BULLETIN OF STOMATOLOGY AND MAXILLOFACIAL SURGERY
Volume 21, Issue 6

DOI: 10.58240/1829006X-2025.21.6-361

ORIGINAL RESEARCH

IMPLEMENTING ARTIFICIAL INTELLIGENCE IN DRUG RESEARCH DEVELOPMENT

Satya Obbalareddy[1], Sanyogita Shahi[2*], Anubhav Dubey[3], Sorabh Sehajpal[4], Kumara Swamy Samanthula[5], Nidhi Saran[6], Deepika Rani[7]

1. Assistant Professor, Department of Health System Management Studies, JSS Academy of Higher Education and Research, Mysuru-570004. India.
2. Department of Science (Chemistry), Kalinga University, Raipur, Chhattisgarh 492101. India.
3. Department of Pharmacology, Maharana Pratap College of Pharmacy, Kanpur, U.P, 209217 India.
4. Principal (Pharmaceutical Sciences department) Amritsar Group of Colleges, Amritsar 143001, India.
5. Faculty of Pharmaceutical Science, Assam down town University, Guwahati, 781026, Assam, India.
6. Assistant Professor, AVIPS, Shobhit University Gangoh. India.
7. Associate Professor, School of Pharmacy and Emerging Science, Baddi university of Emerging Science and Technology, Baddi. India.

Corresponding Author* Sanyogita Shahi Department of Science (Chemistry), Kalinga University, Raipur, Chhattisgarh India.492101 E-mails: drsanyogitashahi@gmail.com

***Received: Jun** 17. 2025; **Accepted:** Jul 18, 2025; **Published:** Jul 25, 2025;*

ABSTRACT

The application of artificial intelligence in drug development marks a momentous shift in the realm of pharmaceutical research. This technological advancement combines advanced computer methods with traditional scientific investigation in order to overcome long-standing challenges. The purpose of this review article is to shed light on the many uses of artificial intelligence as they pertain to the different stages of medication development, highlighting major developments and approaches. This article looks at how AI is used in the design of drugs, Poly-Pharmacology, chemical synthesis, drug repurposing, and the prediction of pharmacological properties like bioactivity, toxicity, and physicochemical features. The paper discusses the obstacles and constraints found in the field of artificial intelligence (AI), including data quality, generalizability, computing needs, and ethical issues. This is in spite of the fact that AI has recently made some promising improvements. This study highlights the potential of artificial intelligence (AI) to dramatically improve drug development by providing a complete review of the role that AI plays in drug discovery. However, it also acknowledges the challenges that need to be solved in order to fully realize the benefits that its use may provide.

***Keywords**:* Artificial intelligence, Bioactivity, Toxicity, Drug development, Repurposing.

INTRODUCTION

Designing, finding, and creating novel pharmaceuticals to improve human health and battle illnesses is a sophisticated process that is known as drug discovery. Finding targets and lead compounds is the first step in this long process. Next come optimization, careful preclinical testing, and then careful clinical trials. All of these steps are necessary to make medicines that work in the real world (Figure 1).

The first four Conventional wisdom suggests that it takes an average of twelve years and $2.6 billion to bring a single chemical from ideation to FDA clearance, highlighting the challenging nature of this procedure.

Even with all of these efforts, the process is marked by high turnover rates, major side effects of modern medications, and ongoing problems with treating long-term illnesses like cancer and diabetes [5, 6].

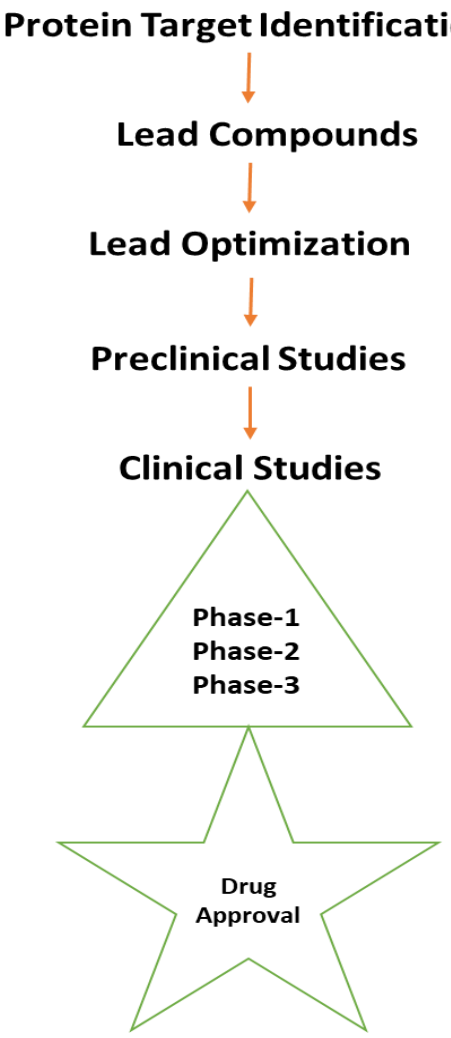

Figure-1 Process of drug discovery

Artificial intelligences (AI) have revolutionized the pharmaceutical industry by offering a range of advanced computational tools designed to enhance human skills rather than replace them. Seven and eight. Artificial intelligence (AI) is changing the pharmaceutical industry by using complex algorithms to make decisions automatically based on data analysis [9–11]. Toxicology, bioactivity, and physicochemical properties are all aspects of this technology. The study discusses the data quality, generalizability, computing needs, and ethical problems that have been encountered in the field of artificial intelligence, in addition to the hopeful improvements that AI has made. Despite recognizing the challenges that must be faced, this study provides a thorough summary of AI's role in drug discovery, under scoring the technology's potential to greatly improve drug research. From computational chemistry and molecular biology to lead compound optimization and clinical trial design, the drug development pipeline stands to gain a great deal of efficiency [12].

AI technologies make processes like protein-ligand docking, molecular dynamics simulations, virtual screening, and de novo drug creation very accurate. This opens up new treatment options and speeds up the search for good drug candidates. Three separate sources Additionally, AI's contributions to systems pharmacology, clinical trial design, and drug-target interaction predictions are transforming drug development tactics. With the use of this technology, we can optimize patient selection, track patient reactions in real-time, and tweak procedures to get the most out of our trials. Ethical considerations, legal compliance, and scientific rigor must all be carefully balanced as we approach the incorporation of AI. Ten and thirteen in this overview, we look at how artificial intelligence has revolutionized medication development. It emphasizes the ways AI speeds up the creation of new therapeutic treatments, simplifies clinical trials, and maintains drug development quality assurance. This study argues that AI should be used wisely in pharmaceutical research because it has the ability to speed up the creation of treatments that save lives, which would be a huge boon to healthcare throughout the world. Automation for Pharmaceutical Research The use of AI is revolutionizing the drug discovery process by making it more efficient, cheaper, and more effective. The use of AI has revolutionized pharmaceutical research by utilizing AI's remarkable skills in data processing, pattern identification, and decision-making[6,15].

We'll examine how artificial intelligence (AI) enhances and streamlines drug development processes in this section. We'll see how it's helping with drug screening, drug repurposing, drug design, chemical synthesis, and Poly-Pharmacology. Artificial intelligence (AI) greatly improves the discovery of promising lead compounds in the pharmaceutical industry, which dramatically shortens the time it takes to create new drugs [1-5].

AI's ability to look at different combinations of chemicals and guess how they will bind has made the process from idea to clinic much better [1,16]. The core of medication creation involves the development of tiny compounds that meet stringent requirements. Among these are the innovative qualities needed to gain intellectual property rights for economic viability, appropriate chemical and biological features, a safe profile, and pharmacological performance[17-18].

While computing tools have revolutionized drug design and discovery, conventional methods still require significant advancements before they can compete. Conventional methods involve a lot of input time, high computing costs, and inconsistent dependability[18,19]. Artificial intelligence (AI) is a promising technology that can overcome these obstacles and improve computational methods used in drug development.

Because protein dysfunction is associated with many illnesses, studying protein architectures is an important part of therapeutic creation. Finding tiny compounds with the ability to selectively bind to certain protein targets is the goal of structural medication design. Predicting the three-dimensional (3D) structure of proteins has historically been an arduous and expensive process, with de novo predictions of 3D structures exhibiting little accuracy [20]. In this facet of medication development has been utterly transformed by the rise of AI, especially in the form of deep learning and feature extraction techniques. We can learn more about the link between structure and sequence with these technologies, which can accurately predict secondary protein structures and map protein contacts [20, 22].

The long-term goal is to make structural drug design better by using deep learning to make more accurate predictions of 3D protein structures. This will allow for more research into how proteins interact with each other (PPI) [20,23].

This incorporation of AI into medication design is a huge step forward, and it has the potential to make drug development endeavors more efficient, faster, and cheaper. Forecasting the Target Protein's Three-Dimensional Structure One important part of structure-based drug design and discovery is making accurate predictions of the target proteins' three-dimensional (3D) structures. Subsets of artificial intelligence (AI) known as machine learning and deep learning algorithms have emerged as critical resources for meeting this problem. references [21, 22, 24]. Building a large database of protein sequences and structures from various sources is the first step in using AI to predict protein structures. Artificial intelligence models may be trained using this dataset to deduce intricate patterns relating 3D shapes to amino acid sequences[25,26]. Artificial intelligence models, especially those built on deep learning, have demonstrated remarkable skill in spotting intricate patterns in protein data by employing state-of-the-art computational methods [6,27].

