Review

How to Expedite Drug Discovery: Integrating Innovative Approaches to Accelerate Modern Drug Development

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Abstract

The drug discovery process, traditionally a lengthy and costly endeavor, is being revolutionized by integrating innovative approaches. This review delves into how modern techniques accelerate drug discovery and development, significantly reducing costs. We focus on the robust synergy of bioinformatics, artificial intelligence (AI), and high-throughput screening (HTS). Bioinformatics aids in the identification and validation of drug targets by analyzing vast genomic and proteomic datasets. AI enhances lead compound identification and optimization through predictive modeling and machine learning (ML) algorithms, slashing the time required for these stages. HTS facilitates the rapid screening of vast compound libraries to pinpoint potential drug candidates. AI-based approaches, such as HTS and predictive modeling, enhance early-stage decision-making, minimize trial-and-error experimentation, and contribute to cost-efficiency across the pipeline. Moreover, advancements in computational chemistry and molecular dynamics simulations provide deeper insights into drug-target interactions, further accelerating the design of effective and selective drugs. In drug discovery, drug candidates are tested in laboratory and live animal settings to assess their effectiveness, pharmacokinetics, and safety. By integrating these preclinical methods, the efficiency and success of drug discovery can be significantly improved, leading to more effective and safer drugs. This review underscores the important role of these technologies in contemporary drug development and explores their promising implications for future research and clinical applications.

Keywords: Artificial Intelligence (AI), Drug Development Pipeline, Drug Discovery, Bioinformatics, AI-Driven Drug Discovery

1. Introduction

Drug development is a complex process encompassing several stages, each essential for ensuring the efficacy and safety of new therapeutics. These phases, from disease-related genomic analysis to clinical testing, are the backbone of the pharmaceutical industry, driving innovation and improving patient outcomes.[1] The drug development process is generally categorized into two primary stages: discovery and development, which are crucial for advancing medicine.[2] Artificial intelligence (AI) has transformed the early phases of drug development, from disease understanding to compound optimization. Drug discovery refers to the early stages of identifying potential drug targets and compounds, whereas drug development includes preclinical and clinical testing phases aimed at bringing a drug to market. This manuscript adopts this distinction consistently throughout. Figure 1 illustrates the integration of AI across key stages of drug development, from disease characterization and target identification to lead compound optimization, preclinical evaluation, and clinical trials.

Drug screening and target identification are not simple tasks but pivotal aspects of drug development. They are aimed at resolving challenges such as insufficient efficacy and substantial adverse effects, which are common hurdles

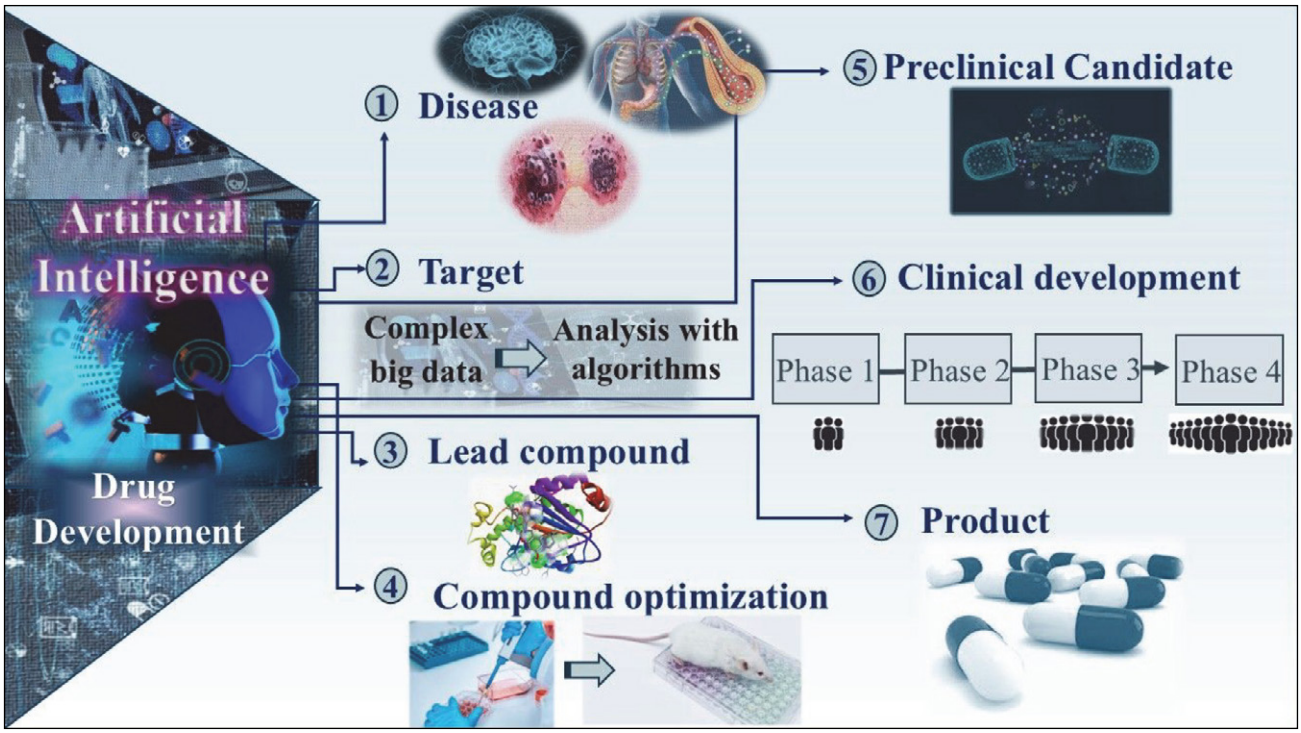

Fig 1. Ilustration of the AI-driven drug development pipeline from disease identification to final product. The schematic outlines key stages, including target selection via analysis of complex big data (Step 2), lead compound identification (Step 3), compound optimization (Step 4), preclinical candidate selection (Step 5), and progression through clinical development phases (Step 6), culminating in an approved therapeutic product (Step 7). This framework highlights how artificial intelligence streamlines the entire pipeline by enhancing data interpretation and decision-making at each stage.

in the process.[3] The drug discovery and development process has become increasingly lengthy and costly over the past decades[4], with current estimates suggesting an average duration of 10–15 years and capitalized R&D costs ranging from $1 to $4.5 billion per approved drug.[5,6] The final stage in the drug development process is not a mere formality but a critical step in product marketing.[7] To reduce the likelihood of failure during drug development, new methodologies have been developed to evaluate absorption, distribution, metabolism, excretion, and toxicity (ADMET) profiles at early stages of the pipeline.[8] Early ADMET profiling helps identify pharmacokinetic and toxicity issues before clinical testing, thereby improving decision-making and reducing the risk of costly late-stage failures.[9,10]

Despite the increasing urgency in minimizing drug resistance, the drug development pipeline incurs significant time and budget costs, with a high failure rate for most drug candidates during the clinical stages.[11] In this regard, drug design and development aspire to acquire a drug that effectively modulates the drug targets while maintaining an optimal balance of physicochemical properties and minimal toxicity.[12] Clinically approved medications, which have completed multiple phases of the drug development process, generally contain extensive information regarding dosage, interactions with other drugs, safety, adverse effects, potential harm, drug movement within the body, and the effects of the drug on the body's functions. The drug discovery and development process has become lengthier and costlier over time, necessitating strategies to reduce attrition rates during drug discovery and development.[13] In this concept, efficient computational methods for the identification of drug targets can help mitigate the high costs associated with experiments, making them crucial for successful drug development.[14]

The swift advancement of computer technologies has led to a notable increase in the screening of compounds using high-throughput methods, the application of combinatorial chemistry, and the ability to synthesize compounds. Additionally, there is an increasing need for ADMET data on lead compounds, and the methods for assessing ADMET *in vitro* are steadily expanding. Numerous effective *in silico* methods have been utilized for the *in vitro* prediction of ADMET, and *in silico* models have been devised to substitute *in vivo* models for forecasting pharmacokinetics, toxicity, and other parameters.[15,16]

Likewise, ADMET, various techniques such as QSAR (Quantitative Structure–Activity Relationship), which models the relationship between a compound's chemical structure and its biological activity using statistical or machine machine learning (ML), pharmacophore modeling, which identifies the essential chemical features required for a molecule to interact with a specific biological target,

molecular docking, and molecular dynamics simulations have proven effective at different stages of drug development, resulting in significant cost and time savings compared to traditional methods.[17] Collaborations and mergers in pharmaceutical research are strategic moves that enhance research and development initiatives. Furthermore, they have been observed to enhance the availability of pharmaceutical products in the market, particularly when these partnerships are forged at the outset of the drug development process.[18]

Integrating innovative approaches is a well-established strategy to enhance the efficiency of drug discovery. The success of utilizing organic synthesis methods compatible with biomacromolecules, machine-assisted synthesis planning, and artificial intelligence (AI) in expediting drug discovery is a testament to their effectiveness.

