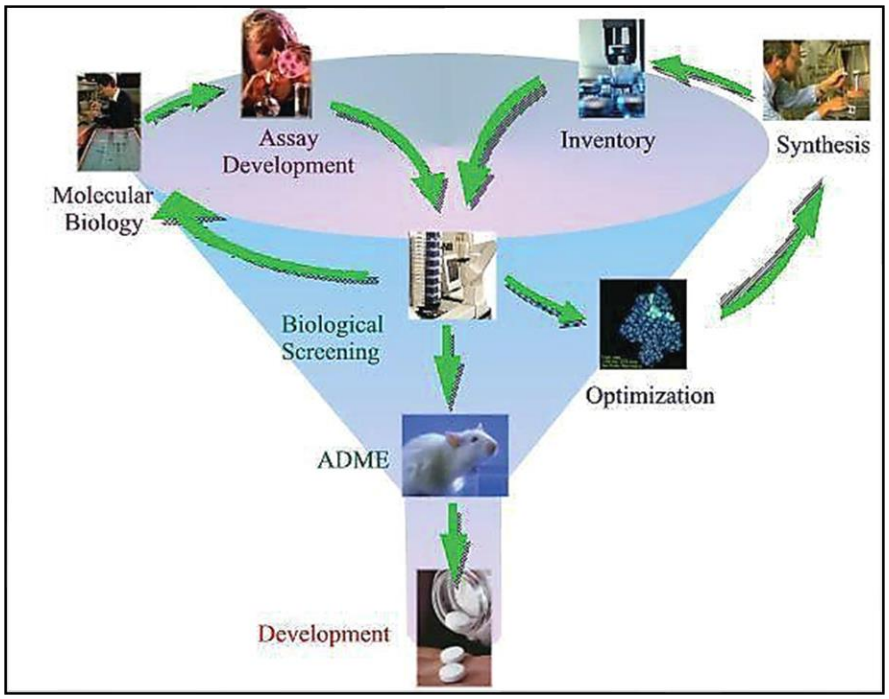

Figure 1 Drug design and discovery [6]

The intrinsic chemical and biological complexity of traditional drug creation presents several difficulties, frequently leading to high clinical trial failure rates. Developments in deep learning, especially generative models, present viable answers to these problems [7].

Computational methods are rapidly being explored, used and admired in the drug design, discovery, and manufacturing procedure. The process of launching a new medication into the market is extremely difficult, dangerous and expensive in terms of labor, money and time [8].

2. Target identification

Deep learning methods use numerous nonlinear modifications of the initial input features to extract higher-dimensional, more complex models from massive biological data. This feature makes it possible to anticipate interactions between drugs and targets using deep learning [9].

From a safety and the clinical application standpoint, it is generally acknowledged that target identification over an active ingredient series is desired in order to assist derisk the project. Over the years, there It was heated discussion about whether it is definitely required for compounds before they enter the clinic [10].

Finding a novel medication and its targets using binding sites is the main goal of the first stage, known as discovery. Pre-clinical research is the second stage, known as development, during which the medication is examined for safety in animals. Human trials are initiated when research is successful. Registration carefully examines all of the supplied drug-related data in the third phase of the registry before determining whether to approve it [11].

The need for target identification and subsequent follow-up play a major role in the choice of medications used for screens or testing. One benefit of genetic testing is that the drug's molecular target need not be identified or have a suspected role in the illness [12].

3. Molecular dynamics in drug design

Through the use of explicit solution MD simulation, findings of the docked postures from Glide were examined in further detail [13].

The currently recognized definition of a molecular chameleon is the capacity of compounds to modify their shapes in such a way that polar bonds are accessible in solutions of water but concealed by the creation of non-bonded interactions between molecules in a nonpolar the environment, like a lipid bilayer [14].