These models carefully pull-out information about amino acid properties, structural motifs, and evolutionary history so that 3D protein structures can be predicted from sequences [28–30].

Developed by Google DeepMind, AlphaFold is a game-changer when it comes to AI-powered protein structure prediction [31–33]. AlphaFold makes a three-dimensional model of the protein of interest by looking at the angles of peptide bonds and how big or small amino acids are compared to each other [28,34] In a recent test, AlphaFold showed a lot of promise in structure-based drug discovery by correctly guessing 25 out of 43 protein structures. While conventional approaches to protein structure determination are accurate, they can be resource-intensive [24].

By producing trustworthy 3D structures from sequence data, AI provides a quicker and cheaper option. Thanks to this breakthrough, we can now forecast the effectiveness and safety of medications early on by designing them according to the structure of the target protein [10,35].

The three-dimensional structures of drugs and proteins that can be found in databases like Drug Bank and Protein Data Bank (PDB) can be used by molecular dynamics (MD) simulations and other AI methods to look into how drug-protein complexes move, change shape, bind, stay stable, and interact over time. the numbers [29,36].

Using graph machine learning techniques, AI has also demonstrated potential in representing intricate relationships within biological data [37,38]. These methods show chemical systems as graphs with atoms as basic units. This makes it possible to see complex patterns and how they relate to each other across medications, illnesses, PPIs, and drug side effects. This could help with drug repurposing and response prediction[29,37,39,40].

Artificial intelligence enables the examination of massive chemical and biological information by employing complex computer methods, such as deep learning and machine learning[40]. Molecular structures, chemical characteristics, and experimental binding affinities are all part of the well-documented DPIs included in these data sets, which have been painstakingly assembled into exhaustive databases.

By analyzing molecular data, AI models are able to predict possible interactions for new drug candidates based on their chemical compositions. This allows them to distinguish and learn the complex patterns and relationships that govern the interactions between drug compounds and protein targets. These repositories offer a rich training environment for AI algorithms [39- 42].

The drug development pipeline streamlines the process of finding effective treatments and saves money on testing by allowing scientists to sort potential medications based on their expected safety and effectiveness. To make a new drug using traditional biological experiments takes a long time and costs a lot of money. It can take 10 to 20 years and a lot of money. Recently, computational methods, such as AI techniques, have become very useful for accurately predicting DPIs, which speeds up the development of high-precision prediction methods. This is particularly true in light of the ongoing evolution of the pharmaceutical landscape, which is shaped by the introduction of new therapeutics and the repurposing of existing drugs for new clinical applications. Predictions of DPI have changed in recent years due to the trend away from traditional machine learning methods and toward the more complex domains of deep learning. Researchers are interested in DPI prediction because deep learning architectures like RNNs, CNNs, and deep neural networks (DNNs) are more accurate than older methods [43–50].

It is very important to be able to accurately predict ligand-protein interactions in order to understand

therapeutic efficacy, allow drug repurposing, and lower the risk of Poly-Pharmacology. Artificial intelligence methods have been very helpful in making these predictions, leading to better therapeutic outcomes. Wang et al. used a model that had been trained on 15,000 interactions between proteins and ligands to find nine new compounds and how they interacted with four important targets in one study. The model was based on small molecule structural features and primary protein sequences. AI techniques can also help with Poly-Pharmacology-based molecule design, which means we can create safer drug candidates that account for possible off-target effects. AI platforms, like self-organizing maps (SOMs), combined with large databases, can link multiple compounds to many targets and off-targets. Bayesian classifiers and SEA algorithms can be used to make connections between drug pharmacological properties and their possible targets. This will help us understand and predict DPIs better [10].

A.I. in New Drug Development

Between 1060 and 10100 drug-like molecules are thought to exist in the chemical space, and de novo drug design entails creating these molecules from scratch without the use of templates or preexisting compounds (Jiménez-Luna et al., 2021). This approach has tremendous promise for discovering new medicines. When it comes to discovering new therapeutic agents, traditional de novo design methods have their limitations, such as difficult synthetic routes and the inability to predict the bioactivity of novel molecules. However, machine learning and deep learning techniques have revolutionized artificial intelligence (AI) by overcoming these challenges. In order to get around these problems, artificial intelligence is using very advanced computer models and algorithms to look through huge amounts of chemical and biological data for patterns that connect the shapes of molecules to the drugs they affect. Examples of effective generative AI models in this field include variational autoencoders (VAEs) and generative adversarial networks (GANs). These models can learn the underlying distributions of molecular representations in order to make new chemicals with the properties that are wanted. One example is the VAE-based method proposed by Gómez-Bombarelli et al. to map chemical structures to a continuous latent space. This method allows for the optimization of the latent representations, which in turn generates new molecules. Deep reinforcement learning (DRL) has also been used for de novo drug design. To generate new molecules, the RLSE software uses generative and predictive DNNs. The generative model suggests new structures, while the predictive model evaluates their attributes. Two examples of compounds with specific targets that have been successfully made using DRL methods and have shown promise as therapeutic agents are retinoic acid and PPAR agonists. AI makes computer-aided synthesis planning better by finding millions of structures that can be synthesized and drawing possible synthesis pathways [20, 24, 63, 64].

This makes lead identification and optimization more efficient. Methods such as online learning, data refining, and strategic synthesis planning allow for this to happen [10, 20]. De novo drug design using AI goes beyond just generating tiny molecules. Combining symbolic AI with deep neural networks (DNNs) and Monte Carlo tree searches (MTCS) has made chemical space exploration more efficient. These methods are used to predict reactions and figure out how they work. AI has also shown potential in predicting PPIs, an underutilized therapeutic intervention area [24, 65, 66].

Artificial intelligence (AI)-driven tools may be used to study PPI interfaces and learn more about the structural factors that control these interactions. This knowledge can then be used to create new medicinal medicines that target PPIs. Although a lot of ground has been covered, researchers are still working on finding the perfect way to use AI for de novo drug creation. Although there are many obstacles to overcome, such as efficiently exploring the vast chemical space, accurately predicting the bioactivity of novel molecules, and creating compounds that can be synthesized, de novo drug design that incorporates AI techniques offers a revolutionary approach that could speed up the search for new, safe, and effective therapeutic agents.

Robotics for Poly-pharmacology

The field of drug discovery is experiencing a major shift. Instead of using the old "one drug, one target" approach, scientists are now looking at Poly-Pharmacology, which involves investigating how drugs interact with multiple targets. This change is driven by the desire to find better treatments and understand complex diseases better. Artificial intelligence (AI) is at the center of these advancements in Poly-Pharmacology because it helps analyze large biological datasets and finds candidates with Poly-Pharmacology potential. The adoption of Poly-Pharmacology is based on a more nuanced understanding of disease mechanisms and the molecular intricacies involved. The integration of databases like AI has made it possible for platforms like Deep DDI to be created. These platforms aim to explain how drugs interact with each other and predict new therapeutic uses with fewer side effects. A lot of information on molecular pathways, binding affinities, and chemical properties is put together in these resources. This makes a rich tapestry for AI algorithms to explore and figure out the complicated relationships in. In addition, AI can predict off-target interactions, which improves our knowledge of a drug's overall effects and leads to safer, more effective treatments. The new way of thinking about poly pharmacology is encouraging for reusing drugs, predicting off-target toxicity, and designing multi-target

drugs (MTDs) in a smart way. Computer methods using AI have shown promise in predicting poly pharmacological profiles and drug repurposing, which means finding new uses for drugs that have already been approved. One reason for this shift toward poly pharmacology is the realization that it may be more effective to target multiple nodes within complex biological networks rather than just one, particularly in cases of multifactorial diseases. Poly pharmacology also affects drug repurposing and drug re-profiling, which can greatly reduce the time and money needed to develop new drugs by using already-approved drugs for different medical purposes. This method considers the complexity, connectivity, and pleiotropy of biological networks, which gives a more complete picture of drug discovery. Researchers have found success in drug repositioning, and artificial intelligence tools can uncover new potential for repurposing [19].

Chemical synthesis using AI

When it comes to drug development, chemical synthesis efficiency and sustainability are paramount. With the arrival of AI, this field has seen a tremendous transformation, with reaction conditions improved and results predicted with astounding precision. Combining chemical knowledge with AI speeds up the production of complicated medicinal compounds, increasing the number of possible new drug discoveries [73]. Several studies have shown that AI has a big effect, especially when it comes to finding the best reaction conditions faster and achieving error-free autonomous synthesis. This is a big step forward in drug development because AI is now being used in chemical synthesis, which makes the processes faster and more accurate. Reaction monitoring, and automation all work together to make experimental workflows much faster and more reliable. However, there are some drawbacks to relying on these systems, like the possibility of oversimplifying chemical reactions, which can happen when AI algorithms are overused. It is important to carefully combine AI technologies with a solid grasp of chemical concepts to avoid inaccurate interpretations of reaction dynamics caused by oversimplifications like these.

