LUPINE PUBLISHERS

Current Trends in Computer Sciences & Applications

DOI: 10.32474/CTCSA.2026.03.000172

ISSN: 2643-6744

Review Article

Recent Computational Advances in Drug Discovery

Abdulrahman A Alsaqabi*

Department of Pharmaceutical Sciences, College of Pharmacy, King Saud Bin Abdulaziz University for Health Sciences, Saudi Arabia.

***Corresponding author:** Abdulrahman A Alsaqabi, Department of Pharmaceutical Sciences, College of Pharmacy, King Saud Bin Abdulaziz University for Health Sciences, Saudi Arabia.

Received: July 13, 2026 **Published:** August 16, 2026

Abstract

The integration of computational technologies into medicinal chemistry and drug discovery is fundamentally reshaping pharmaceutical research. Over the past few years, there has been a paradigm shift propelled by advances in artificial intelligence (AI), machine learning, and high-performance computing. This review provides a comprehensive analysis of the most recent computational breakthroughs accelerating the drug discovery pipeline. Key areas discussed include the transformative impact of deep learning on target identification, the revolutionary capabilities of AlphaFold in predicting protein structures, and the utility of generative AI models in de novo molecular design. We also examine enhancements in structure-based virtual screening, ultra-large library docking, and refined molecular dynamics simulations that are improving the prediction of protein-ligand interactions. Additionally, modern machine learning-driven models for predicting Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) properties are evaluated, showcasing their ability to reduce late-stage attrition rates. By summarizing the state-of-the-art computational methods and highlighting major real-world implementations, this article emphasizes how computational platforms serve not merely as supplementary tools, but as primary drivers of therapeutic innovation, ultimately promising faster and more cost-effective pathways to market for life-saving therapeutics.

Keywords: *Artificial Intelligence; Computational Drug Discovery; AlphaFold; Generative AI; Virtual Screening; Machine Learning*

Introduction

The process of discovering and developing a novel therapeutic agent is traditionally characterized by high costs, extended timelines averaging over a decade, and substantial attrition rates. However, modern drug discovery has been dramatically reshaped by a surge in sophisticated computational capabilities [1]. Today, advanced computational methods and artificial intelligence (AI) play a central role across the entire drug discovery pipeline, from early-stage target identification to late-stage clinical risk assessment.

Data-driven and intelligence-driven processes are overtaking traditional trial-and-error paradigms. This transition is marked by the deployment of robust algorithms to analyze enormous arrays of biomedical and molecular data. Recent developments in predictive modeling, deep learning architectures, and natural language processing techniques have paved new pathways for identifying targets, anticipating toxicity, and modeling complex biological systems [2]. This review comprehensively explores recent major computational milestones, primarily focusing on breakthroughs in structural biology, AI-mediated de novo design, advanced virtual screening, and predictive pharmacology.

Structural Biology Breakthroughs: AlphaFold and Beyond

A primary bottleneck in rational drug design has historically been the absence of high-resolution three-dimensional protein structures. The release of AlphaFold by DeepMind represented a monumental leap forward, establishing a robust deep learning framework to accurately predict protein structures based solely on amino acid sequences. This advancement is particularly crucial for identifying small-molecule binding sites on previously understudied or 'undruggable' targets.

While AlphaFold has achieved near-experimental accuracy for many targets, evaluating these generated structures in downstream docking applications is vital. Recent studies have demonstrated that combining AlphaFold structural representations with molecular generative models significantly enhances generalized target learning and multi-target chemical design [3]. Moreover, optimized AlphaFold models have successfully been integrated into virtual screening pipelines, allowing researchers to successfully identify selective inhibitors, such as against HDAC11, where conventional homology modeling previously fell short [4]. However, researchers continue to emphasize that raw AlphaFold models often require refinement and careful assessment, as direct integration into high-throughput docking can sometimes yield less reliable results without appropriate preparation [5].

Generative AI for De Novo Drug Design

De novo drug design relies on the generation of novel chemical entities that comply with predefined pharmacological and structural constraints. Generative AI models, including recurrent neural networks, variational autoencoders, and diffusion-based models, have catalyzed a shift in how medicinal chemists explore chemical space [6]. These models can autonomously assemble and optimize molecules to fit specific targets, effectively automating hit generation and lead optimization.