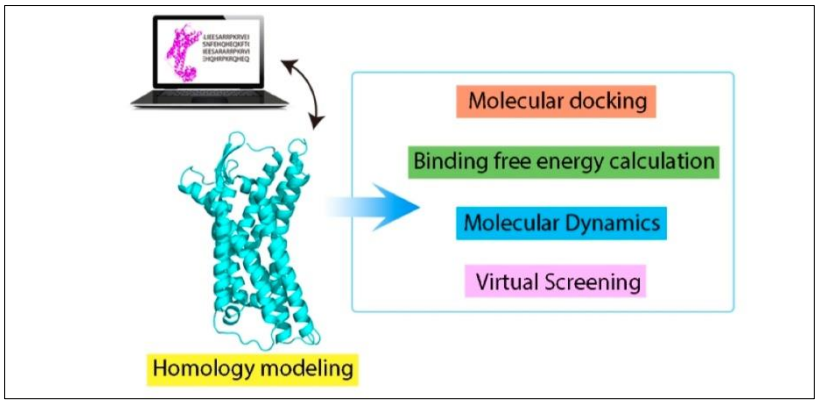

Figure 2 Molecular dynamics in drug design [15]

Beginning with basic constituents such oligonucleotides, oligosaccharides, phospholipids which peptides that or proteins, structural internal organization and self-assemble are the processes that create complex multidimensional multicomponent buildings with well-defined functions [16].

4. Structure based drug design

One of the most important tasks in the development of drugs is creating 3D ligands that fit into a target binding site. Current structured-based drug design approaches treat every ligand atom equally, ignoring the various roles that atoms play in the ligand for drug design. This can make them less effective for examining the vast universe of drug-like molecules [17].

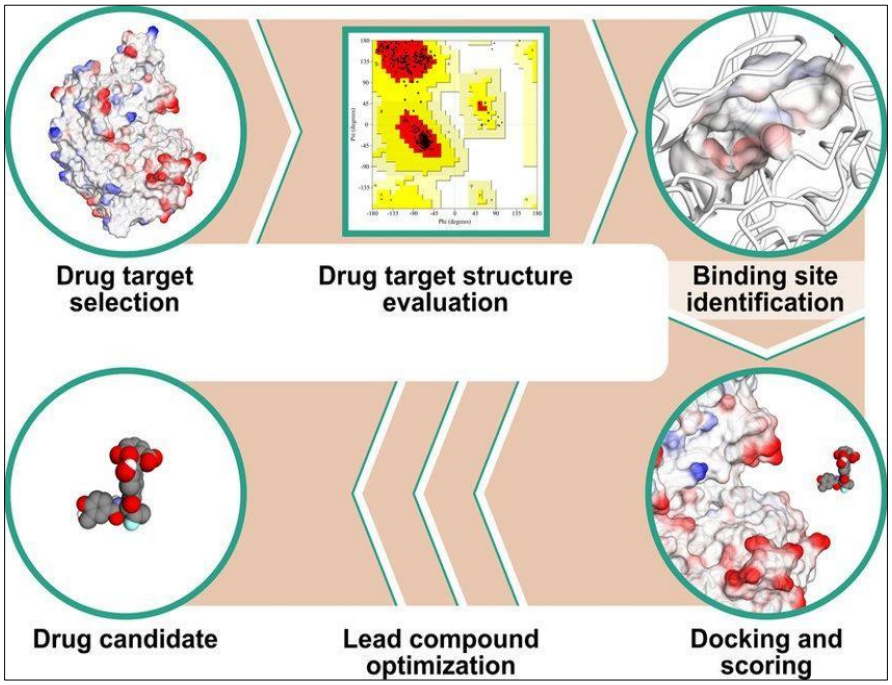

Figure 3 workflow of structure-based drug design [18]

Structure based drug design is becoming a more significant method of drug discovery as a result of the synthesis of numerous chemicals and their biological activity testing in lab model of human diseases using tissues, cells and other tissues and organs [19].