Robotics for Retrosynthesis Path Forecasting

A major step forward in medication discovery has been the integration of AI with the field of chemical synthesis, particularly retrosynthesis. With the help of state-of-the-art deep learning and machine learning algorithms, AI can sort through massive databases of chemical interactions. With this capability, retrosynthesis pathways can be more easily discovered, which is important for the development of new medicinal compounds. The first step is to compile a large dataset of known chemical reactions so that AI models can identify intricate relationships between the reactants and the products. As a result, these models This means that these models can accurately predict successful retrosynthesis pathways for certain target molecules by finding common reaction mechanisms and changes in functional groups. AI-enhanced retrosynthesis also saves time and effort by looking at synthetic routes in a planned way. It also helps chemists by suggesting the best bond cleavages and reaction sequences, which leads to more efficient and cost-effective synthetic methods. To help scientists come up with new ways to make things, AI can find other ways to do retrosynthesis that human chemists might miss. Thanks to recent breakthroughs in AI, systems that can accurately anticipate retrosynthesis have been developed. For example, using 3.5 million reactions to train DNNs has led to top-tier accuracy rates for reaction prediction and retrosynthetic analysis. These accomplishments demonstrate that AI is better than traditional rule-based methods at solving complex retrosynthesis problems. In addition, neural sequence-to-sequence models have demonstrated encouraging accuracy, even when trained on niche datasets like US patent data. Since the beginning, retrosynthesis has tried to break down target compounds into their most basic parts by using a series of reactions to find starting materials that can be bought in stores. Retrosynthetic analysis has changed from heuristic methods that relied on human knowledge to more advanced AI-driven methods that make planning synthesis easier and faster. The objective of this project is to find workable reactants by breaking bonds and build the target molecule from simpler parts. This project involves both single-step and multi-step retrosynthesis predictions. The ability to generalize to new molecular structures and reaction types is a common challenge for traditional rule-based systems. However, artificial intelligence (AI) and machine learning (ML), especially deep learning, have been used to overcome these limitations and provide flexible predictions with much reduced computational costs. Chemists now have cutting-edge tools to design synthetic pathways for novel molecules thanks to AI's revolutionary role in retrosynthesis route prediction. This capability is essential for drug discovery and other scientific fields like medicinal chemistry, materials science, and natural product synthesis. The move toward retrosynthesis powered by artificial intelligence marks a significant improvement in chemical thesis techniques in terms of logic, methodology, and efficiency. This highlights the crucial importance of computational technology in determining the trajectory of pharmaceutical research going forward.

Application of AI to the Repurposing of Drugs

Figure 2 summarizes important differences and benefits of drug repurposing approaches compared with traditional drug discovery pipelines. Drug repurposing, also known as drug repositioning or re-tasking, is the process of finding new therapeutic applications for drugs that were originally developed for other medical conditions. This approach has gained significant attention because it has

the potential to speed up the drug development process, reduce costs, and bring medications to patients more rapidly. AI has become an important part of the drug repurposing process because it can work through huge amounts of data, such as medication databases, clinical records, and genetic insights. One major advantage of AI-driven drug repurposing is the ability to skip early-phase clinical trials and toxicological evaluations. This is because AI can find new connections between current medications and new disease targets through a variety of methodologies, such as network-based, feature-based, and matrix-based approaches. Repurposed pharmaceuticals can skip Phase I trials for new indications and go straight to Phase II trials, cutting development times and costs in half [71, 87, 88]. Digital neural networks (DNNs), generative adversarial networks (GANs), and reinforcement learning are some of the artificial intelligence techniques that have demonstrated enormous promise in the field of drug design. DNNs can categorize drugs into therapeutic groups according to their efficacy, therapeutic use, toxicity, and functional class. GANs can create new molecular structures based on real data, which opens up new possibilities for innovative drug design. Instead, these algorithms can identify strategic trends in drug molecule design, potentially leading to the development of medications with fewer side effects. You can make repurposed drugs even safer by teaching AI systems to tell the difference between compounds that are harmful to the heart and compounds that are not [71,93].AI has also shown promise in precision medicine by making it possible to make therapeutic compounds that are specific to certain genetic profiles and disease subtypes. The potential for better treatment results and fewer side effects is high with this individualized approach [71,92]. Artificial intelligence methods, in the era of big data and network medicine, offer advanced information science applications that accurately define illnesses, medications, treatments, and identify targets. Figure 3. summarizes of AI techniques to pharmaceutical analysis. To find potential treatments for disorders like COVID-19, researchers have used extensive knowledge graphs that show the connections between publications, biological pathways, and targets. Managing and analyzing large-scale networks requires tremendous processing resources, among other obstacles [74,94-95]. AI has enormous promise in medication repurposing. Additionally, innovative methods such as creating machine-learning models that focus on drug side effects could open up new drug repurposing opportunities by revealing areas that need more research [74]. The incorporation of AI into drug repurposing signals a revolutionary age in drug discovery, ready to accelerate the development of new therapeutic agents, reduce expenses, and speed up the delivery of effective treatments, particularly for rare and complex diseases that do not have many treatment options [96].

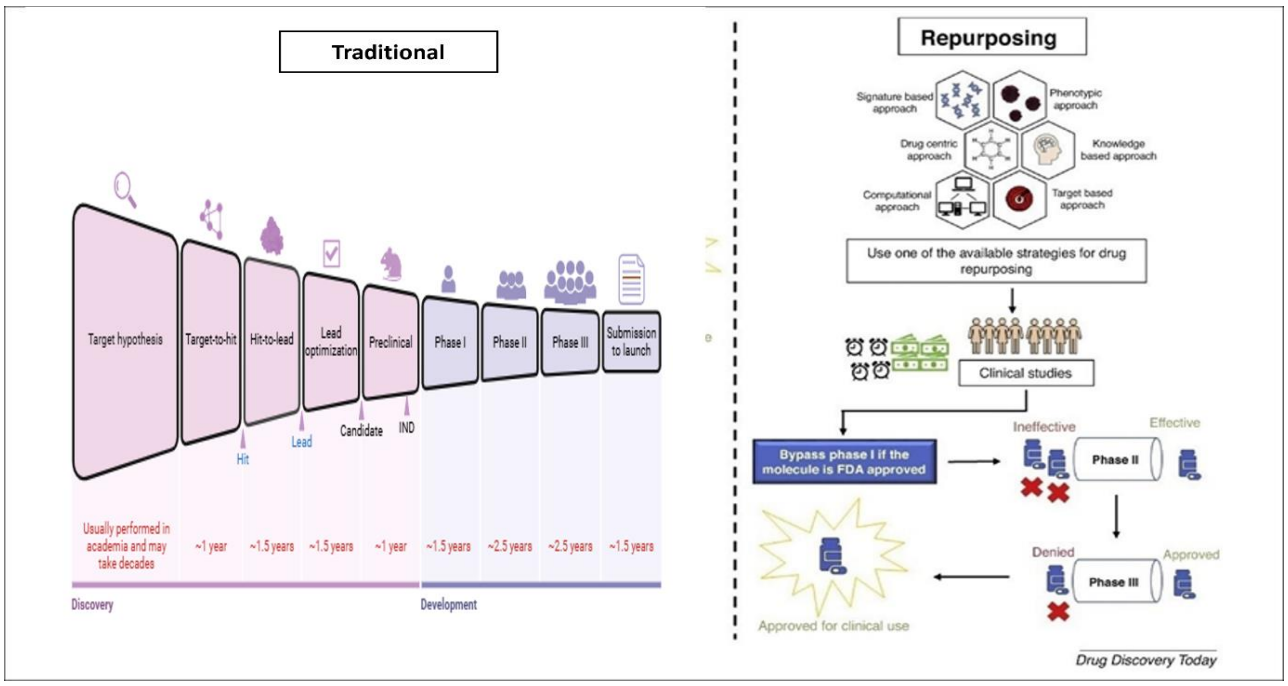

Figure 2. Comparison between traditional drug discovery process versus drug repurposing

Predicting Drug Adverse Effects

The emergence of AI has significantly advanced drug toxicity prediction by identifying potential side effects of new medication candidates. Artificial intelligence models can accurately outline toxicity profiles by training and validating themselves thoroughly. This allows them to zero in on the possibility of damage to certain organs or biological processes. This capability enables the prioritization of compounds with minimized adverse effects, refining the selection of safer drug candidates [10,58].

Toxicity, a key indicator of a substance ‘s harmful effects, remains a central concern in drug development [61]. Traditional toxicity assessments often rely on in vivo animal testing, which not only raises ethical concerns but also significantly increases the cost of drug discovery [61,119]. In contrast, AI-powered computational methods present an efficient, cost-effective alternative for estimating chemical toxicity [61,120]. Projects like the Toxicology in the 21st Century (Tox21) challenge show how useful these computer methods are, with AI being particularly good at predicting how toxic substances will be [61].

The DeepTox algorithm, utilizing a DNN architecture, showcases AI’s potential in this realm by predicting substance toxicity with high precision, outperforming conventional models in comparative studies [61].