Computer-aided drug design (CADD) techniques have been instrumental in expediting drug discovery, reducing costs, minimizing failures, and laying a solid foundation for future endeavors. Moreover, advancements in computational methodologies, such as generative chemistry and deep learning models, are promising and showing tangible results in hastening drug discovery. Strategies like repurposing existing therapeutics, leveraging traditional medicines, and employing large-scale data analytics and AI can enrich and revolutionize contemporary drug development. These multidimensional approaches, encompassing target identification, structure-based virtual screening, and *in vitro* assays, have proven to be the drivers of drug discovery, leading to more effective and successful outcomes. Figure 2 presents a conceptual framework of drug design, depicting the interplay among computational and experimental strategies, such as CADD, bioassays, and AI/ML, in identifying and refining drug candidates.

2. Identification of Drug Target: How to Get from DNA to Drug?

The journey from DNA to drugs in the drug discovery process is a complex and multi-stage process that begins with genomic information and culminates in the development of effective therapeutic molecules. The initial and crucial step in this process is identifying the correct target. In drug discovery, a 'target' refers to a specific biomolecule, often a protein, that is involved in a disease and can be modified by a drug to treat the disease. The design of drugs to target these specific molecules can lead to better therapeutic outcomes by directly influencing the function of the target. This approach can be more effective and less harmful to other cells or organ systems, potentially increasing the success rate in clinical trials.[19,20]

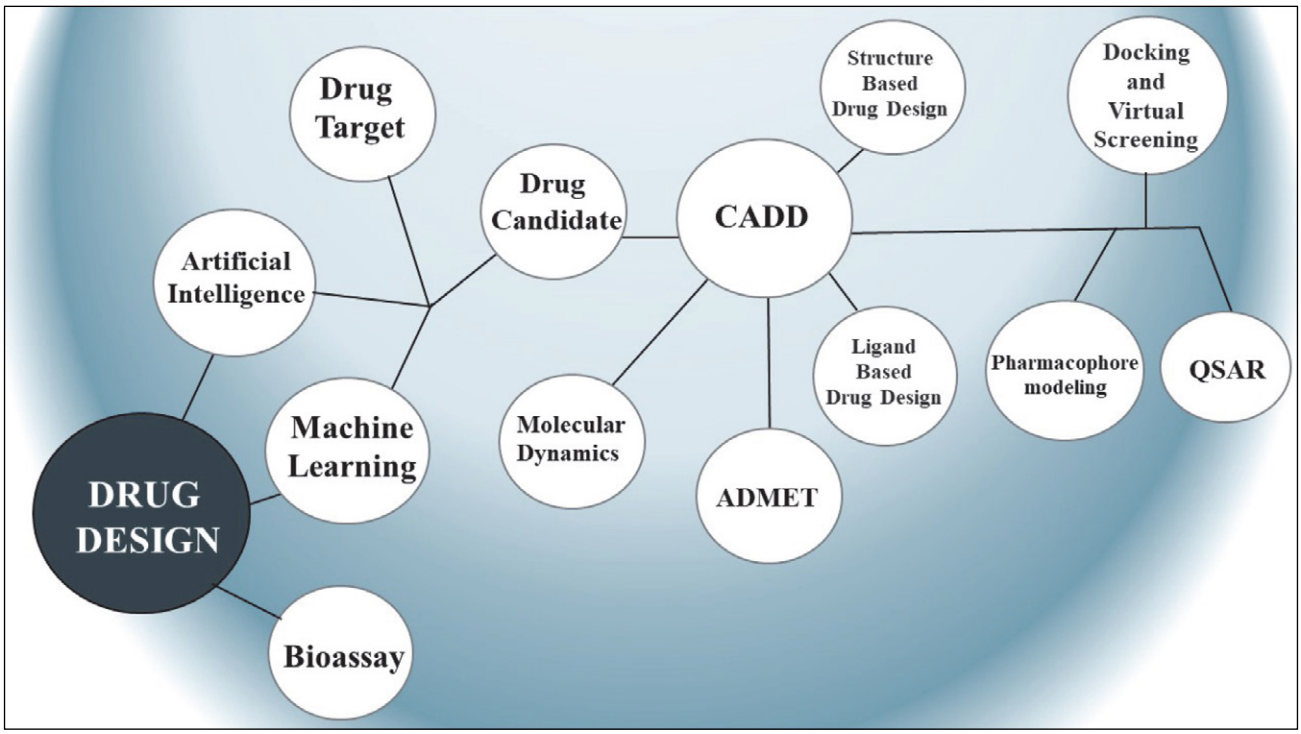

Fig 2. Conceptual map illustrating the interconnected components of modern drug design. The diagram illustrates the integration of artificial intelligence (AI), machine learning (ML), and computer-aided drug design (CADD) tools, including structure-based and ligand-based design, molecular dynamics, and ADMET prediction, to generate drug candidates. Additional elements, such as pharmacophore modeling, QSAR analysis, and bioassay validation, are also shown to be essential parts of the iterative drug discovery process.

In drug discovery, the pivotal role of data mining through bioinformatics approaches using sources such as genomic methods like Genome-Wide Association Studies (GWAS) and gene expression profiling, proteomic analyses, transgenic phenotyping, and compound profiling data is of paramount importance. This process is integral to the target identification process, providing crucial information for further analysis. Conducting mutation and polymorphism analysis to examine disease-associated mutations and genetic changes, as well as functional genomic analysis to investigate the function of specific genes and their impact on the disease, is a targeted approach in this process.[21]

With the striking progress in computer systems, integrating AI/ML in genomics has become increasingly essential. This is primarily due to the vast amount of data generated by advanced technologies in biomedicine. In clinical genomics, deep learning algorithms process large and complex genomic datasets, enabling more efficient analysis and interpretation of genetic information.[22] AI/ML algorithms, such as convolutional neural networks (CNNs), have been widely employed to interpret complex genomic data. Tools like DeepVariant utilize deep learning to accurately call genetic variants,[23] while AlphaFold leverages AI to predict protein 3D structures with unprecedented accuracy,[24] significantly aiding in structure-based target identification and validation. The systematic analysis of genomic data using AI/ML technologies has led to measurable advancements in precision medicine, particularly in chronic airway diseases such as asthma and COPD.[25] For instance, convolutional neural networks and ensemble models have been successfully applied to predict asthma exacerbations from electronic health records with high accuracy (AUC ≈ 0.85),[26] while AI-driven biomarker discovery has facilitated the stratification of asthma endotypes to support individualized treatment strategies.[27]

The application of AI in genomics is still in its nascent stages, but its potential impact is already significant. With the rapid growth of biomedical data facilitated by advanced experimental technologies, AI/ML have emerged as indispensable tools for drawing meaningful insights and improving decision-making processes in various areas, including drug discovery.[28] In the context of cancer genomics, the development of AI-based platforms capable of integrated analyses of large-scale multiomics data is pivotal for enhancing the diagnosis and therapy of cancer patients.[29] Furthermore, the use of AI/ML in cancer genomics is seen as a key component in integrating genomic analysis for precision cancer care, underscoring the importance of these technologies in advancing personalized medicine.[30] Yet, using AI/ML in genomics is not without challenges. Before AI/ML applications can be widely adopted in clinical care, rigorous studies are needed to test the safety and effectiveness of these technologies in real-world settings.[31] Efforts must be made to overcome these challenges, harness the potential benefits of AI/ML in genomics, and firmly ensure their successful integration into clinical practice.

The application of AI-powered spatial analysis in microenvironments, particularly in the context of cancer drug identification, represents a paradigm shift in research. This innovative study area significantly uses ML and AI techniques to enhance drug discovery processes. The tumor microenvironment (TME) is a complex ecosystem comprising various cell types, signaling molecules, and extracellular matrix components that interact dynamically to influence tumor growth, progression, and response to therapy.[32] Understanding the intricate interactions within the TME is crucial for developing effective cancer treatments. Recent technological advancements, such as AI-supported spatial analysis and multiplex assays, have significantly enhanced our ability to dissect the tumor microenvironment (TME) with high precision and resolution.[33] By integrating deep learning techniques with spatial omics data modeling methods like SOTIP[34], researchers can gain insights into spatial heterogeneity and differential microenvironments within tumors. This approach provides a comprehensive understanding of the tumor microenvironment, identifying potential drug targets and responses to treatment.[35]

The advent of multiplexed methodologies has opened doors for the simultaneous examination of different components of the TME, providing insights into the biological cross-talk occurring at the tumor-host interface.[36] By harnessing digital analysis tools, researchers can scrutinize paraffin tumor tissues at subcellular and cell population levels, illuminating the complex interactions within the TME.[36] These approaches enable identifying biomarker-positive cells and their spatial colocalization within tumor regions, offering valuable information for predicting treatment outcomes.[37] Furthermore, AI-powered spatial analysis tools, such as Lunit SCOPE IO, have been developed to automate the segmentation and quantification of histologic components in hematoxylin and eosin-stained whole-slide images (WSI).[33] These tools enhance the characterization of tumor-infiltrating lymphocytes (TILs) and serve as complementary biomarkers for immune checkpoint inhibition in non-small-cell lung cancer.[33]Additionally, ML and AI-driven spatial analysis techniques applied to pathology slides have facilitated a deeper understanding of the tumor immune microenvironment.[38]