4.1. History of drug design

To combat the rise in drug resistance and the newly identified forms of illnesses, including mutant bacteria, pharmaceutical companies must constantly find and develop new medications, especially in anti-infective agents [20]. Over the past few decades, the conventional model drug development technique has been time-consuming, demanding of resources and has had significant challenges in finding potential therapeutic candidates [21].

4.2. Computer -aided drug design

At a quick pace, computational approaches to drug design, discovering things and production are being investigated, used, and appreciated [22].

The process of creating compounds that may interact with a certain biomolecular target and guaranteeing their binding is known as computer-aided drug design or CADD. The basic functional groups of tiny particles (SMs)-based chemotherapeutic drugs, particularly overall stereo-arrangement and stereo-selectivity, impact their therapeutic potential to enhance therapeutic outcomes [23].

Finding and creating a novel drug is frequently viewed as a time-consuming and costly process. To increase the effectiveness of the process of discovering and developing drugs, computer-aided drug design techniques are now widely used [24].

4.3. Approaches for drug discovery

A system of suggestions that suggests new indications depending on established drug-disease relationships can be used to computationally mimic the drug repositioning challenge. Using a vector of concealed characteristics to represent a medicine or a disease, matrix factorization the most common drug repositioning technique projects therapeutics and disorders under a shared latent environment. The drug-disease link is subsequently described as the internal product of their hidden orientations [25].

Standard single-and multi-SNP evaluation methods are guaranteed to be paired by machine learning (ML) techniques in order to better grasp the overall genomic architecture of complex human disorders [26].

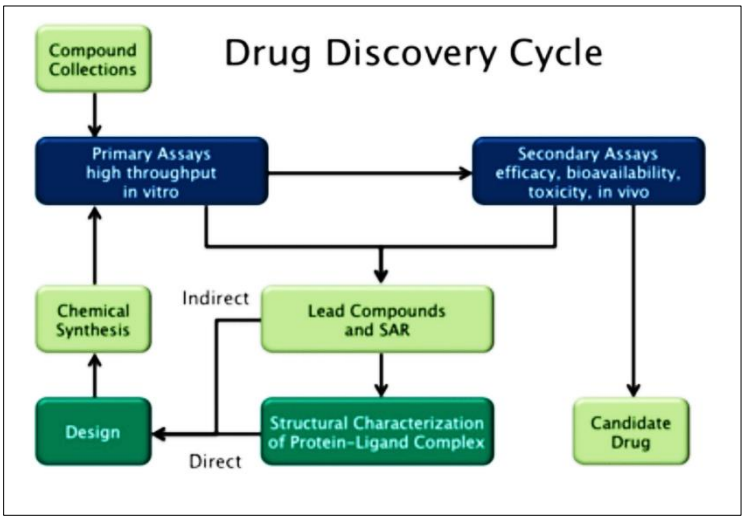

Figure 4 Drug discovery cycle [27]

4.4. How to design a drug?

The creation of safe and efficient molecules that can be used as medications in clinical medication is one of medicinal chemistry's main goals. To do it, a combination of chemists, biologists, doctors, pharmacists, pharmacologists, along with other experts are necessary. Therefore, it is crucial to comprehend a drug candidate's PK (pharmacokinetics) profile (intake, distribution, metabolism and removal or ADME) during the drug research and development phase [28].

A user using the upgraded mercury in addition graphics program at an interactive drawings station starts the design phase [29].

4.5. Protein flexibility in drug design

Maintaining human health is crucial and unfettered access to drugs is necessary for general well-being. Pharmaceuticals are essential to healthcare because they contain a vast array of medicinal compounds that are used to identify, treat, and improve a variety of illnesses and ailments. Nonetheless, the lengthy, taxing and expensive character of the drug scientific and technological development process is well known. Interdisciplinary teams have come together to improve the efficiency of this intricate process, creating the subject known as "bioinformatics" [30]

Despite recent reports of its significance in the development of non-peptide peptidomimetics, the inherent mobility of proteins has frequently been disregarded in therapeutic design [31].