The application of AI in toxicity prediction serves as a vital tool in mitigating risks associated with drug development. Using tools like DeepTox, toxicological issues can be identified and addressed early on in the development process, preventing potential adverse effects. AI's predictive power is crucial for pre-market drug safety, as it helps to anticipate side effects, therapeutic targets, and safety profiles before clinical trials begin. By taking this precaution, the chances of failed trials due to unexpected toxicity are lowered. This makes drugs safer and lowers side effects after they are sold. AI has also made it easier to predict toxicity, including off-target toxicity, genotoxicity, organ toxicity, cytotoxicity, and mitochondrial toxicity. AI models can accurately predict in vivo toxicity effects by using large datasets, such as gene expression and cell imaging data. Quantitative structure-activity relationship (QSAR) models that use ensemble approaches like support vector machines (SVMs) and random forests (RF) are better than traditional methods at predicting toxicity [18].

Prediction of Drug Bioactivity

A revolutionary step forward in drug development, especially for bioactivity prediction, has been the use of AI into drug screening procedures. One of the biggest obstacles in drug development is determining how effective a drug will be in the body. This is particularly true for medications that are naturally occurring, as they may not have enough bioactivity to be effective. Traditional methods of assessing drug bioactivity include expensive and time-consuming in vitro and in vivo experiments. However, AI is changing all of that by discovering new targets through predictive interactions and predicting a compound's affinity for specific proteins or receptors. A directed message-passing neural network model proposed by Stokes et al. exemplifies the innovative use of AI in predicting antimicrobial activity.

AI methodologies have emerged as powerful tools for predicting pharmacological activities, including anticancer, antiviral, and antibacterial properties, by leveraging their cost-effectiveness and efficiency. A streamlined approach for the discovery of new antimicrobial agents is provided by this model, which accurately assesses the antibacterial potential of molecules by building molecular graphs from SMILES notations and extracting detailed feature vectors. The prediction of drug-target binding affinity (DTBA) is essential for evaluating the efficacy of drug molecules. The chemical properties of drugs and targets are taken into account in AI-based strategies through feature-based interactions and similarity-based interactions. To accurately predict DTBA, tools like ChemMapper and the similarity ensemble approach (SEA) have been used, along with machine learning and deep learning techniques such as KronRLS, SimBoost, DeepDTA, and PADME.

Artificial intelligence techniques have expanded the possibilities for drug-protein interaction prediction by using sophisticated computer models that are not dependent on the availability of three-dimensional protein structures. This allows for far more accurate predictions than were previously possible. 10 and 130Deep learning models, such as Deep Affinity and PADME, stand out for their ability to predict drug-target interactions by integrating comprehensive drug and target features [10]. Deep- Affinity, for instance, combines RNN and CNN with both labeled and unlabeled data, providing a nuanced understanding of DPIs [10]. Similarly, PADME utilizes feed-forward neural net- works to forecast the interaction strength between drugs and target proteins, paving the way for more accurate predictions of therapeutic efficacy and mechanism of action [10].

Moreover, AI's application extends to the prediction of ADME (Absorption, Distribution, Metabolism, and Excretion) properties, crucial for understanding the pharmacokinetics of drug molecules. By improving the prediction of drug clearance pathways and adding to our understanding of drug metabolism, tools such as XenoSite and SMARTCyp help discover metabolic sites and particular CYP450 isoforms involved in drug metabolism.

Artificial Neural Networks

Artificial neural networks (ANNs), modeled after the electrical operations of the human brain, mark a significant breakthrough in computer science. In the same way that biological neural networks process information collaboratively, ANNs do the same. At their core, ANNs have multiple layers: an input layer that takes in raw data, one or more hidden layers that process it through complex relationships, and an output layer that makes all the final predictions or classifications. This layered structure is what makes ANNs excel at learning from data, finding patterns, and making well-informed predictions in all sorts of different domains. Artificial neural networks (ANNs) include a wide variety of network types, each tailored to a particular task. The Multi-layer Perceptron (MLP) is one example of an ANN, while RNNs are used for sequential data processing and CNNs are used for image analysis. ANNs are versatile because they can handle both feed-forward and feedback mechanisms and have a flexible training procedure. ANNs have historically found applications in many fields, including medicine, engineering, biology, and pharmacology.

Analytical data analysis, process optimization, and drug delivery studies have all been greatly advanced by ANNs in the pharmaceutical industry. With their help, we can better understand the nonlinear relationships that are necessary for finding new drugs. They have been very helpful in high-throughput virtual screening (HTVS), quantitative structure-activity relationship (QSAR) studies, and pharmacokinetic and pharmacodynamic modeling. To begin with, artificial neural networks (ANNs) were utilized in the early 1970s to categorize molecules according to their activity. Since then, they've been used to predict molecular interactions and biological activity.

This has made ANNs even more useful for studying and modeling the quantitative structure-activity relationship (QSAR). Artificial neural networks (ANNs) have become an essential part of artificial intelligence (AI) due to their ability to accomplish both categorization and prediction. An artificial neural network (ANN) is a simplified model of the human brain's architecture that consists of layers of input, hidden, and output neurons. In this model, each hidden neuron has a weighted input, an activation function, and an output, and the process involves transmitting information from the input layers to the output layers via these hidden neurons.

As a result of their architecture, ANNs can create nonlinear models that can do a wide range of tasks, including classification, prediction, decision-making, and visualization. ANNs have become known as "digitized model brains" in the field of drug discovery, thanks to their ability to handle the nonlinearities and complexity of the process. Artificial neural networks (ANNs) have a lot of uses in drug development, from finding better ways to deliver drugs to finding new drugs based on targets and structures. This shows how revolutionary ANNs could be in finding new therapeutic solutions.

Renewal Neural Systems

Recurrent Neural Networks (RNNs) are an advanced type of artificial neural networks (ANNs) designed to process data in a sequential way. They are used in areas like genomics, drug discovery, and natural language processing. Recurrent Neural Networks (RNNs) are different from regular ANNs because they have architectural loops that let the network remember and use information from earlier steps.

This makes it easier for the network to process input sequences of varying lengths. RNNs can record changing temporal behaviours, which are important for studying time series data, genomic sequences, protein structures, and SMILES strings. However, traditional RNNs have problems learning long-term dependencies within data sequences because of the vanishing gradient problem, which makes it challenging to retain information over extended sequences. To overcome this limitation, new RNN architectures such as Long Short-Term Memory (LSTM) networks and Gated Recurrent Units (GRUs) have been introduced.

These improvements get rid of the vanishing gradient problem by adding ways to choose which information to keep and which to discard during the sequence. This keeps important long-term relationships. Due to the sequential nature of genetic and molecular data, RNNs are very useful in the context of drug development. One important use of RNNs is the prediction of drug molecule binding affinities to target proteins. RNNs are

particularly effective at this because they can recognize the sequential connections among atoms in ligands and amino acids in proteins. When assessing the possible medicinal effects of pharmaceutical candidates, such forecasts are vital. One distinctive feature of RNNs is their design, which allows them to process sequences internally via feedback loops [60]. This design's feedback connections allow signals to return to earlier levels, distinguishing it from feed-forward networks. Because of their built-in memory capabilities, RNNs are highly successful in analysing sequential data, including text, protein sequences, and other signals. They comprehend sequences and their contexts.

Renewal Neural Systems

Recurrent Neural Networks (RNNs) are an advanced type of artificial neural networks (ANNs) designed to process data in a sequential way. They are used in areas like genomics, drug discovery, and natural language processing. Recurrent Neural Networks (RNNs) are different from regular ANNs because they have architectural loops that let the network remember and use information from earlier steps. This makes it easier for the network to process input sequences of varying lengths.

RNNs can record changing temporal behaviors, which are important for studying time series data, genomic sequences, protein structures, and SMILES strings. However, traditional RNNs have problems learning long-term dependencies within data sequences because of the vanishing gradient problem, which makes it challenging to retain information over extended sequences. To overcome this limitation, new RNN architectures such as Long Short-Term Memory (LSTM) networks and Gated Recurrent Units (GRUs) have been introduced. These improvements get rid of the vanishing gradient problem by adding ways to choose which information to keep and which to discard during the sequence. This keeps important long-term relationships.

Due to the sequential nature of genetic and molecular data, RNNs are very useful in the context of drug development. One important use of RNNs is the prediction of drug molecule binding affinities to target proteins. RNNs are particularly effective at this because they can recognize the sequential connections among atoms in ligands and amino acids in proteins. When assessing the possible medicinal effects of pharmaceutical candidates, such forecasts are vital. One distinctive feature of RNNs is their design, which allows them to process sequences internally via feedback loops [60].

This design's feedback connections allow signals to return to earlier levels, distinguishing it from feed-forward networks. Because of their built-in memory capabilities, RNNs are highly successful in analyzing sequential data, including text, protein sequences, and other signals. They comprehend sequences and their contexts.

Advanced Neural Networks

A revolutionary development in artificial intelligence, Convolutional Neural Networks (CNNs) stand out when it comes to processing and analyzing visual data. CNNs use filter-equipped convolutional layers to extract spatial and hierarchical features from input data, which makes them very good at identifying patterns in images [117].