Recent applications of large language models (LLMs) and transformer-based architectures have further expanded the frontier of drug generation. For instance, advanced modular systems incorporating LLM frameworks demonstrate a remarkable ability to integrate biomedical data retrieval with molecular structure generation [7]. Furthermore, exhaustive surveys into generative models reveal their power to transcend human-curated chemical libraries by producing highly viable, unique candidates [8]. This expansive exploration mitigates the bias toward known molecular classes, ensuring that the structural modifications proposed by AI systems contribute substantially to discovering novel treatments.

Innovations in Virtual Screening and Molecular Docking

Virtual screening has evolved from docking thousands of molecules to interrogating ultra-large chemical libraries comprising billions of compounds. Deep learning tools are actively facilitating this scale-up. Notably, deep neural network-based virtual screening systems empower the rapid and explicit docking of immense databases. Such approaches have recently led to the discovery of potential inhibitors for novel targets, including choline acetyltransferase for targeted cancer theranostics [9].

To bypass the exorbitant computational costs of explicit docking for every molecule, contemporary machine learning methodologies are deployed to predict docking scores directly. Utilizing algorithms like attention-based long short-term memory (LSTM) neural networks, researchers can train models on minimal subsets of docked ligands and accurately predict the scores for millions of unseen molecules, accelerating the process exponentially [10]. Moreover, coupling machine learning with rigorous molecular docking and molecular dynamics has repeatedly demonstrated superior hit rates, such as in the robust computational identification of indolocarbazole scaffolds against mutant EGFR in lung cancer [11]. Molecular dynamics simulations now benefit from automated workflows capable of evaluating ligand-protein complex stability across entire pre-docked libraries in a high-throughput fashion, cementing the bridge between static structures and dynamic physiological environments [12].

Enhancing ADMET Predictions with Advanced Computational Models

Late-stage clinical trial failures are frequently attributed to poor pharmacokinetic properties or unforeseen toxicity. Thus, incorporating quantitative structure-activity relationship (QSAR) and Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) profiling early in the discovery phase is critical. Machine learning has revitalized QSAR modeling by providing profound, non-linear insights into molecular bioactivity [13].

Recent integrations of deep neural networks have enhanced the precision of pharmacokinetic modeling across diverse settings. For example, machine learning-driven QSAR models have been adeptly applied to accurately predict the plasma half-lives of drugs, illustrating advanced predictive capabilities that inform optimal dosing and withdrawal times [14]. By capturing complex relationships through sophisticated structural descriptors and fingerprints, these AI-driven ADMET models rapidly sift out high-risk candidates, focusing resources efficiently on the most promising lead compounds.

Graph Neural Networks and Target Interaction

Due to their inherent capacity to represent data via topological structures, graph neural networks (GNNs) are highly suited for cheminformatics and computational pharmacology. Molecules are naturally represented as graphs—atoms as nodes and bonds as edges—allowing GNNs to process chemical data without forcing fixed-vector limitations [15]. In the current landscape, GNNs demonstrate exceptional accuracy in predicting complex biological mechanisms such as drug-gene interactions, offering over 97% accuracy in specialized areas like periodontal regeneration targeting the RTK-VEGF4 family [16] Table 1.

Table 1: Summary of Recent Computational Technologies in Drug Discovery.

Computational Technology	Primary Applications in Drug Discovery	Notable Benefits / Capabilities
AlphaFold & Deep Learning Structural Models	3D protein structure prediction; resolving 'undruggable' targets.	Provides near-experimental accuracy without reliance on prior homology structures.
Generative AI (Transformers, Diffusion, LLMs)	De novo molecular design; autonomous compound optimization.	Explores vast novel chemical spaces; capable of incorporating multi-parameter constraints.
Machine Learning-driven Virtual Screening	High-throughput evaluation of ultra-large chemical databases (billions of compounds).	Exponentially faster than explicit docking; robust binding affinity predictions.
Automated Molecular Dynamics (MD)	Evaluating protein-ligand stability over time; flexibility analysis.	Bridges static structural data with dynamic physiological contexts at high throughput.
Graph Neural Networks (GNNs)	Drug-target interaction mapping; molecular property abstraction.	Captures complex structural topologies without strict formatting limits.
AI-Integrated QSAR & ADMET Models	Predicting pharmacokinetics, toxicity, and plasma half-lives.	Reduces late-stage clinical attrition; speeds up optimization processes.