4.6. Druglike properties in drug discovery

Finding substances with characteristics similar to those of drugs is essential to the formation of novel drugs. One crucial factor in evaluating a compound's chances of therapeutic development is its drug-likeness [32]. In order to provide extra affinity across the non-covalent bonds responsible for drug binding, covalent medicines use a slightly reactive functional group to generate a covalent connection with protein targets [33].

Over the past ten years, there has been an increased focus on the physicochemica characteristics of potential chemical compounds for drug development. Limitations and cutoff points for basic physicochemical or "drug-like" characteristics, including molecular weight [34].

5. Discovery and development

engrossing and topical analysis of the revolutionary possibilities of machine learning in biologics study, with an emphasis on antibodies, a key pharmacological field propelling the development of drugs innovation [35]. A promising method for the mechanized design of structures with certain pharmacological characteristics, like synthetic permeability and similarities to drugs, is molecules production techniques [36]. There is constant pressure on the pharmaceutical sector to improve its success rate in bringing medications to market [37]. Drug development is a complicated process that includes a number of steps, such as locating possible targets, screening for starting compounds, refining lead candidates, performing pre-clinical testing and starting clinical trials [38].

According to medical history, the majority of early discoveries came about by accident and were based on poisoners' sources rather than traditional medicines [39].

6. Fragment -based drug discovery:

Future drug development may be significantly influenced by fragment-based drug design. The pharmaceutical target space has been broadened to include RNAs and RNA-binding proteins (RBPs) due to recent developments in the field of molecular biology and bioinformatics, providing unrealized potential for medical treatment beyond conventional protein targets [40]. Fragments are tiny chemical molecules having a low molecular weight and size. Finding tiny chemical fragments that the bind to biological substances weakly and then combining or expanding them to produce a lead with a higher affinity is the idea behind FBDD [41].

It has demonstrated its usefulness over the past 20 years. Spectroscopy of NMR, the surface plasmon resonance technique and X-ray crystallography are some of the most widely used screening techniques for FBDD, which has increased in use in tandem with the growing prominence of RNA as a pharmacological target [42].

6.1. Screening

A fragonomics endeavor cannot be successfully carried out without a physicochemical screening component. Segment screenings can be driven by biologic assays, biophysical methods (X-ray, NMR, the Society for the Promotion etc.) or an intersection of all these methods [43].

6.2. NMR

This gap could be filled by in-cell NMR spectroscopy, which offers a novel approach to examining the dynamics and structure of ligand-target relationships in the natural cellular setting by enabling structural analyses of amino acids and proteins immediately. in living cells, from microorganisms to human-derived. In-cell NMR offers valuable information

on binding characteristics and selectivity towards a biological target when used for drug screening, making it a potent tool for enhancing drug potency early in the drug development process [44].

6.3. X-ray crystallography

However, there are a number of challenges that slow down the rate at which new crystal structures are solved when utilizing X-ray crystallography to clarify the structure of proteins [45].

7. Structure activity relationship (SAR)

One of the earliest possible applications of protein structures in drug discovery was the creation of the significant ACE inhibitors captopril and enalopril. Modeling of these medications, which are used to treat hypertension and other disorders, was aided by crystal structure of this enzyme A, which has an active site that is comparable and contains a catalytically significant zinc ion [46].

An analysis of how modifications to small-molecule structure impact activity in relation to a specific molecular target gives rise to structural-activity relationships or SARs [47].

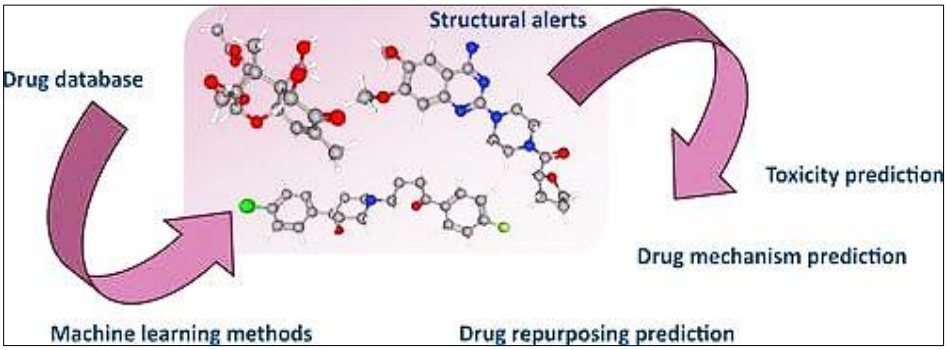

Figure 5 Structure activity relationship of drug discovery [48]