Image classification, object detection, and segmentation are just a few of the many tasks that have made convolutional neural networks (CNNs) indispensable. CNNs are trained mostly using supervised learning from labelled examples and have proven adept at accurately classifying and analysing images across various domains. CNNs have also proven useful in drug discovery, particularly for predicting the bioactivity of drug-like molecules. One example of this is the DeepChem model, created by Stanford University researchers, which uses a CNN to analyse two-dimensional images showing molecular structures. In addition, CNNs can learn representations directly from molecular structures without the need for predefined structure descriptors, which distinguishes them from traditional machine learning methods.

This allows them to discern intricate patterns and predict a compound's bioactivity with respect to specific target proteins. The image of each compound encapsulates chemical features, such as atom and bond types. Due to their superior performance in computer vision applications, CNNs have also found use in biological image processing. This differentiation does away with the traditional need for feature reduction and selection, which streamlines the analysis process. By combining convolution and subsampling layers, their design effectively decreases the amount of free parameters, which in turn decreases memory needs and increases learning speed. CNNs are better at identifying pictures than other machine learning algorithms because they are so efficient. They are also necessary for mining biological data for useful insights.

CNNs have many potential uses in many different fields of biology, including pharmacogenomics, which

goes much beyond simple picture analysis [60].

In the field of customized and precision medicine, where convolutional neural networks (CNNs) and other AI systems provide new avenues for drug discovery, this flexibility is becoming more and more important. Notably, researchers have used convolutional neural networks (CNNs) to evaluate nucleotide and protein sequences, examples of one-dimensional biological data. This has allowed for breakthroughs in several areas of biological study. The Siamese network and other creative implementations of CNN's design have increased the breadth of CNN's use, which now includes the prediction of drug interactions in drug development as well as the reunification of missing individuals with their relatives.

The adaptability of CNNs highlights their revolutionary potential in several fields, one of which is the prediction of interactions between ligands and proteins. However, it is important to note that CNN models could help improve drug discovery predictions by making big improvements to scoring functions in ligand-protein interaction studies by predicting binding affinities [20].

Network for Feed-Forward

In the original design of artificial neural networks (ANNs), there was a single-direction, linear flow of data from the input layer to the output layer. This is called a feed-forward neural network (FNN). There are no cyclic or backward connections in this design. The structure is essential for FNNs to be user-friendly and successful in many fields, especially drug development. FNN design can be very different, ranging from simple single-layer perceptions to more complex ones like multi-layer perceptions (MLP), radial basis function (RBF) networks, self-organizing maps (SOM), and deep feed-forward networks.

In FNNs, which work like biological neurons, layers of neuron-like units, or nodes, that are connected to each other improve the ability to make decisions. The choice of architecture is application dependent, with each variant providing distinct advantages for pattern recognition, prediction, and data analysis. The prediction or classification made by this network is based on the data that these nodes processed using activation functions and weighted sums.

Streamlined and reliable, FNNs allow for simple data processing without the complexity of feedback loops because of their feed-forward functioning. When it comes to drug development, FNNs are priceless for simulating intricate pharmacological and biological interactions, which helps find treatment targets and optimizes medication candidates. The rapidity and accuracy of therapeutic development are greatly affected by their computational abilities, which shorten the time it takes to get from experimental data to practical discoveries.

Supervised Regression

The feed-forward structure of the Multilayer Perceptron (MLP), which is an important part of ANN architecture, is what lets data move from the input layer to the output layer in a certain order after going through one or more hidden layers. The structured approach and strong supervised learning capabilities of MLP make it highly adaptable to various applications, especially in the field of drug discovery [31].

MLP is essentially a type of feed-forward neural network that can be used to map inputs to their corresponding outputs. The backpropagation method is used in the training process. This lets the network's weights be changed based on the difference between what was expected and what happened. By utilizing this error-correcting technique, MLPs are able to improve the accuracy of their predictions as time goes on. Because it is set up like a directed graph, the network can improve its ability to predict complicated patterns and relationships in data by changing connections and weights on the fly based on errors in the output nodes.

MLPs can do difficult nonlinear modelling tasks with the help of activation functions like the hyperbolic tangent or the logistic sigmoid. This capability has found practical applications in many areas of natural language processing, such as machine translation, speech recognition, and handwriting recognition. Integrating MLPs into CNNs is a huge step forward as it allows for the sequential linking of several MLPs, which boosts their analytical powers even further. In the realm of artificial neural networks (ANNs) predictive modelling, MLPs are an effective tool for data-driven analysis.

Typically, a multi-layer perceptron (MLP) has three main layers: input, hidden, and output. Neurons in each of these layers are connected by weights, and a bias term is added to each layer to determine the activation threshold. With this setup, MLPs may take in data, process it, and then provide outputs that can guide important parameters in a number of processes, such as the creation of new drugs. Biological gas treatment operations use MLPs to model variables like gas residence time and inflow pollutant concentration. Machine learning

PLPSes show how flexible they are by using datasets from biological treatment trials to build models that accurately predict how well removal will work.

Tools for Drug Discovery Utilizing AI

By streamlining the exploration of massive datasets, the creation of novel chemical structures, and the prediction of the effectiveness of prospective drug candidates, artificial intelligence is poised to revolutionize the drug development industry [29].

The many AI technologies utilized in the drug development process are shown in Table 1. AlphaFold is a framework. Built on DNNs, the groundbreaking AI tool AlphaFold has shown remarkable progress in predicting three-dimensional protein structures [28]. Using peptide bond angles and lengths between amino acids, AlphaFold successfully predicts the structure of target proteins. AlphaFold's remarkable powers in protein structure prediction have been demonstrated by its 25 accurate predictions out of 43 [10]. Both the speed and accuracy of protein structure predictions have been enhanced in the evolution of AlphaFold into its later iteration, AlphaFold2 [29].

It is still difficult, nevertheless, to translate these forecasts into in vivo situations. Although many drug discovery applications need knowledge of protein-small molecule complexes, AlphaFold2 is mostly trained to predict structures of unattached proteins. Additionally, AlphaFold2 is not yet capable of reaching the sub-angstrom resolution that is frequently required for drug creation. While ultra-high resolution is not required for the design of protein-based therapeutics such as antibodies and peptides, AlphaFold2's promise nevertheless shines in this area. AlphaFold has become an indispensable tool for comprehending the structure-function interactions of proteins, and its influence goes far beyond drug development. By decoding complicated protein structures and detecting dam- aged proteins, AlphaFold assists in comprehending various dis- eases, expediting medicine development, and assisting to pandemic response efforts [28].

IBM's smart AI

The enormous natural language processing capabilities of IBM Watson, a watershed moment in AI development, allowed it to glean logical answers from both organized and unstructured data [6]. Its 2011 triumph over two human champions on the game show "Jeopardy" brought widespread acclaim for its abilities. Thanks to DeepQA, an advanced piece of IBM's natural language processing software, Watson was able to understand queries with an unprecedented level of detail and produce precise replies, allowing this accomplishment [70-80]. DeepQA gathers information from numerous databases to support each probable answer it proposes for a given question. It functions by merging various modules. During the training phase, these replies are assessed using a multilayer logistic regression. The most convincing answers are then tested extensively to determine the most correct response [6].

Despite setbacks, Watson continues to make important contributions to healthcare, which has dampened expectations of its revolutionary influence. In order to help oncologists, Watson analyses patient data in conjunction with pertinent medical literature to suggest tailored cancer treatment programs. Additionally, it improves the identification of anomalies in medical imaging, which in turn increases radiological accuracy.

Advanced-Chemistry

The goal of the open-source deep learning platform Deep Chem is to make it easier to use AI methods for cheminformatics and drug development [33]. From virtual screening and lead optimization to predictive modeling of drug characteristics, DeepChem offers a suite of tools for utilizing deep learning across different areas of drug research. It is a Python-based platform. The Molecule Net dataset, which is a part of Deep Chem and contains the characteristics of more than 700,000 molecules, is an excellent tool for drug discovery deep learning model training and validation. Several algorithmic research initiatives have made use of Deep Chem. These include creating one-shot deep learning algorithms for drug discovery, modeling inhibitors for Alzheimer's disease targets, and evaluating protein structures, among other varied uses. Notably, Deep Chem isn't only used in academic research; it has also been embraced by industry for use in commercial drug development. This includes tasks like driving ligand screening for commercial pharmaceuticals, fitting and evaluating complicated models, and creating models. In order to speed up calculations and improve the efficacy of deep learning models in medication development, Deep Chem makes use of NVIDIA GPUs [50-

[60]. Deep-Chem offers a full suite of features and tools for using deep learning in several parts of drug research and discovery; it may be accessed through its GitHub repository (https://github.com/deepchem/deepchem).