This collaborative effort underscores the importance of our collective work in characterizing the molecular, cellular, and spatial properties of tumor microenvironments across different cancer types.[39] By combining image analysis algorithms with multiplex staining, researchers can conduct in-depth quantitative and spatial analyses of the broader TME, enhancing our comprehension of tumor-immune interactions.[40] These advancements underscore the potential of automated methodologies in characterizing tumor microenvironments' molecular, cellular, and spatial properties across different cancer types, ultimately leading to improved patient outcomes.[41] These in-

Table 1: Pharmaceutical companies that are using AI-supported spatial analysis in their drug development processes

Pharmaceutical Company	AI Provider/ Tool	Application	Description
AstraZeneca	DeepMind	Drug discovery, tissue analysis	Utilizing AI for spatial analysis of tissue samples to understand disease mechanisms and identify new drug targets.
Pfizer	IBM Watson	Oncology research	Applying AI-supported spatial analysis to study tumor microenvironments and improve cancer treatment strategies.
Novartis	PathAI	Pathology, diagnostic advancements	Using AI to analyze spatial patterns in tissue samples for better diagnostics and treatment planning.
Sanofi	Insilico Medicine	Biomarker discovery	Leveraging spatial analysis to identify biomarkers and understand disease progression.
Roche	Genentech	Personalized medicine	Implementing AI for spatial analysis to tailor treatments based on individual tissue profiles.
Merck	NVIDIA	Immunotherapy research	Using spatial analysis to study immune cell interactions within tissues to enhance immunotherapy approaches.
Johnson & Johnson	Atomwise	Drug target identification	Applying AI-supported spatial analysis to identify and validate new drug targets.
GlaxoSmithKline	BenevolentAI	Drug discovery	Utilizing spatial analysis to understand disease mechanisms at the cellular level and identify potential drug candidates.
Eli Lilly	Flatiron Health	Clinical trials	Using spatial analysis in clinical trial data to improve patient stratification and treatment efficacy.
Bristol-Myers Squibb	GNS Healthcare	Drug development	Implementing AI-supported spatial analysis to enhance understanding of tissue responses to treatments.

novative approaches highlight the importance of advanced imaging and analysis techniques in unraveling the complexities of the TME. In parallel with these developments, some pharmaceutical companies (see Table 1) use AI-supported spatial techniques.

Several pharmaceutical companies listed in Table 1 are actively applying AI-supported spatial analysis to address complex biomedical questions. For instance, AstraZeneca collaborates with DeepMind to analyze tissue samples for elucidating disease mechanisms and identifying targets. Pfizer uses IBM Watson's AI to study tumor microenvironments in oncology research. Novartis, through PathAI, advances diagnostic accuracy by identifying spatial patterns in tissue. Companies like Roche (via Genentech) and Sanofi (via Insilico Medicine) apply spatial tools for personalized medicine and biomarker discovery, respectively. These applications demonstrate how AI is enabling a precise, spatially resolved understanding of tissue pathology, thereby enhancing decision-making in both the early discovery and clinical phases.

2. 1. Computer Aided Drug Discovery (CADD)

CADD is a crucial approach that utilizes computer models, data analyses, and artificial intelligence (AI) techniques to improve the efficiency and effectiveness of drug development processes. The integration of ML algorithms, deep learning technologies, and AI-driven solutions has transformed various stages of drug discovery and development.[42,43] These technologies are essential for tasks such as structure- and ligand-based virtual screening, de novo drug design, physicochemical property prediction, and drug repurposing.[42] Pharmaceutical companies and research groups increasingly rely on computer-aided drug discovery techniques.[44]

CADD is recognised as a cutting-edge strategy with numerous advantages, including cost and time savings, high efficiency and success rates, better alignment and selectivity to the target, rational drug design, ADMET prediction, environmentally friendly approaches and ethical benefits, such as reduced reliance on animal testing. Structure-based drug discovery (SBDD) and ligand-based drug discovery (LBDD) are the two primary methods used in CADD.[45]

2. 1. 1. Structure-based Drug Design (SBDD)

SBDD, a method that comes into play when the three-dimensional structure of the target molecule is known or can be predicted, is a testament to precision in drug design and optimization. It strives to create and enhance drug candidates that will bind specifically to the target, thereby exhibiting biological activity. This is achieved by leveraging the structural information of the target protein or nucleic acid.[46]

SBDD is the method of choice when the crystal structure of the target protein has been resolved, a feat accomplished through techniques like X-ray crystallography or Cryo-EM (electron microscopy). These methods provide high-resolution structural data, offering a clear view of the binding sites of ligands and the active regions of the target. Similarly, it is employed when the three-dimensional structure of the target protein in solution is deter-

mined using NMR spectroscopy, a particularly valuable tool for small proteins and protein complexes. If the structure of the target protein is unknown, homology modeling steps in, creating a predicted structure based on a known structure. This process involves using the structure of a closely related protein as a reference.[47] In this regard, researchers access approximately 1 million Computed Structure Models (CSMs) from AlphaFoldDB and RoseTTAFold (from the Model Archive) and ~200,000 empirically determined PDB structures at https://www.rcsb.org/.

Docking and virtual screening:

Finding and improving therapeutic compounds requires understanding the binding mechanism between proteins and small molecules.[48] Molecular docking is a widely used SBDD method. Molecular docking estimates the optimal position, orientation, and conformation of a drug candidate (small molecule) when binding to a protein. Most docking systems currently in use achieve success rates between 70% and 80% in terms of accurately reproducing known ligand binding poses, typically within a root mean square deviation (RMSD) of 1.5 to 2 Å when compared to crystallographic reference structures.[49] A virtual screening computational technique evaluates a vast library of compounds to determine if they can bind to specific locations on target molecules, such as proteins and, well-compounds examined.[50] It focuses on rapidly searching enormous chemical structure libraries using computers to find those structures most likely to bind to a therapeutic target, usually an enzyme or protein receptor.

Structure-based virtual screening (SBVS): SBVS is a computer-aided drug discovery method that uses the three-dimensional structure of a target molecule (usually a protein) to identify potential drug candidates.[51] SBVS screens an extensive library of chemical compounds, predicting how these compounds might bind to the target molecule and identifying the most promising candidates.[48] Docking techniques are frequently employed in SBVS on extensive chemical libraries due to their rapidity in scanning millions of molecules with a simplified scoring function. Scoring functions are utilized by docking tools like DOCK, AutoDock, Glide, FRED, GOLD, and Surflex-Dock to assess protein–ligand binding.[48]

Ligand-based virtual screening (LBVS): LBVS is a computer-aided drug discovery method that uses the properties of known active ligands to predict the binding potential of chemical compounds to specific biological targets. LBVS uses the molecular similarity concept to analyze the structural details and physicochemical characteristics of the chemical scaffold of known active and inactive compounds. Accordingly, similarity measurements utilizing appropriate chemical descriptors are used to investigate the links between compounds in a particular library and one or more known actives.[51] These measurements can be carried out using 3D descriptors related to molecular fields, shape, and volume as well as pharmacophores, as well as 1D and 2D descriptors that often include information on the chemical nature of compounds and their topological properties. The following circumstances make LBVS a better choice: (a) when little is known about the molecular target's structure. Additionally, it is used to enhance the database for SBVS experiments; (b) LBVS methods are generally superior to SBVS methods for targets with a large amount of available experimental data or where the drug-binding site is not well defined; (c) using both approaches simultaneously can improve the accuracy of the VS by removing some false-positive compounds that the SBVS technique identified as promising, increasing the likelihood of obtaining positive results.[52] When information on the structure of ligand-target complexes and similarity relationships to active compounds are available, combining the methods of SBVS and LBVS may be a viable approach that can result in a comprehensive framework that can improve the success of drug discovery efforts.[51]

Despite their widespread use, both SBVS and LBVS come with notable limitations. SBVS often suffers from high false-positive rates due to inaccuracies in scoring functions, may fail to rank active compounds over decoys reliably. Additionally, the quality and resolution of protein structures especially for flexible or disordered regions can significantly affect docking results. LBVS, on the other hand, is inherently limited by its dependence on the availability of well-characterized ligands with known activity. This restricts its application to targets with rich ligand databases, making it unsuitable for novel or poorly studied targets. Both approaches also entail substantial computational costs, especially in large-scale screenings, and are sensitive to the quality of input data, which can impact the robustness of the outcomes.