8. Conclusion

Machine learning has emerged as a powerful tool in drug discovery, enabling the development of novel and effective therapies for various diseases. The integration of ML-driven approaches, such as deep learning and neural networks, has accelerated the discovery process, reducing the time and expense involved in traditional drug development. Computational tools and software have made the drug research and development process more convenient, enabling the use of online screening, structure-based design, and lead optimization. As the pharmaceutical industry continues to evolve, the application of ML in drug discovery is expected to play an increasingly important role in shaping the future of healthcare. With its potential to transform the drug discovery process, ML is poised to revolutionize the pharmaceutical industry, enabling the development of innovative therapies that can improve human health and well-being. Further research is needed to fully realize the potential of ML in drug discovery and to explore its applications in various disease areas.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] AI and Negut I. Integrating Artificial Intelligence for drug discovery in the context of revolutionizing drug delivery. Life. 2024;14 (2):233.

[2] Patel, J. R. Joshi, H. V. Shah, U. A. and Patel, J. K. A review on computational software tools for drug design and discovery. Indo Global Journal of Pharmaceutical Sciences. 2022;12, 53-81.

[3] De Oliveira, A. M. and Rudrapal, M. Introduction to drug design and discovery. In Computer aided drug Design (CADD): from ligand-based methods to structure-based approaches. Elsevier. 2022; 1-15.

[4] Bharath, E. Thilagavathi, T. S. Jeeva, D. Anbazhagan, S. and Vadivel, S. A. Advances in Artificial Intelligence for drug discovery and development: A review of current trends and applications. Asian journal of pharmaceutical research and development, 2025;13(2): 67-78.

[5] An, Q. Huang, L. Wang, C. Wang, D and Tu, Y. New strategies to enhance the efficiency and precision of drug discovery. Frontiers in Pharmacology. 2025; 16, 1550158.

[6] Prajapat, P. Agarwal, S. and Talesara, G. L. Significance of computer aided drug design and 3D QSAR in modern drug discovery. J Med Org Chem. 2017;1(1): 1.

[7] Sheikholeslami, M. Mazrouei, N. Gheisari, Y. Fasihi, A. Irajpour, M., and Motahharynia, A. Druggen: advancing drug discovery with large language models and reinforcement learning feedback. Arxiv preprint arxiv. 2024; 2411-14157.

[8] Muhammed M. T. and Akı-yalcın, E. Pharmacophore modeling in drug discovery: methodology and current status. Journal of the turkish chemical society section A: Chemistry. 2021; 8(3): 749-762.

[9] Suruliandi, A. Idhaya, T. and Raja, S. P. Drug target interaction prediction using machine learning techniques–a review. 2024;8(6):86-100.

[10] Huang, D. Yang, M. and Zheng, W. Integrating AI and deep learning for efficient drug discovery and target identification.2024, 2(1):44–63.

[11] Vincent, F. Nueda, A. Lee, J. Schenone, M. Prunotto, M. and Mercola, M. Phenotypic drug discovery: recent successes, lessons learned and new directions. Nature Reviews Drug Discovery. 2022; 21(12): 899-914.

[12] Suruliandi, A. Idhaya, T. and Raja, S. P. Drug target interaction prediction using machine learning techniques–a review. 2024;8(6):86-100.

[13] Patton, E. E. Zon, L. I. and Langenau, D. M. Zebrafish disease models in drug discovery: from preclinical modelling to clinical trials. Nature reviews Drug discovery. 2021; 20(8): 611-628.