Thorough-Detox

One notable piece of software is DeepTox, which is developed to forecast the possible toxicity of certain medications. Its usefulness in the vital process of medication safety evaluation is enhanced by its capacity to evaluate several medicines concurrently. One kind of machine learning that excels at processing complicated, multi-layered data is deep learning, which DeepTox makes use of. In the end, DeepTox is able to extract very instructive chemical properties since it is able to learn and forecast a broad variety of possible harmful consequences using a single neural network [61]. To start the Deep Tox process running, the drug's chemical representations are standardised. This permits more fruitful comparisons and guarantees uniformity. The next step is to input a complete collection of chemical descriptors into the machine learning algorithms. Deep-Tox builds strong prediction ensembles by repeatedly training, evaluating, and assembling the best models. In the end, Deep Tox can forecast the toxicity of novel substances, which helps scientists evaluate the dangers of possible medications while they are being developed. Researchers from all across the globe may use this technology at www.bioinf.jku.at/research/DeepTox and use it to improve drug safety and reduce side effects [33,61]. An effective tool for producing compounds with desired features, ORGANIC (Objective-Reinforced Generative Adversarial Networks for Inverse-Design Chemistry) is a valuable resource for researchers [71]. The Using a state-of-the-art architecture that merges RL with a Generative Adversarial Network (GAN), this tool is able to use machine learning to its full potential. While the GAN part generates reasonable, non-repetitive molecular species, the RL part ensures that the created molecules satisfy the requirements by biassing the generative distribution toward certain qualities. Developing new compounds with targeted medicinal characteristics is an important first step in the drug development process, and ORGANIC is an invaluable tool at this point [71]. The To optimize pharmacokinetic properties, improve target binding affinity, or minimize potential adverse effects, researchers may rapidly explore the large chemical space using this tool and develop compounds customized to fulfil particular aims [33]. Drug discovery researchers from all over the globe may take advantage of the ORGANIC framework's robust features because it is open source and hosted on the project's GitHub repository (https:// github.com/aspuru-guzik-group/ORGANIC). The scientific community as a whole and individual patients alike stand to gain from this open-source strategy, which promotes collaboration and speeds up the creation of new treatment methods [33,71].

Table 1. List of AI-based software for drug discovery

Tools	Details	Website URL	Refs
DeepNeuralNetQSAR	Python-based system driven by computational tools that aid detection of the molecular activity of compounds	https://github.com/Merck/ Deep- NeuralNet-QSAR	[10]
DeepChem	MLP model that uses a python-based AI system to find a suitable candidate in drug discovery	https://github.com/deepche m/ deepchem	[10]
ORGANIC	A molecular generation tool that helps to create molecules with desired properties https://github.com/aspuru-guzik-group/ORGANIC	https://github.com/aspuru-guzik- group/ORGANIC	[10]
PotentialNet	Uses NNs to predict binding affinity of ligands https://pubs.acs.org/doi/full/ 10.1021/acscentsci.8b00507	https://pubs.acs.org/doi/full/ 10.1021/acscentsci.8b00507	[10]
Hit Dexter	ML technique to predict molecules that might respond to biochemical assays hitdexter2.zbh.uni-hamburg.de/	http://hitdexter2.zbh.uni-ham- burg.de	[10]
DeltaVina	A scoring function for rescoring drug–ligand binding affinity https://github.com/ chengwang88/deltavina	https://github.com/chengw ang88/ deltavina	[10]

Neural graph finger-print	Helps to predict properties of novel molecules https://github.com/HIPS/neural- fingerprint	https://github.com/HIPS/neural- fingerprint	[10]
DeepTox	Software that predicts the toxicity of total of 12 000 drugs www.bioinf.jku.at/ research/DeepTox	www.bioinf.jku.at/research/ Deep- Tox	[10]
AlphaFold	Predicts 3D structures of proteins https://deepmind.com/blog/alphafold	https://deepmind.com/blog /alpha- fold	[10]
Chemputer	Helps to report procedure for chemical synthesis in standardized format https:// zenodo.org/record/1481731	https://zenodo.org/record/ 1481731	[10]

Punch Dexter

Struck Dexter, an AI system, has the ability to identify chemicals that frequently encounter strikes. By including primary screening and confirmatory dose-response tests, this technique improves upon its predecessor. The development process employed several ML methods, including Bagging Classifiers, AdaBoost, Extremely Randomized Trees (ETC), and Random Forests (RF). Matthews Correlation Coefficient (MCC) values between 0.56 and 0.58 indicate that the ETC model performed best. Validation from outside sources showed that the best models could correctly classify substances as either promiscuous or not promiscuous, with MCC values as high as 0.64 and AUROC values as high as 0.96. Hit Dexter's ability to forecast promiscuity among marketed medications is a major plus. The model found promiscuous properties in slightly over one-fifth of all pharmaceuticals, with six percent deemed extremely so. Natural products, drug-like molecules, aggregators, high-throughput screening (HTS) chemicals, drug-like substances, pan-assay interference compounds (PAINS), and the web server itself all show how versatile it is. You may get Hit Dexter online at http://hitdexter2.zbh.uni-hamburg.de. It has ML models and rules that can help you find substructures that could be harmful to your drug development efforts and frequent hitters.

Case-Based Approaches

One kind of learning algorithm is instance-based techniques, which are sometimes called memory-based methods. They save the training cases in memory rather than building an explicit model during training, which is different from standard techniques. Pattern recognition, classification, and regression are just a few of the many domains that commonly employ these techniques, such as k-nearest neighbors (KNN) and case-based reasoning (CBR). One strategy involves searching a huge library of chemical compounds for molecules with structural or functional similarities to existing medications or drug targets using instance-based approaches for virtual screening.

Key-Nearest Neighbors (KNN)

The KNN algorithm excels in drug discovery and massive data mining. It uses very large sets of chemical compounds as training data, and uses molecular weight and lipophilicity to sort molecules into groups. A multidimensional space is conceptualized for the purpose of plotting compounds, where each dimension is a description. When we add a new compound to the dataset, KNN locates its K nearest neighbors by comparing their positions in this space. The value of K is often determined as the square root of the total number of compounds in the dataset, but it may also be a predetermined value. As an illustration, K would be around 20 for a set of 400 compounds. KNN looks at the properties and bioactivities of the closest neighbors to guess how well the new compound will work as a medicine, how toxic it will be, and how it will move through the body. This is based on the similarity principle, which says that chemicals and structures that are similar have similar biological effects. By utilizing the abundance of existing data on known chemicals, KNN enables researchers to quickly screen and rank prospective drug candidates in drug discovery. By finding potential lead compounds and improving their attributes, this data-driven strategy helps speed up the early phases of drug development. This is done before moving on to the more resource-intensive experimental validation and clinical trials [65-70].

Reasoning Based on Cases (CBR)

CBR is an AI method that tackles new issues by reusing answers from comparable previous instances. A case base is an archive of cases that have been resolved by the CBR system. Each case includes a description of the problem and the applied solution. When a new issue emerges, CBR looks for comparable instances in the case database using a similarity metric. To address the new challenge, we adapt or reuse the solution from the most comparable situations.

Methods like rule-based reasoning and machine learning can be used to fine-tune the answer if it cannot be immediately implemented based on the most comparable examples. Several important considerations have led to CBR's demonstrated usefulness in healthcare problem-solving and decision-support applications. Medical students learn a great deal from case histories, and there are many anecdotal examples in the literature that describe specific therapies for individual patients. Due to the absence of formal models or universal recommendations, a more case-specific approach is required for many disorders. Even if there are guidelines, they still need to be interpreted based on background information gathered in real-life situations. This helps make the guidelines more useful. Even with well-studied diseases, the complexity of the human body makes generalized models difficult to use, and symptoms are frequently caused by a combination of diagnoses. It is in line with the normal cognitive processes of healthcare practitioners to reason from examples. Also, systems that can draw conclusions from past cases found in electronic medical records or data mining provide customized, fact-based help with decisions. This is especially helpful in medicine because it uses so much data. The intrinsic reasoning processes of healthcare practitioners, the complexity of biological systems, and the nature of medical information all contribute to CBR's generalizability.

Analytical Decision

Trees Decision tree algorithms are models that depict a series of decisions based on attributes or input data value predictions using a tree-like structure. Tasks involving categorization or prediction often make use of them [117].

At the root node of a decision tree model is the whole training dataset. Then, at the decision nodes, the data is divided into two or more categories. Until a last choice, or terminal node, is reached, this division continues, gradually subdividing the data into ever smaller subgroups by binary decisions. Although it would be ideal for each terminal node to represent a single data point and its label, the splitting process is stopped before reaching this level of granularity to avoid overfitting and improve the model's generalizability .

However, there are several limits to decision tree models. Decision tree algorithms have a high variance, which makes them vulnerable to overfitting. Thus, they are susceptible to picking up on noise or patterns that aren't related to the training data. The other side is that they could be biased if they simplify too many complicated data linkages. We invented the notion of random forests to solve these restrictions. An ensemble of decision trees, a random forest uses a randomly selected portion of the training data to train each tree. To help in the identification and advancement of probable revolutionary drugs, pharmaceutical organizations have utilized decision tree algorithms throughout various phases of drug research .

To illustrate the point, Yoon et al. used decision tree algorithms to construct a model that could be used to prioritize drugs based on their probability of inhibiting the protein kinase DYRK1 A. This particular target is implicated in the development of several neurological diseases.