Conclusion

The synergy between computer science and medicinal chemistry is rapidly ushering in a new era of drug discovery. The integration of structural prediction mechanisms such as AlphaFold, generative AI for molecular design, high-throughput virtual screening, and precise machine learning models for ADMET estimation reduces developmental bottlenecks. As these technologies grow more sophisticated, computational drug discovery will continually enhance the efficiency, cost-effectiveness, and success rate of identifying novel therapeutics.

References

1. Qureshi R, Irfan M, Gondal TM, Khan S, Wu J, et al. (2023) AI in drug discovery and its clinical relevance. Heliyon 9(7): e17575.
2. Tripathi S, Gabriel K, Tripathi PK, Kim E (2024) Large language models reshaping molecular biology and drug development. Chemical Biology & Drug Design 103(6): 14568.
3. Bernatavicius A, Šícho M, Janssen APA, Hassen AK, Preuss M, et al. (2024) AlphaFold Meets De Novo Drug Design: Leveraging Structural Protein Information in Multitarget Molecular Generative Models. Journal of Chemical Information and Modeling 64(21): 8113-8122.
4. Baselious F, Hilscher S, Robaa D, Barinka C, Schutkowski M, et al. (2024) Comparative Structure Based Virtual Screening Utilizing Optimized AlphaFold Model Identifies Selective HDAC11 Inhibitor. Chemrxiv pp. 1-34.
5. Scardino V, Di Filippo JI, Cavasotto C (2022) How good are AlphaFold models for docking-based virtual screening? Chemrxiv pp. 1-17.
6. Crucitti D, Pérez Míguez C, Díaz Arias JÁ, Fernandez Prada DB, Mosquera Orgueira A (2024) De novo drug design through artificial intelligence: an introduction. Frontiers in Hematology 3: 1-14.
7. Ock J, Meda RS, Badrinarayanan S, Aluru NS, Chandrasekhar A (2025) Large Language Model Agent for Modular Task Execution in Drug Discovery. arXiv.
8. Tang X, Dai H, Knight E, Wu F, Li Y, Li T, Gerstein M (2024) A Survey of Generative AI for de novo Drug Design: New Frontiers in Molecule and Protein Generation. arXiv.
9. Baidya ATK, Goswami AK, Das B, Darreh Shori T, Kumar R (2024) AI-Enabled Ultra-large Virtual Screening Identifies Potential Inhibitors of Choline Acetyltransferase for Theranostic Purposes. ACS Chemical Neuroscience 15(22): 4156-4170.
10. Bande AY, Baday S (2023) Accelerating molecular docking using machine learning methods. Research Square.
11. Das AP, Mathur P, Agarwal SM (2024) Machine Learning, Molecular Docking, and Dynamics-Based Computational Identification of Potential Inhibitors against Lung Cancer. ACS Omega 9(4): 4528-4539.
12. Brueckner AC, Shields B, Kirubakaran P, Suponya A, Panda M, et al. (2024) MDFit: automated molecular simulations workflow enables high throughput assessment of ligands-protein dynamics. Journal of Computer-Aided Molecular Design 38(24).
13. Xu Z (2023) Machine Learning-Based Quantitative Structure-Activity Relationship and ADMET Prediction Models for ERα Activity of Anti-Breast Cancer Drug Candidates. Wuhan University Journal of Natural Sciences 28: 257-270.
14. Wu P Y, Chou W C, Wu X, Kamineni V N, Kuchimanchi Y, et al. (2024) Development of machine learning-based quantitative structure–activity relationship models for predicting plasma half-lives of drugs in six common food animal species. Toxicological Sciences 203(1): 52-66.
15. Yao R, Shen Z, Xu X, Ling G, Xiang R, et al. (2024) Knowledge mapping of graph neural networks for drug discovery: a bibliometric and visualized analysis. Frontiers in Pharmacology 15: 1-19.
16. Yadalam P, Barbosa F, Natarajan P, Ardila C (2024) Graph Neural Networks-Based Prediction of Drug Gene Interactions of RTK-VEGF4 Receptor Family in Periodontal Regeneration. Journal of Clinical and Experimental Dentistry 16(12): e1454-e1458.