[14] Tripathi, S. M. Akash, S. Rahman, M. A., and Sundriyal, S. Identification of synthetically tractable MERS-cov main protease inhibitors using structure-based virtual screening and molecular dynamics potential of mean force (PMF) calculations. Journal of biomolecular structure and dynamics. 2025; 43(2):787-797.

[15] Poongavanam, V. Wieske, L. H. Peintner, S. Erdélyi, M. and Kihlberg, J. Molecular chameleons in drug discovery. Nature Reviews Chemistry. 2024;8(1); 45-60.

[16] Gu X, Wang Y, Wang H, Wu H, Li W, Wang J, and Li N. Homology modeling, molecular dynamics and virtual screening of endothelin-A receptor for the treatment of pulmonary arterial hypertension. Journal of Biomolecular Structure and Dynamics.2021; 39(11): 3912-3923.

[17] Guan, J. Zhou, X. Yang, Y. Bao, Y. Peng, J. Ma, J and Gu, Q. Decompdiff: diffusion models with decomposed priors for structure-based drug design. Arxiv preprint arxiv. 2024;2403-07902.

[18] Hardianto A, Yusuf M, Liu F, and Ranganathan S. Structure-based drug design workflow.2019.

[19] Zhang, S. Liu, K. Liu, Y. Hu, X. and Gu, X. The role and application of bioinformatics techniques and tools in drug discovery. Frontiers in Pharmacology. 2025;16: 1547131.

[20] Pant, S. Verma, S. Pathak, R. K. and Singh D. B. Structure-based drug designing. In Bioinformatics . Academic Press.2022; 219-231.

[21] Alizadehsani, R. Oyelere, S. S. Hussain, S., Jagatheesaperumal, S. K. Calixto, R. R., Rahouti, M., roshanzamir, M. and de Albuquerque, V. H. C. Explainable Artificial Intelligence for drug discovery and development: A comprehensive survey. IEEE Access. 2024; 12, 35796-35812.

[22] Padole, S. S. Asnani, A. J. Chaple, D. R. and Katre S. G. A review of approaches in computer-aided drug design in drug discovery. GSC Biological and pharmaceutical sciences.2022;19(2):075-083.

[23] Siddiqui, B. Yadav, C. S. Akil, M. Faiyyaz, M. Khan, A. R. Ahmad, N and Azad, I. Artificial Intelligence in Computer-Aided Drug Design (CADD) tools for the finding of potent biologically active small molecules: Traditional to modern approach. Combinatorial chemistry and high throughput screening.2025;1-50

[24] Perišić, O. Sevim Bayrak, C. and Gunady, M. K. Machine learning in computer-aided drug design. Frontiers in molecular biosciences.2025;12, 1568437.

[25] Meng, Y. Lu, C. Jin, M. Xu, J. Zeng, X. and Yang, J. A weighted bilinear neural collaborative filtering approach for drug repositioning briefings in bioinformatics. 2022; 23(2):1-13.

[26] Nayarisseri, A. Khandelwal, R. Tanwar, P. Madhavi, M. Sharma, D. Thakur, G. and Singh, S. K. Artificial Intelligence, big data and machine learning approaches in precision medicine and drug discovery. Current drug targets. 2021; 22(6): 631-655.

[27] Sharma P. Quantum Computing in Drug Design: Enhancing precision and efficiency in pharmaceutical development. Sage science review of applied machine learning.2024; 7(1): 1-9.

[28] Riccardi L, Genna V, and De Vivo, M. Metal–ligand interactions in drug design. Nature Reviews Chemistry.2018; 2(7):100-112.

[29] Kumar, G. Yadav, S., Mukherjee, A. Hassija, V. and Guizani, M. Recent advances in quantum computing for drug discovery and development. 2024; 6(3): 64491-64509.

[30] Iglesias J, Saen-oon S, Soliva R and Guallar V. Computational structure-based drug design: Predicting target flexibility. Wiley interdisciplinary reviews: Computational molecular science.2018; 8(5): e1367.