AI for the design of clinical trials

An important part of developing and designing clinical trials to bring new medications to market is figuring out how many events are needed to get results that are statistically significant. This phase is important for determining the number of patients to recruit and the length of time to keep track of them in order to reach the goal event count; it also helps estimate the event rate within the target group. During the trial, we closely monitor patients until we meet the set number of occurrences. Developing and releasing a new pharmaceutical takes a lot of time and money. Successfully navigating the drug development pipeline typically takes 10–15 years and costs 1.5–2.0 billion USD [29]. The clinical trial phases take around six to seven years and a lot of money; thus, they take up a lot of time and resources [10].

The safety and effectiveness of a medication product in treating a specific illness in people can only be determined through these clinical studies. Unfortunately, the industry suffers a huge loss due to the dismal success rate; just 10% of compounds that

enter clinical trials manage to get clearance. Inappropriate patient selection, insufficient technological requirements, and inadequate infrastructure are all potential causes of these failures. Half of the budget for R&D goes toward preclinical work, which includes things like finding new compounds, doing pilot tests, and complying with regulations [29].

A clinical trial's success hinges on recruiting the right patients, as inadequate patient selection accounts for over 86% of trial failures. The patient enrollment phase alone takes up one-third of the clinical trial timeframe[10,29]. We urgently need innovative ways to improve and expedite the clinical trial process, reduce costs, and shorten time-to-market. The current methods are burdensome and expensive, and the failure rates are high. Given the wealth of digital medical data at our disposal, artificial intelligence (AI) has emerged as a potential transformative tool for clinical trial design and execution, aiming to accelerate the development and dissemination of innovative therapeutic interventions [10,89-90].

By modeling the interactions between therapeutic molecules and biological targets, AI systems can quickly screen hundreds of compounds, drastically cutting down on the time and resources needed for early-stage drug discovery [29].

The use of atomic techniques based on physics, such as molecular dynamics (MD), to simulate biomolecule structures is an essential part of biotechnology and drug development. In these models, MD simulations are run on the three-dimensional structures of drugs and proteins that come from databases like DrugBank and the Protein Data Bank (PDB) or are predicted by cutting-edge AI models like AlphaFold2. This method gives a timeline of atomic motions, which can be used to study the shape, stability, dynamics, and binding efficiency of protein-drug complexes. By analyzing these trajectories using advanced data analysis methods, such as deep learning, we may learn more about the structural changes and interactions in complicated biological systems. Diseases, pathways, and the processes of medication response and resistance can all be better understood with this information. Experts in artificial intelligence (AI) for drug development, such as Atom wise, have used their platform to screen thousands of tiny compounds against defined protein targets in search of new therapeutic possibilities. For example, by using virtual screening of current medications, they were able to find two compounds that effectively suppress the Ebola virus, which might be used as a treatment for Ebola. By simplifying the process of identifying possible candidates, this method greatly speeds up early-stage drug research.

Problems and Solutions: Using Artificial Intelligence for Pharmaceutical Research

In order for AI to fully achieve its promise of revolutionizing drug development, we still need to overcome a number of tough obstacles. Maintaining high-quality and easily accessible data is a major obstacle. Because AI models are data-driven, the quality and variety of the training data determine how well they perform. Because of data dispersion and privacy regulations, it is challenging to get high-quality biological data. Also, gathering all the required data may be a real time- and money-sucker, particularly for smaller research groups. Consequently, activities for data sharing and cooperation are crucial in making comprehensive datasets available. Additional major constraints are data bias and generalizability. Training AI models using biased data could lead to erroneous predictions. Underrepresentation of certain groups in clinical trials, differences in data sources' locations, or individual differences in healthcare practitioners are all potential causes of these biases. Overfitting, which means that a model does well with training data but poorly with unknown data, can also lead to false positives or medication candidates that don't work. During the training phase of AI models, researchers can use bias correction strategies to reduce the impact of biases on model outputs. One example of a bias correction method used in an AI-powered drug discovery investigation is SMOTE (Synthetic Minority Oversampling Technique). To even out the dataset and reduce the effect of bias, SMOTE creates synthetic data points for underrepresented groups. Despite the lack of a universal solution, researchers are constantly seeking more effective ways to reduce bias. But researchers may mitigate data bias in AI applications by carefully selecting datasets, processing them, and using bias correction techniques. Particularly for deep learning models, there are substantial difficulties related to processing power and resource intensity. Academic research teams and smaller pharmaceutical corporations sometimes lack the necessary computing capabilities to train and infer these models. In order to lower computing costs and increase accessibility, AI technology vendors are collaborating, and cloud-based AI services are being used [112-118]. Artificial intelligence models used in medication discovery must also go through the rigorous processes of regulatory approval and validation. In order to acquire regulatory approva land establish trust in the pharmaceutical industry, it is crucial to prove that AI-

generated results are safe, efficacious, and reproducible. In order to build validation methods and standards, it is essential that regulatory authorities, pharmaceutical firms, and AI researchers work together. Initial expenditures on technology, data collection, and trained staff will be substantial, which adds to the cost concerns. We should investigate government incentives, strategic alliances, and collaborative financing methods, along with a long-term view, to address these financial difficulties.

CONCLUSIONS

An important step forward in the pharmaceutical industry's quest to improve the quality and effectiveness of therapeutic interventions has been the use of artificial intelligence (AI) in drug development and discovery. Aside from speeding up the drug development process, artificial intelligence has opened up new possibilities for repurposing medications, identifying targets, and predicting new therapeutic uses through its many applications. AI is an important tool for finding new medicines, and its ability to be used in new ways makes it even more powerful in changing the way drugs are usually made. Artificial intelligence's ability to improve drug development methodologies is demonstrated by its use in virtual screening and the careful design of medications. Artificial intelligence (AI) allows researchers to accurately evaluate medication candidates by identifying and classifying target cells. Poly pharmacology, chemical synthesis, and medication repurposing are all areas where AI has the ability to significantly improve healthcare results worldwide due to its computational efficiency. Recent advancements in machine learning, a subfield of artificial intelligence, have facilitated the development of models capable of self-learning and prediction, significantly enhancing the state of drug discovery. Large datasets need to be processed using networks such as the Multi-Layer Perceptron (MLP), Recurrent Neural Network (RNN), Convolutional Neural Network (CNN), and Feed-Forward Network (FFN). This will improve the accuracy and reliability of drug development predictions. HitDexter, ORGANIC, Deep Chem, and IBM Watson are just a few examples of the cutting-edge AI technologies and software that are available to help speed up the drug development process. Further, a variety of artificial intelligence (AI) approaches may be used to optimize pharmacological characteristics and find potential new therapeutic options, such as K-Nearest Neighbors (KNN), Case-Based Reasoning (CBR), and Decision Tree Algorithms. Although the pharmaceutical industry has made significant progress in using AI, there are still obstacles to overcome. Important challenges include data bias, worries about ROI, a lack of knowledge of medication processes, difficulties in complying with validation protocols, and the possibility of losing one's employment. Researchers, industry stakeholders, and regulatory agencies must work together to tackle these difficulties by maximizing AI's promise and reducing its limits. Ultimately, AI has significantly transformed the pharmaceutical industry, paving the way for improved and customized medical care. To fully realize AI's potential and bring forth revolutionary advances in healthcare and therapeutic development, the pharmaceutical sector must overcome the inherent difficulties of AI.

LIST OF ABBREVIATIONS

AI- Artificial intelligence

PDB -Protein Data Bank

MD -Molecular dynamics

VAEs -Variational autoencoders

GANs-Generative adversarial networks

Deep reinforcement learning (DRL)

ML-Machine learning

DNNS-Digital neural networks

LBVS-Ligand-based virtual screening

SBVS-Structure-based virtual screening

SVMS -Support vector machines

RFS-Random forests

HTVS-High-throughput virtual screening

QSAR- Quantitative structure-activity relationship

SOM-Self-organizing maps

CNN-Convolutional Neural Network (CNN)

DECLARATIONS

CONSENT FOR PUBLICATION

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

The authors are very much grateful to Prof. Vikram Kumar Sahu, principal of Maharana Pratap College of Pharmacy Kanpur for his inspiration and facilities.

REFERENCES

(1) Hasselgren, C.; Oprea, T. I. Artificial Intelligence for Drug Discovery: Are We There Yet? Annu. Rev. Pharmacol. Toxicol. 2024, 64 (1), 527–550. https://doi.org/10.1146/annurev-pharmtox-040323-040828.

(2) Wagner, J.; Dahlem, A. M.; Hudson, L. D.; Terry, S. F.; Altman, R. B.; Gilliland, C. T.; DeFeo, C.; Austin, C. P. A Dynamic Map for Learning, Communicating, Navigating and Improving Therapeutic Development. Nat Rev Drug Discov 2018, 17 (2), 150–150. https://doi.org/10.1038/nrd.2017.217

(3) Tambuyzer, E.; Vandendriessche, B.; Austin, C. P.; Brooks, P. J.; Larsson, K.; Miller Needleman, K. I.; Valentine, J.; Davies, K.; Groft, S. C.; Preti, R.; Oprea, T. I.; Prunotto, M. Therapies for Rare Diseases: Therapeutic Modalities, Progress and Challenges Ahead. Nat Rev Drug Discov 2020, 19 (2), 93–111. https://doi.org/10.1038/s41573-019-0049-9.