2. 1. 2. Ligand-based Drug Design (LBDD)

To anticipate the properties of a novel compound, LBDD examines current activities using techniques such as pharmacophore modeling, QSAR models, and 3D shape matching.[48]

Pharmacophore modeling: An abstract representation of the structural characteristics needed by a biological macromolecule to identify a ligand is called a pharmacophore. To develop a pharmacophore model, an initial set of compounds is chosen with a variety of structural features. Compatibility analysis is performed to make a list of low-energy conformations for each chosen molecule, including the likely bioactive conformation. The low-energy conformations of molecules in every possible combination are stacked. Functional groups (such as carboxylic acid groups or phenyl rings) that are common to all the compounds in the collection can be added. It is thought that the collection of conformations that yields the best fit is the active conformation. Molecules are stacked and repre-

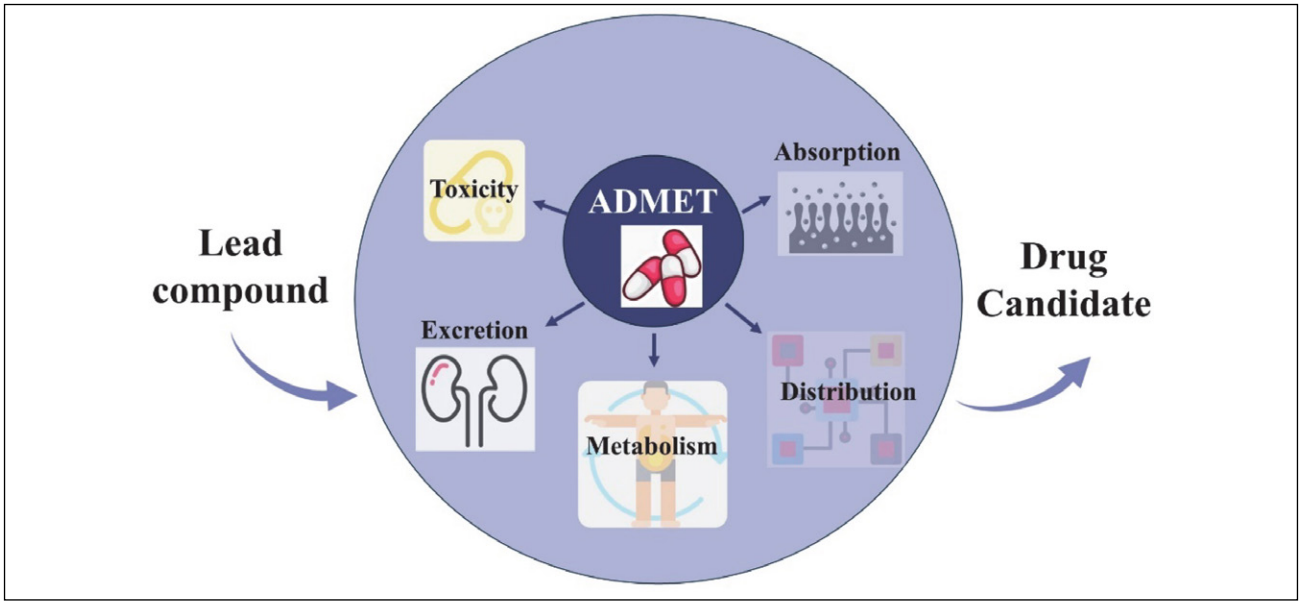

Fig 3. Schematic representation of ADMET evaluation in the drug development pipeline. The diagram outlines how absorption, distribution, metabolism, excretion, and toxicity assessments are used to screen lead compounds before selecting viable drug candidates. These properties collectively determine the pharmacokinetic and safety profile of a compound, significantly influencing its success in preclinical and clinical stages.

sented abstractly. The pharmacological effects of a collection of substances that bind to the same biological target are evaluated.[53]

Quantitative structure-activity relationships (QSAR): One of the traditional uses of ML techniques in drug discovery is QSAR.[54] Building prediction models of biological activities based on the structural and molecular details of a compound library is known as quantitative structure-activity relationship, or QSAR, modeling. The idea of quantitative structure-property relationship, or QSAR, was first applied in drug discovery and development. Since then, it has found widespread use in the correlation of molecular data with various physicochemical properties as well as biological activities.[50] In QSAR, the selection of molecular descriptors and the evaluation of molecular similarity are crucial. It is important to note that, regardless of the field of study, comparing object representations, similarity metrics, and the interactions between related attributes and relationships among objects are generally relevant for data modeling.[55] Important pharmacological characteristics, like ADMET, have been thoroughly modeled using QSAR techniques. To develop novel and safe medications, it is imperative to minimize toxicity and optimize pharmacokinetics; inaccurate assessment of these factors may cause unfavorable side effects and impair in vivo efficacy, which could ultimately lead to a drug candidate's failure.[55]

Moreover, AI–driven virtual screening, particularly through deep learning and ultra-large compound library docking, has significantly accelerated early-stage drug discovery. These approaches reduce the number of false positives and eliminate resource-intensive failures during hit-to-lead stages.[56,57] For instance, deep docking strategies can rapidly screen over a billion compounds, drastically decreasing both time and experimental cost compared to traditional *in vitro* methods. A landmark example is the discovery of Halicin, a novel broad-spectrum antibiotic, identified using a deep learning model trained on molecular structures an achievement that conventional screening pipelines had missed.[58] This case illustrates the practical application of AI in streamlining discovery pipelines and alleviating the economic burden of early-stage drug development.

2. 1. 3. ADMET Prediction

Drugs that are both safe and effective have precisely calibrated pharmacokinetics and pharmacodynamics, which include sufficient absorption, distribution, metabolism, excretion, and acceptable toxicity (ADMET), as well as high potency, affinity, and selectivity against the molecular target.[59] It was observed that the inadequacies in ADMET characteristics cause a lot of clinical trials to fail. Although it is ideal to profile ADMET early in the drug discovery process, there is a lack of data and a high expense associated with experimentally evaluating ADMET characteristics. Additionally, computational analyses of ADMET during the clinical trial phase can be a useful design approach that enables researchers to focus more on the most promising drugs.[60] Today, there is a large range of tools available for ADMET prediction, including ADMETlab[61], QikProp[62], MetaTox, SwissADME, pKCMS[63], DataWarrior[64], MetaSite and StarDrop[65] to mention a few. By easily excluding inappropriate compounds, ADMET prediction tools can cut down on the amount of costly late-

stage failures and synthesis-evaluation cycles.[59] Figure 3 exhibits the ADMET evaluation process, highlighting how absorption, distribution, metabolism, excretion, and toxicity profiling are employed to refine lead compounds into viable drug candidates.

Furthermore, AI-powered predictive toxicology and ADMET modeling enable early elimination of compounds with poor safety profiles, thus lowering attrition rates in later phases and saving substantial R&D resources. Machine learning techniques have been shown to outperform conventional rule-based methods in predicting toxic effects.[66] In addition, Kelleci Çelik and Karaduman[67] employed a one-vs-all QSTR (OvA-QSTR) approach to accurately predict drug-induced hepatotoxicity using structural and molecular descriptors, reinforcing the utility of AI in early-stage toxicological assessments.

2. 1. 4. Incorporated Artificial Intelligence and Molecular Dynamics (AI-MD)

AI and MD methods have demonstrated significant potential in various scientific fields, particularly drug design, chemistry, and materials science. The integration of AI with MD simulations not only enables the development of innovative computational workflows but also underscores the significance of combining AI with mechanistic insights from MD, a crucial aspect of this integration. Elend et al.[68] present a computational drug design work-

Table 2A: AI Applications in Drug Discovery Phase

Application	Description	AI Techniques Used	Tools
Target Identification	Identifying biological targets linked to diseases	ML, NLP	IBM Watson, DeepMind
Lead Compound Identification	Screening large compound libraries	VS, Deep Learning	Atomwise, Schrödinger, DeepChem
Lead Optimization	Improving efficacy and reducing toxicity	QSAR, Generative Models	MOE, ChemDraw, ADMET Predictor
ADMET Predictions	Early profiling of pharmacokinetics and toxicity	ML, Predictive Modeling	ADMET Predictor, pkCSM
Drug Repurposing	New uses for existing drugs	ML, Network Analysis	IBM Watson
Protein Structure Prediction	Predict 3D structures for interaction studies	Deep Learning	AlphaFold
Genomic Data Analysis	Disease-related genetic profiling	ML, Data Mining	GATK, DeepVariant
Biomarker Discovery	Identifying biomarkers that predict response to therapies	ML, Data Mining	BenevolentAI, GNS Healthcare
Virtual Screening and Docking	Simulating molecular docking to predict how drugs bind to their targets	VS, Molecular Docking	AutoDock, Schrödinger Suite