[31] Li, B. Wang, Z. Liu, Z. Tao, Y., Sha, C. He, M. and Li, X. Drugmetric: quantitative drug-likeness scoring based on chemical space distance. Briefings in Bioinformatics. 2024;25(4): bbae321.

[32] Boike, L. Henning, N. J. and Nomura, D. K. Advances in covalent drug discovery. Nature Reviews Drug Discovery. 2022; 21(12): 881-898.

[33] Pantaleão, S. Q. Fernandes, P. O. Gonçalves, J. E. Maltarollo, V. G. and Honorio, K. M. Recent advances in the prediction of pharmacokinetics properties in drug design studies: a review. Chemmedchem. 2022;17(1): e202100542.

[34] Villoutreix, B. O. Poyet, J. L. and Tsaioun, K. Drug discovery and development explained: introductory notes for the general public. Frontiers in Drug Discovery. 2024;4,1528467.

[35] Wang, D. Chen, J. Liang, Z. Fu, T. and Liu, X. Y. Quantum-inspired reinforcement learning for synthesizable drug design. Arxiv preprint arxiv. 2024;2409-09183.

[36] Rautio J, Meanwell NA, Di L, and Hageman MJ. The expanding role of prodrugs in contemporary drug design and development. Nature reviews drug discovery.2018; 17(8): 559-587.

[37] Kumar, G., Yadav, S., Mukherjee, A., Hassija, V., and Guizani, M. (2024). Recent advances in quantum computing for drug discovery and development. IEEE Access. 2024; 12,64491-64509.

[38] Weng HB, Chen HX and Wang MW. Innovation in neglected tropical disease drug discovery and development. Infectious diseases of poverty.2018; 7(03): 1-9.

[39] Woodhead, A. J. Erlanson, D. A. De Esch, I. J. Holvey, R. S. Jahnke, W. and Pathuri, P. Fragment-to-lead medicinal chemistry publications in 2022. Journal of medicinal chemistry. 2024;67(4): 2287-2304.

[40] Xu, W. and Kang, C. Fragment-based drug design: From then until now, and toward the future. Journal of Medicinal Chemistry. 2025; 68(5): 5000-5004.

[41] Shinde, P. P. and Shinde, M. G. Fragment Based Drug Design: A Review. International journal of pharmaceutical sciences. 2024; 2(7): 171–176.

[42] Bon M, Bilsland A, Bower J and mcaulay K. Fragment-based drug discovery—the importance of high-quality molecule libraries. Molecular Oncology.2022;16(21):3761-3777.

[43] Lundquist KP, Panchal V, Gotfredsen CH, Brenk R and Clausen MH. Fragment-based drug discovery for rna targets. Chemmedchem.2021;16(17): 2588-2603.

[44] Luchinat, E. and Banci, L. In-cell NMR: From target structure and dynamics to drug screening. Current opinion in structural biology. 2022;74 102374.

[45] Kermani, A. A. Aggarwal, S. and Ghanbarpour, A. Advances in X-ray crystallography methods to study structural dynamics of macromolecules. In Advanced spectroscopic methods to study biomolecular structure and dynamics. 2023; 309-335.

[46] Wei, H., and mccammon, J. A. Structure and dynamics in drug discovery. Npj drug discovery. 2024; 1(1): 1-8.

[47] Cosmas S, Ekpo DE, Asomadu RO, Assor JO, Nnamani VI and Durojaye OA. Review on structure-activity relationship (Sar) using antimalarial drug design as a case study. Int. J. Sci. Eng. Res.2018;9: 1743-1751.

[48] Staszak M, Staszak K, Wieszczycka K, Bajek A, Roszkowski K and Tylkowski B. Machine learning in drug design: Use of Artificial Intelligence to explore the chemical structure–biological activity relationship. Wiley interdisciplinary reviews: Computational molecular science.2022;12(2): 1568.