Table 2B. AI Applications in Drug Development Phase

Application	Description	AI Techniques Used	Tools
Preclinical Testing	Evaluating efficacy & safety pre-clinically	Image Analysis, ML	Insilico Medicine, PathAI
Clinical Trial Design	Patient recruitment, protocol optimization	AI Analytics, Predictive Modeling	Medidata, REDCap
Predictive Toxicology	Forecasting toxicity and safety issues	ML, Neural Networks	DeepTox, Tox21 Challenge
Molecular Dynamics Simulations	Atomistic simulations of drug-target interactions	Molecular Dynamics	GROMACS, NAMD
Chemical Synthesis Optimization	Improving synthesis yield and routes	AI-driven Planning	ChemPlanner, Reaxys
Synthetic Biology	Designing novel biological systems	ML, Synthetic Biology	Benchling
Patient Stratification	Subgrouping based on genetic/clinical data	Clustering, ML	Illumina BaseSpace, Synthego
Personalized Medicine	Individualized therapy planning	ML, Data Analytics	23andMe, Foundation Medicine
Image Analysis	Tissue/pathology image evaluation	AI Diagnostic Systems	ImageJ, PathAI
Data Mining	Identifying patterns from large datasets	ML, Data Mining	RapidMiner, Weka

Abbreviations: ML: Machine Learning, NLP: Natural Language Processing, VS: Virtual Screening, QSAR: Quantitative Structure–Activity Relationship, ADMET: Absorption, Distribution, Metabolism, Excretion, and Toxicity, AI: Artificial Intelligence.

flow that merges AI methods and MD simulations to create potential drug candidates, showcasing the effectiveness of AI-MD integration in drug discovery. Baum et al.[69] discuss the impact of AI implementations in chemistry, highlighting their role in reducing experimental effort and optimizing reaction conditions, underscoring the transformative potential of AI in scientific research. Tran et al.[70] utilize MD simulations to gain insights into AI-generated cell-penetrating peptides, stressing the significance of combining AI with mechanistic insights from MD. Terayama et al.[71] underscore the importance of integrating ML techniques with simulations and experiments in research. Meuwly[72] explores the application of ML techniques in chemical reactions, illustrating the historical use of AI in chemistry research. Zhang et al.[73] focus on enhancing molecular simulations with AI, emphasizing the computational intensity of such applications and the necessity for advanced methodologies. Xu et al.[74] combine chemical descriptors with AI/ML tools to predict synthesis reactions, demonstrating the potential of AI in predicting chemical outcomes. Elbaz et al.[75] investigate the use of MD simulations to study diffusion mechanisms, highlighting the importance of detailed simulations in understanding molecular processes. In conclusion, the amalgamation of AI and MD methods provides a robust tool for expediting scientific discovery, streamlining experimental processes, and designing innovative materials and drugs. Researchers can unlock new frontiers in various scientific disciplines by leveraging AI's strengths in data analysis and prediction with detailed insights from MD simulations.

Table 2A summarizes AI-driven tools and methods employed in the drug discovery phase, including target identification, virtual screening, and biomarker discovery. Table 2B, on the other hand, outlines applications in the drug development phase, such as preclinical testing, clinical trial design, and predictive toxicology. This separation facilitates a clearer understanding of the sequential use of AI technologies across the whole drug development pipeline.

2. 1. 5. Key Takeaways in AI-Aided Drug Development in CADD

AI has significantly impacted drug development processes by offering various benefits. AI plays a crucial role in rational drug design, decision-making support, personalized therapies, clinical data management, and expediting drug development.[76] AI/ML platforms are instrumental in determining the correct dosage form, optimizing it, and facilitating quick decision-making for efficient manufacturing of high-quality products.[77] Advances in AI-powered Language Models (LMs) have shown the potential to enhance drug discovery and development processes.[78] CADD techniques are essential for accelerating drug discovery, reducing costs, and minimizing failures in the final stages of development.[44]

AI is involved in every drug design and development stage, from target identification to trial design and post-market product monitoring.[79] Pharmaceutical companies have utilized AI to speed up drug discovery processes, automate target identification, and enhance development speed.[80] AI assists in developing treatment regimens, prevention strategies, and drug/vaccine development, particularly crucial during health crises like the COVID-19 pandemic.

AI algorithms enable the design of advanced drug development pipelines, reducing time and costs in the drug discovery process.[81] AI advancements in radiotherapy show promise in improving treatment efficiency and effectiveness.[82] AI has been extensively used in computer-aided drug design, including repurposing existing drugs against specific targets like COVID-19 receptor proteins.[83] Open data sharing and model development are crucial for the progress of drug discovery with AI.[84]

The application of AI/ML in synthetic drug substance process development presents significant untapped opportunities.[85] AI's role in drug discovery spans from compound screening to clinical trial conduct and repurposing, enhancing various phases of drug development.[86] AI/ML trends impact clinical pharmacology by aiding target identification, generative chemistry, and clinical trial outcome evaluation.[87] Effective multimodal approaches integrating big data, chemistry, biology, and medicine with AI capabilities optimize drug discovery.[87]

2. 1. 6. AI/ML in Drug Development

Artificial intelligence (AI) and machine learning (ML) have become indispensable tools in drug development, offering advanced capabilities across both discovery and development stages. Their unique contributions are particularly pronounced in clinical trial optimization, post-market surveillance, and biomarker-driven drug repositioning areas less emphasized in earlier sections of this review.

AI algorithms are now extensively used to enhance clinical trial design by predicting patient enrollment dynamics, optimizing inclusion/exclusion criteria, and estimating dropout risks, thus improving efficiency and reducing costs.[88] In the post-marketing phase, AI-powered pharmacovigilance systems can detect adverse drug events faster and more reliably than traditional methods by analyzing real-world data from electronic health records and patient forums.[89]

In preclinical development, AI models support compound screening, molecular property prediction, and de novo drug design through deep learning techniques that handle complex datasets, expediting lead optimization and safety profiling.[90,91] These tools are especially valuable in oncology and rare diseases, where patient stratification and precision targeting are essential.

Table 3 summarizes real-world implementations of AI/ML by leading pharmaceutical companies. For in-

Table 3: Pharmaceutical Companies Using AI For Drug Development

Pharmaceutical Company	Collaboration Focus	AI Provider/Tool	Year Started
Pfizer	Drug discovery and development using AI-driven data analysis	IBM Watson, Atomwise	2016
Novartis	Drug discovery, personalized medicine, drug discovery, and clinical trial design	Microsoft, PathAI	2017
Sanofi	Drug discovery and design, biomarker development	Exscientia, Insilico Medicine	2019
AstraZeneca	Discovery of new drug targets and develop therapies	BenevolentAI, DeepMind	2018
GlaxoSmithKline	Drug discovery, clinical trials, and biomarker development	Insilico Medicine, GNS Healthcare	2019
Johnson& Johnson	Pathology, diagnostic advancements	Atomwise, PathAI	2016
Merck	Drug discovery, predictive toxicology	PathAI, DeepTox	2017
Roche	Personalized medicine, drug development	Genentech, Flatiron Health	2018
Bristol-Myers Squibb	Drug discovery, immunotherapy research	NVIDIA, Flatiron Health	2019
Eli Lilly	Drug discovery, lead optimization	Atomwise, BioSymetrics	2017
Takeda	Drug discovery, clinical trials	Atomwise, BioSymetrics	2018
AbbVie	Drug discovery, target validation	IBM Watson, BioSymetrics	2019
Amgen	Drug discovery, biologics development	GNS Healthcare, Atomwise	2017
Bayer	Drug discovery, patient stratification	GNS Healthcare, BenevolentAI	2018
Biogen	Drug discovery, neurodegenerative diseases	IBM Watson, Atomwise	2019

stance, AstraZeneca has collaborated with DeepMind to enhance tissue analysis in oncology, while Novartis leverages Microsoft AI for patient segmentation and trial efficiency. Similarly, Pfizer, Sanofi, and GlaxoSmithKline employ AI platforms such as IBM Watson, Exscientia, and Insilico Medicine to accelerate drug discovery, biomarker development, and clinical trial design. These collaborations reflect AI's expanding role from preclinical modeling to post-marketing applications.

The table has been structured to clearly distinguish AI use cases in discovery (e.g., target identification, virtual screening) versus development (e.g., trial optimization, toxicity prediction), thereby improving reader comprehension and aligning with the pharmaceutical R&D workflow.

3. Bioassay of Drug Candidate

The integration of *in silico*, *in vitro*, and *in vivo* studies is essential for effective and efficient drug discovery. *In silico* studies provide a cost-effective and rapid initial screening of potential drug candidates, which are then rigorously tested through *in vitro* and *in vivo* experiments to ensure their safety and efficacy before proceeding to clinical trials in humans. This multi-stage approach helps streamline the drug discovery process, reducing time and costs while increasing the likelihood of success in developing new treatments.[92]

Recent advances in biomedical engineering and genetic technologies have introduced innovative *in vitro* and *in vivo* techniques that significantly enhance the predictive power and translational relevance of preclinical drug testing.

CRISPR-based assays represent a transformative *in vitro* approach, enabling precise genome editing to model disease-specific mutations and assess gene-drug interactions in human-derived cell lines. These systems would allow researchers to dissect target-specific pathways and identify synthetic lethal interactions, which are particularly valuable in oncology and for rare genetic disorders.[93] CRISPR screening platforms have also been integrated into drug repurposing pipelines, offering scalable tools for high-throughput functional genomics.

In the realm of *in vivo* models, the development of humanized animal models has bridged critical translational gaps by introducing human genes, cells, or tissues into immunodeficient animals. These models are beneficial for studying immunotherapies, infectious diseases, and drug responses related to metabolism.[94] Unlike conventional rodent models, humanized systems enable the evaluation of drug efficacy and toxicity in a context that closely mimics human physiological conditions.

Additionally, organ-on-a-chip technologies, although not strictly *in vitro* or *in vivo*, offer a hybrid system that simulates the dynamic interactions of human tissues and fluids. These microfluidic devices recreate the multicellular architectures and mechanical forces of organs like the lung, liver, and gut, providing valuable insights into drug absorption, distribution, and organ-specific toxicity.[95]

Together, these cutting-edge approaches complement traditional bioassays by enhancing mechanistic understanding, improving predictive accuracy, and supporting the development of safer and more effective drugs.

3. 1. *In vitro* Studies

In vitro studies provide valuable information on the efficacy and safety of drug candidates before *in vivo* animal studies and clinical trials. *In vitro* studies evaluate the effects of potential drug candidates on specific biological

targets in an *in vitro* setting. During this phase, cell culture studies are conducted to assess the impact of the candidate drug on cell viability, its apoptotic and necrotic effects, and its genotoxicity as part of toxicity and safety tests to understand the mechanism of action of the drug candidate, its effects on cellular signaling pathways, receptor interactions, and biomolecular processes are examined in detail.[96–99] Pharmacokinetic studies are conducted to investigate how the drug candidate is absorbed, distributed, metabolized, and excreted by the cells.[100] Additionally, pharmacodynamic studies are performed to determine the biological effects and efficacy of the drug on the cells. *In vitro* studies utilizing three-dimensional (3D) cell cultures and organoid models provide more complex and realistic cellular environments, helping to achieve more reliable results.[101,102]

3D cell cultures and organoid systems offer significant advantages over traditional two-dimensional (2D) cultures, as they more accurately mimic the structural and functional complexity of human tissues. They replicate cell–cell and cell–matrix interactions, nutrient and oxygen gradients, and tissue-specific architecture more effectively, enhancing their predictive value for *in vivo* outcomes. However, these models are not without limitations. They can be expensive to establish and maintain, often require specialized scaffolds or materials, and exhibit variability in reproducibility and scalability for high-throughput applications. Furthermore, while *in vitro* systems whether 2D or 3D are invaluable for mechanistic insights, they lack biokinetic context, which may lead to misinterpretation of toxicity or efficacy profiles when extrapolating results to human physiology.[103]

3. 2. *In vivo* Studies

In vivo studies involve testing drug candidates in animal models to evaluate their efficacy, pharmacokinetics, and safety within a living organism.[104] These studies are a critical step to verify the findings from *in vitro* experiments and to evaluate the efficacy and safety of the drug in more complex biological systems.[105] At this stage, ADME studies are conducted to determine the bioavailability and half-life of the drug as part of pharmacokinetic studies. Pharmacodynamic studies are performed to establish dose-response relationships and the degree of efficacy. Acute, subacute, and chronic toxicity tests are conducted as part of toxicity and safety studies. Potential side effects, organ damage, and mortality rates are examined.[106–108] *In vivo* models are crucial for studying the progression of the disease and the effects of the drug on this process. Additionally, they play an important role in observing the response to treatment and in identifying and validating biomarkers to monitor disease progression.[105] Compared to *in vitro* experiments, animal models are more dependable, despite certain limitations such as variations in biokinetics parameters and the inability to extrapolate results to humans.[103] Nonetheless, significant physiological and metabolic differences between animal models and humans can limit the translatability of preclinical findings, necessitating cautious interpretation and validation in human-relevant systems.

4. Discussion

4. 1. What are the Gaps in Drug Development?

The landscape of drug development is characterized by challenges that impede the efficient translation of scientific discoveries into safe and effective therapies. For instance, one of the significant issues in the pharmaceutical industry is the innovation gap, where drug development costs are escalating. In contrast, the number of new drugs approved remains relatively stable.[109] This discrepancy underscores a fundamental challenge in the field, where the increasing financial burden of bringing a new drug to market is not met with a proportional increase in successful outcomes. The high attrition rate in clinical development significantly contributes to the rising drug development costs.[110] This attrition emphasizes the urgent need for more efficient and reliable methods to identify viable drug candidates early in development to alleviate the financial strain on pharmaceutical companies.

The funding landscape is a critical aspect that exacerbates the gaps in drug development. While a significant portion of foundational research for drug discovery receives public funding, there often needs to be more in transitioning these discoveries into viable drug candidates due to funding limitations.[111] This gap between early-stage research and late-stage development highlights the necessity for bridging mechanisms to ensure that promising leads are not abandoned due to financial constraints. Moreover, challenges in developing new drugs are further compounded by the need for more effective therapies despite significant advancements in preclinical research.[112] This gap between preclinical data and clinical success is attributed to suboptimal drug development strategies, particularly in addressing critical genetic alterations in diseases like cancer.

Another crucial gap in drug development lies in pediatric drug therapy, historically lacking a focus on developing medications specifically tailored for children.[113] Pediatric drug development continues to lag behind adult therapeutics due to several scientific, ethical, and regulatory challenges. Children are often excluded from clinical trials, leading to widespread off-label drug use without robust evidence of safety or efficacy in pediatric populations. Ethical concerns such as obtaining informed consent and minimizing risk further complicate trial design. Regulatory agencies have implemented specific frameworks to bridge this gap. In the United States, the Pediatric Research

Equity Act (PREA) mandates pediatric assessments for certain new drugs, and the Best Pharmaceuticals for Children Act (BPCA) provides incentives such as extended market exclusivity for conducting pediatric studies.[114,115] The European Union's Paediatric Regulation (EC No 1901/2006) requires Pediatric Investigation Plans (PIPs) for new medicines. Despite these advances, barriers persist, including limited pediatric patient numbers, age-dependent pharmacokinetics, and formulation challenges. Addressing these obstacles is essential to ensure the development of safe and effective therapeutics for children.

Additionally, gaps in predicting drug metabolism and toxicity—particularly in the liver—pose significant challenges in drug development.[116] The underperformance in this area is largely attributed to limited understanding of the mechanisms driving hepatic injury, highlighting the urgent need for more comprehensive and physiologically relevant approaches to assess drug safety.

Another challenge is that the interval between biomarker discovery and clinical utility hinders drug development progress.[117] While there is a focus on identifying biomarkers for various conditions, there often needs to be more clarity in translating these findings into clinically meaningful applications. This highlights the importance of streamlining the drug approval process and enhancing the translational impact of biomarker research to bridge this gap effectively. Furthermore, the gap in predicting drug-drug interactions (DDIs) poses a substantial complexity in drug development, emphasizing the need for robust predictive models to assess the potential interactions of new drug entities.[118] Improving our ability to predict and manage DDIs is crucial for ensuring the safety and efficacy of drug therapies.

The lack of proactive drug development is evident in infectious diseases, particularly in addressing emerging viral diseases such as COVID-19.[119] The reactive nature of drug development in response to emerging infectious diseases underscores the need for a more proactive approach to shorten the gap between identifying new diseases and developing effective treatments. Additionally, gaps in understanding the ontogeny of drug metabolism and transport present challenges in predicting drug disposition, especially in vulnerable populations like children and the elderly.[120] The reactive nature of drug development in response to emerging infectious diseases underscores the need for a more proactive approach to shorten the gap between identifying new diseases and developing effective treatments. Additionally, gaps in understanding the ontogeny of drug metabolism and transport present challenges in predicting drug disposition, especially in vulnerable populations like children and the elderly.[121] This gap accentuates the importance of addressing fundamental gaps in disease pathophysiology to drive practical drug discovery efforts. Moreover, gaps in drug design and discovery for diseases like the Ebola virus showcase the potential of computational tools in advancing target-based drug design.[122]

In conclusion, the gaps in drug development are multifaceted and span various stages of the drug discovery and development process. They are not challenges that we can afford to ignore. Addressing these gaps requires a concerted and immediate effort from researchers, industry stakeholders, regulatory bodies, and funding agencies. By implementing innovative strategies, leveraging emerging technologies, and enhancing collaboration, we can drive impactful and efficient drug development efforts, underlining the urgency and importance of the issue.

To bridge the innovation gap and overcome funding limitations in drug development, actionable strategies are needed. Public–private partnerships (PPPs) have proven effective. For example, the Innovative Health Initiative (IHI) a €2.4 billion joint undertaking by the European Union and pharmaceutical industry brings together stakeholders from academia, industry, regulators, and patient organizations to accelerate health innovation.[123] In the United States, the Accelerating Medicines Partnership (AMP) supports cross-sector collaboration in fields such as Alzheimer's disease, type 2 diabetes, ALS, and schizophrenia, facilitating the discovery and validation of biomarkers.[124] These partnerships offer standardized frameworks, pooled resources, and data-sharing mechanisms that enhance translational efficiency. Additionally, open-access datasets like AMP-PD democratize research participation and support reproducibility. Regulatory tools such as the FDA's Biomarker Qualification Program (BQP) provide structured processes for developing biomarkers as validated drug development tools.

4. 2. Unlocking the Potential: How AI/ML are Revolutionizing Drug Development

The 20th anniversary of the completion of the draft human genome sequence was observed in 2021, exemplifying a significant milestone that has revolutionized genomics research and generated a substantial amount of genomic data. Genomics research is projected to produce between 2 and 40 exabytes of data in the next decade.[125] With this giant data, AI/ML have emerged as powerful tools in bridging the gaps in genomics by facilitating the integration of complex data sets, enabling more accurate predictions, and enhancing decision-making processes in various fields such as clinical diagnostics, agriculture, oncology, and personalized medicine. The application of AI in genomics has been highlighted in several studies, showcasing its potential to revolutionize the way genetic information is analyzed and utilized.[22,126–128] By leveraging AI technologies, researchers can overcome challenges in understanding genome evolution, function, and disease mechanisms, ultimately leading to groundbreaking discoveries.[129]

In clinical and genomic diagnostics, AI has been instrumental in linking image-derived phenotypes to their genetic origins, offering insights into disease mechanisms and potential treatments.[22] This imaging and genomic data integration can potentially enhance diagnostic accuracy and personalized treatment strategies. Moreover, in the context of precision medicine, AI plays a crucial role in analyzing genomic determinants along with patient symptoms and clinical history to enable personalized diagnosis and prognostication.[130] Moreover, AI applications to medical images, such as MRI classification tasks for neurological and psychiatric diseases[131], have demonstrated the potential of AI-based algorithms in clinical diagnosis with high quality and efficiency. These advancements spotlight the transformative impact of AI/ML in enhancing diagnostic capabilities and treatment outcomes across various medical disciplines. Regarding this, by combining genomic data with AI/ML analyses, researchers can identify novel biomarkers, optimize treatment approaches, and improve patient outcomes.

AI is not just a theoretical concept in oncology, but a practical tool that is already delivering tangible benefits. It simplifies the analysis of imaging-genomics data in diseases like glioblastoma[132], thanks to deep learning algorithms that have made significant strides in image recognition and genome analysis. The integration of molecular and imaging signatures through AI technologies offers practical advantages for early cancer detection, diagnosis, and treatment planning. In the cancer immunity, AI-driven approaches have not only opened up new avenues for comprehensive analyses of tumor immunity using genomics, transcriptomics, proteomics, and cytomics, but also led to the emergence of tumor immunomics as a novel discipline.[133] This is a clear example of how AI is shaping the future of oncology. In addition, the application of AI in bridging the gap between genomes and chromosomes, as demonstrated through single-chromosome sequencing (ChromSeq), has provided valuable insights into genome organization and function.[129,134] By overcoming challenges related to genome and chromosome analysis, researchers can advance our understanding of genetic mechanisms and their implications for various biological processes.

The integration of AI in genomics has extended to fields such as cardiology[135] and kidney cancer[136] management, bringing with it a host of practical benefits. AI technologies, such as machine and deep learning algorithms, can model complex interactions, identify new phenotype clusters, and enhance prognostic capabilities, thereby significantly improving patient care and outcomes. In kidney cancer management, AI can analyze radiographic, histopathologic, and genomic data to tailor personalized treatment strategies.[136]

AI/ML are not just reshaping the landscape of drug development but also effectively addressing critical gaps and challenges, providing a reassuring solution to complex problems. Their impact is particularly evident in drug repurposing, where these technologies enable researchers to systematically identify potential leads, thereby accelerating the drug development process and reducing associated risks through computational means.[137] In this manner, AI/ML have been instrumental in rapidly identifying drugs effective against the coronavirus, bridging the gap between repurposed drugs, laboratory testing, and final authorization.[138] The rapid growth of biomedical data, facilitated by advanced experimental technologies, has made AI/ML indispensable tools for drawing meaningful insights and improving decision-making in drug discovery, particularly in central nervous system diseases.[28] Again, during the COVID-19 pandemic, AI algorithms have played a crucial role in surveillance, diagnosis, drug discovery, and vaccine development, enabling the design of sophisticated drug development pipelines that reduce the time and costs associated with traditional methods.[81] However, it is essential to address biases in ML-based algorithms to ensure their robustness and reproducibility for integration into clinical practice.[139] AI has also been instrumental in developing treatment regimens and prevention strategies and advancing drug and vaccine development for COVID-19 and other infectious diseases.[140] In orthodontics and chronic airway diseases like asthma and chronic obstructive pulmonary disease (COPD), AI/ML have demonstrated effectiveness in mining and integrating large-scale medical data for clinical practice, showcasing their potential in improving patient care and treatment outcomes.[25,141]

The application of AI, particularly deep learning, offers opportunities to discover and develop innovative drugs by analyzing vast datasets and predicting potential drug candidates.[42] Internationally renowned experts have identified key challenges in small-molecule drug discovery using AI and have put forward strategies to address them, emphasizing the groundbreaking potential of AI in this critical area.[142] Importantly, regulatory bodies like the FDA have not only recognized, but also strongly endorsed the importance of AI/ML in medical devices. They have defined ML as a system capable of learning from specific tasks through performance tracking[143], providing a solid framework for the integration of AI in healthcare. This robust endorsement from the FDA has led to an increase in the approval of AI/ML-based medical devices in the USA and Europe. The FDA, for instance, has actively participated in the approval process of over 60 AI-equipped medical devices[144], indicating a growing trend toward incorporating AI technology into the future of medicine.

ML contributes to the automation of various stages in the traditional drug development pipeline. This is evident in studies such as that of Li et al.[145] and Vatansever et al.[28] As for antibiotic discovery, AI has emerged as a powerful ally, accelerating the identification of novel antimicrobial agents, as highlighted in studies like that of Melo et al.[146] By applying AI to computer-aided drug design, we can expedite the discovery of antibiotics and antimicrobial

peptides, addressing the global challenge of antibiotic resistance. This is a crucial task that our collective ML research has significantly advanced. By integrating natural language processing (NLP) in AI, we can scan vast amounts of literature to identify potential drug targets. At the same time, AI-driven synthesis robots, a testament to our shared vision, enable the exploration of new reaction spaces to discover novel drug candidates. This automation, a result of our combined expertise, accelerates the drug discovery process and enhances the reproducibility of chemical reactions, leading to the discovery of new compounds with therapeutic potential.

Furthermore, the advancements in AI-driven drug discovery, as discussed in studies like those of Zhavoronkov et al.[87], have not only paved the way for innovative approaches to target identification and generative chemistry but also hold the promise of a brighter future for clinical pharmacology. By leveraging AI/ML trends, researchers can enhance target identification processes, optimize small-molecule drug discovery, and evaluate clinical trial outcomes with greater accuracy and efficiency. These developments can potentially transform the field of clinical pharmacology, offering new avenues for enhancing drug development and therapeutic interventions and instilling a sense of optimism for the future.

Concisely, when harnessed collaboratively, AI/ML can usher in a new era in the pharmaceutical industry. They have the potential to address key gaps in the process, such as expediting drug discovery, optimizing lead compounds, and enhancing clinical outcomes, offering innovative solutions to longstanding challenges. By utilizing these technologies, researchers can significantly improve the efficiency and effectiveness of drug development, ultimately discovering novel treatments for various diseases. However, further research and collaboration, in which each stakeholder plays a crucial role, are imperative to fully realize this potential. As AI continues to evolve, its impact on drug development is poised to revolutionize the field and pave the way for more effective and personalized therapeutic interventions.

4. 3. Overpowering Restraints in AI-Aided Drug Development

The transformative potential of AI in revolutionizing the discovery of new materials is not just tremendous but also holds the promise of developing materials with tailored properties for diverse applications, sparking optimism for the future of pharmaceutical research. However, it's crucial to recognize and address the challenges and limitations to ensure its practical application.[147]

One significant challenge is the necessity for high-quality data, as AI algorithms heavily depend on data for accurate predictions.[148] The interpretability of AI-driven drug discovery processes is another critical limitation, as researchers often need help comprehending how AI algorithms reach conclusions and recommendations.[149] Moreover, the sustainability of resources is a growing concern due to the significant computational resources and data required for AI techniques.[150] Additionally, the current methods and tools may only partially exploit the potential of AI in drug discovery.[151] Overcoming challenges related to data quality, interpretability, resource sustainability, and tool development is not just important, but essential for maximizing the benefits of AI in revolutionizing the drug discovery process. Moreover, one of the other issues is Ethics. Regarding ethical issues in IA regulation, the EU Council recently proclaimed that member states have acknowledged the "Artificial Intelligence Law," which will establish the world's first comprehensive rules for artificial intelligence.[152]

It is crucial to emphasize the importance of addressing challenges in AI-aided drug development. By implementing strategies based on insights from reputable sources, we can overcome these challenges and maximize the benefits of AI in revolutionizing the drug discovery process. The use of specific AI models, such as deep learning and natural language processing, has become crucial for expediting the drug development process and reducing failures.[44] These AI-powered language models have demonstrated potential in assisting drug discovery and development by summarizing advancements and providing computational tools for efficiently identifying new compounds.[78] Additionally, AI/ML, including neural networks and decision trees, have proven to be essential tools for deriving meaningful insights and enhancing decision-making in drug discovery, particularly in diseases such as central nervous system disorders.[28]

Moreover, AI, in collaboration with human expertise, plays a crucial role in facilitating rational drug design, aiding decision-making processes, personalizing therapies, and effectively managing clinical data for future drug development.[76] By incorporating advancements in computer-aided drug design, automated synthetic chemistry, and high-throughput biological screening, initiatives like the NCATS ASPIRE program aim to explore novel chemical spaces more efficiently and cost-effectively. This underscores the importance of human-AI collaboration in maximizing the potential of AI in drug development.[153] Figure 4 summarizes critical applications of AI in both genomics and clinical domains, such as data integration, variant detection, biomarker discovery, and drug repurposing, underscoring its broad utility in precision medicine.

Overall, while AI offers significant potential in drug development, it's important to acknowledge and address potential risks and limitations. These include the need for large, diverse, and high-quality datasets, to avoid **ancestral bias,** which can result in reduced predictive accuracy for underrepresented populations.[154] Another challenge is **model interpretability**: many deep-learning systems remain "black boxes," limiting clinical adoption. For example, recent explainable AI techniques such as *concept-whit-*

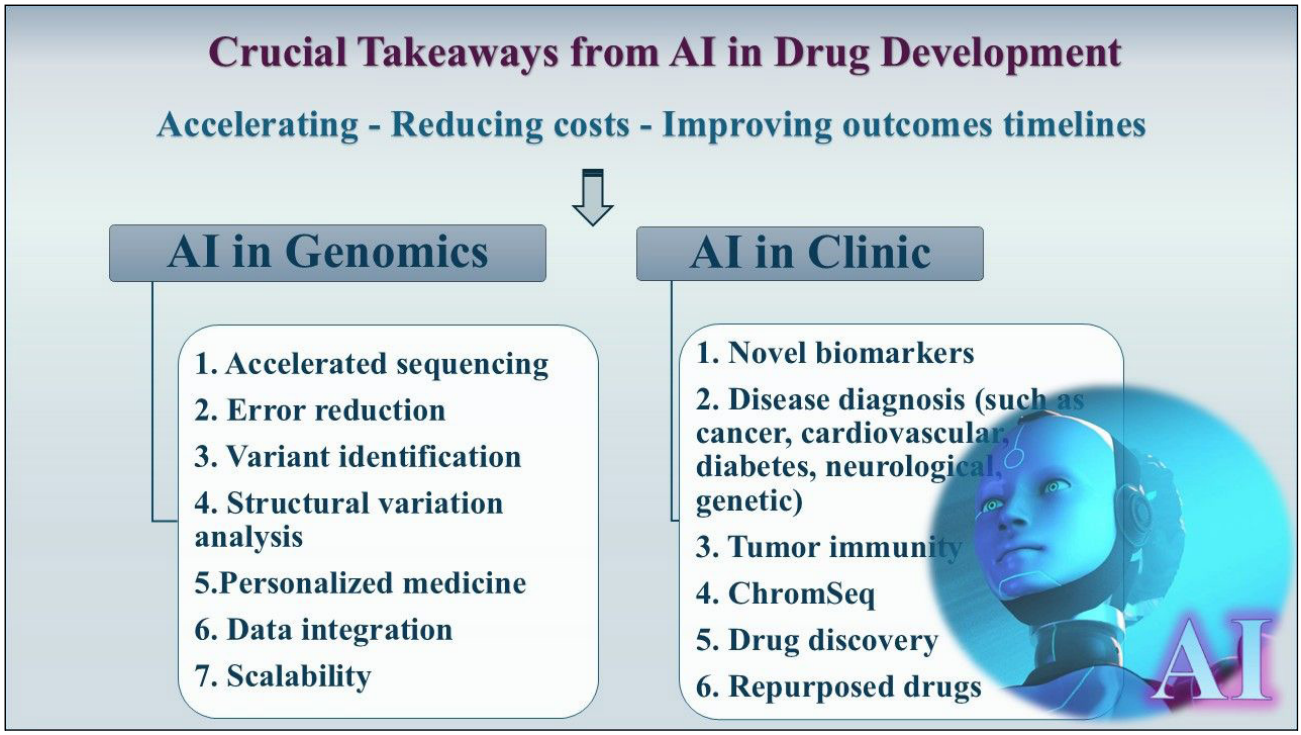

Fig 4. Summary of artificial intelligence applications in drug development, highlighting key contributions in genomics (e.g., data integration, variant analysis) and clinical contexts (e.g., biomarker discovery, disease diagnosis, and drug repurposing).

ening applied in graph neural networks reveal which molecular features drive predictions, thereby enhancing transparency.[155] Additionally, **generalizability between datasets** remains imperfect: models validated on public benchmarks often perform poorly when applied to proprietary or real-world datasets, underscoring the need for rigorous cross-platform validation.[156,157]

By proactively addressing these challenges through explainable frameworks, ancestry-aware model training, and broad validation pharmaceutical researchers can fully leverage AI's promise while maintaining safety, fairness, and confidence in the drug development process.

5. Conclusion

The integration of advanced Technologies particularly AI and ML, computational modeling, and HTS has significantly reshaped the landscape of modern drug development. These tools have demonstrated concrete progress in AI-driven target identification, lead compound optimization, and early-stage ADMET profiling. Together, they contribute to reduced development timelines, improved cost efficiency, and lower failure rates in clinical phases.

Furthermore, emerging *in vitro* 3D models, organoids, and improved *in vivo* models have enhanced translational relevance, thereby bridging the gap between preclinical findings and clinical outcomes. Despite these advancements, challenges remain particularly in areas such as pediatric drug development, biomarker validation, and the development of ethical and regulatory frameworks for the integration of AI.

Future research directions should focus on enhancing the interpretability of AI algorithms, integrating multi-omics datasets for comprehensive decision-making, and developing standardized, reproducible workflows for early-stage evaluation. These efforts will further solidify the role of computational and AI-based systems in delivering safe, effective, and patient-centered therapeutics.

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Povzetek

Postopek odkrivanja zdravil tradicionalno dolgotrajen in drag proces, vendar doživlja revolucijo z vključevanjem inovativnih pristopov. V tem članku smo povzeli, kako sodobne tehnike pospešujejo odkrivanje in razvoj zdravil ter hkrati znatno zmanjšujejo stroške. Osredotočamo se na močno sinergijo bioinformatike, umetne inteligence (UI) in visokozmogljivega testiranja (HTS). Bioinformatika pomaga pri identifikaciji in potrjevanju tarč zdravil z analizo obsežnih genomskih in proteomskih podatkovnih zbirk. UI izboljšuje identifikacijo in optimizacijo spojin vodnic s pomočjo napovednega modeliranja in algoritmov strojnega učenja, kar močno skrajša čas, potreben za te faze. HTS omogoča hitro pregledovanje obsežnih knjižnic spojin za odkrivanje potencialnih kandidatov za zdravila. Pristopi, ki temeljijo na UI, kot sta HTS in napovedno modeliranje, izboljšujejo odločanje v zgodnjih fazah, zmanjšujejo poskuse in napake ter prispevajo k stroškovni učinkovitosti skozi celoten proces. Poleg tega napredek v računalniški kemiji in simulacijah molekulske dinamike omogoča globlji vpogled v interakcije med zdravilom in tarčo, kar dodatno pospešuje načrtovanje učinkovitih in selektivnih spojin. Pri odkrivanju zdravil kandidate testirajo v laboratorijskih in živalskih modelih, da se oceni njihova učinkovitost, farmakokinetika in varnost. Z vključevanjem predkliničnih metod se lahko učinkovitost in uspešnost odkrivanja zdravil bistveno izboljšata, kar vodi do učinkovitejših in varnejših zdravil. Ta pregled poudarja pomembno vlogo računalniških tehnologij v sodobnem razvoju zdravil ter raziskuje njihove obetavne implikacije za prihodnje raziskave in klinično uporabo.