(4) Khan, S. R.; Baghdasarian, A.; Fahlman, R. P.; Michail, K.; Siraki, A. G. Current Status and Future Prospects of Toxicogenomics in Drug Discovery. Drug Discovery Today 2014, 19 (5), 562–578. https://doi.org/10.1016/j.drudis.2013.11.001.

(5) DiMasi, J. A.; Grabowski, H. G.; Hansen, R. W. Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs. Journal of Health Economics 2016, 47, 20–33. https://doi.org/10.1016/j.jhealeco.2016.01.012.

(6) Khan, S. R.; Al Rijjal, D.; Piro, A.; Wheeler, M. B. Integration of AI and Traditional Medicine in Drug Discovery. Drug Discovery Today 2021, 26 (4), 982–992. https://doi.org/10.1016/j.drudis.2021.01.008.

(7) Chen, W.; Liu, X.; Zhang, S.; Chen, S. Artificial Intelligence for Drug Discovery: Resources, Methods, and Applications. Molecular Therapy - Nucleic Acids 2023, 31, 691–702. https://doi.org/10.1016/j.omtn.2023.02.019.

(8) Bordukova, M.; Makarov, N.; Rodriguez-Esteban, R.; Schmich, F.; Menden, M. P. Generative Artificial Intelligence Empowers Digital Twins in Drug Discovery and Clinical Trials. Expert Opinion on Drug Discovery 2024, 19 (1), 33–42. https://doi.org/10.1080/17460441.2023.2273839.

(9) Hamet, P.; Tremblay, J. Artificial Intelligence in Medicine. Metabolism 2017, 69, S36–S40. https://doi.org/10.1016/j.metabol.2017.01.011.

(10) Paul, D.; Sanap, G.; Shenoy, S.; Kalyane, D.; Kalia, K.; Tekade, R. K. Artificial Intelligence in Drug Discovery and Development. Drug Discovery Today 2021, 26 (1), 80–93. https://doi.org/10.1016/j.drudis.2020.10.010.B.

(11) Brady, A.; Naikar, N. Development of Rasmussen's Risk Management Framework for Analysing Multi-Level Sociotechnical Influences in the Design of Envisioned Work Systems. Ergonomics 2022, 65 (3), 485–518. https://doi.org/10.1080/00140139.2021.2005823..

(12) Ali, K. A.; Mohin, S.; Mondal, P.; Goswami, S.; Ghosh, S.; Choudhuri, S. Influence of Artificial Intelligence in Modern Pharmaceutical Formulation and Drug Development. Futur J Pharm Sci 2024, 10 (1), 53. https://doi.org/10.1186/s43094-024-00625-1.

(13) Lamberti, M. J.; Wilkinson, M.; Donzanti, B. A.; Wohlhieter, G. E.; Parikh, S.; Wilkins, R. G.; Getz, K. A Study on the Application and Use of Artificial Intelligence to Support Drug Development. Clinical Therapeutics 2019, 41 (8), 1414–1426. https://doi.org/10.1016/j.clinthera.2019.05.018.V.

(14) Patel, V.; Shah, M. Artificial Intelligence and Machine Learning in Drug Discovery and Development. Intelligent Medicine 2022, 2 (3), 134–140. https://doi.org/10.1016/j.imed.2021.10.001.

(15) Chen, Z.; Liu, X.; Hogan, W.; Shenkman, E.; Bian, J. Applications of Artificial Intelligence in Drug Development Using Real-World Data. Drug Discovery Today 2021, 26 (5), 1256–1264. https://doi.org/10.1016/j.drudis.2020.12.013.J.

(16) Deng, J.; Yang, Z.; Ojima, I.; Samaras, D.; Wang, F. Artificial Intelligence in Drug Discovery: Applications and Techniques. Briefings in Bioinformatics 2022, 23 (1), bbab430. https://doi.org/10.1093/bib/bbab430.

(17) Segall, M. D.; Barber, C. Addressing Toxicity Risk When Designing and Selecting Compounds in Early Drug Discovery. Drug Discovery Today 2014, 19 (5), 688–693.

https://doi.org/10.1016/j.drudis.2014.01.006.

(18) Vanden Eynde, J. J. Drugs and Drug Candidates: Year in Review. DDC 2024, 3 (1), 52–53. https://doi.org/10.3390/ddc3010004.

(19) Lavecchia, A.; Cerchia, C. In Silico Methods to Address Polypharmacology: Current Status, Applications and Future Perspectives. Drug Discovery Today 2016, 21 (2), 288–298. https://doi.org/10.1016/j.drudis.2015.12.007.3

(20) Dara, S.; Dhamercherla, S.; Jadav, S. S.; Babu, C. M.; Ahsan, M. J. Machine Learning in Drug Discovery: A Review. Artif Intell Rev 2022, 55 (3), 1947–1999. https://doi.org/10.1007/s10462-021-10058-4.

(21) Abbas, M. K. G.; Rassam, A.; Karamshahi, F.; Abunora, R.; Abouseada, M. The Role of AI in Drug Discovery. ChemBioChem 2024, 25 (14), e202300816. https://doi.org/10.1002/cbic.202300816

(22) Spencer, M.; Eickholt, J.; Cheng, J. A Deep Learning Network Approach to Ab Initio Protein Secondary Structure Prediction. IEEE/ACM Trans. Comput. Biol. and Bioinf. 2015, 12 (1), 103–112. https://doi.org/10.1109/TCBB.2014.2343960.

(23) Xue, L. C.; Dobbs, D.; Bonvin, A. M. J. J.; Honavar, V. Computational Prediction of Protein Interfaces: A Review of Data Driven Methods. FEBS Letters 2015, 589 (23), 3516–3526. https://doi.org/10.1016/j.febslet.2015.10.003.

(24) Sarkar, C.; Das, B.; Rawat, V. S.; Wahlang, J. B.; Nongpiur, A.; Tiewsoh, I.; Lyngdoh, N. M.; Das, D.; Bidarolli, M.; Sony, H. T. Artificial Intelligence and Machine Learning Technology Driven Modern Drug Discovery and Development. IJMS 2023, 24 (3), 2026. https://doi.org/10.3390/ijms24032026.

(25) Lim, H.; Cankara, F.; Tsai, C.-J.; Keskin, O.; Nussinov, R.; Gursoy, A. Artificial Intelligence Approaches to Human-Microbiome Protein–Protein Interactions. Current Opinion in Structural Biology 2022, 73, 102328. https://doi.org/10.1016/j.sbi.2022.102328.

(26) Liu, B.; He, H.; Luo, H.; Zhang, T.; Jiang, J. Artificial Intelligence and Big Data Facilitated Targeted Drug Discovery. Stroke Vasc Neurol 2019, 4 (4), 206–213. https://doi.org/10.1136/svn-2019-000290.

(27) S Kandathil, S. M.; Lau, A. M.; Jones, D. T. Machine Learning Methods for Predicting Protein Structure from Single Sequences. Current Opinion in Structural Biology 2023, 81, 102627. https://doi.org/10.1016/j.sbi.2023.102627.

(28) Jumper, J.; Evans, R.; Pritzel, A.; Green, T.; Figurnov, M.; Ronneberger, O.; Tunyasuvunakool, K.; Bates, R.; Žídek, A.; Potapenko, A.; Bridgland, A.; Meyer, C.; Kohl, S. A. A.; Ballard, A. J.; Cowie, A.; Romera-Paredes, B.; Nikolov, S.; Jain, R.; Adler, J.; Back, T.; Petersen, S.; Reiman, D.; Clancy, E.; Zielinski, M.; Steinegger, M.; Pacholska, M.; Berghammer, T.; Bodenstein, S.; Silver, D.; Vinyals, O.; Senior, A. W.; Kavukcuoglu, K.; Kohli, P.; Hassabis, D. Highly Accurate Protein Structure Prediction with AlphaFold. Nature 2021, 596 (7873), 583–589. https://doi.org/10.1038/s41586-021-03819-2.

(29) Qureshi, R.; Irfan, M.; Gondal, T. M.; Khan, S.; Wu, J.; Hadi, M. U.; Heymach, J.; Le, X.; Yan, H.; Alam, T. AI in Drug Discovery and Its Clinical Relevance. Heliyon 2023, 9 (7), e17575. https://doi.org/10.1016/j.heliyon.2023.e17575.

(30) Kryshtafovych, A.; Schwede, T.; Topf, M.; Fidelis, K.; Moult, J. Critical Assessment of Methods of Protein Structure Prediction (CASP)—Round XIV. Proteins 2021, 89 (12), 1607–1617. https://doi.org/10.1002/prot.26237.

(31) Prajapati, R. N.; Bhushan, B.; Singh, K.; Chopra, H.; Kumar, S.; Agrawal, M.; Pathak, D.; Chanchal, D. K.; Laxmikant. Recent Advances in Pharmaceutical Design: Unleashing the Potential of Novel Therapeutics. Current Pharmaceutical Biotechnology 25 (16), 2060–2077. https://doi.org/10.2174/0113892010275850240102105033.

(32) Smith, J. S.; Roitberg, A. E.;

Isayev, O. Transforming Computational Drug Discovery with Machine Learning and AI. ACS Med. Chem. Lett. 2018, 9 (11), 1065–1069. https://doi.org/10.1021/acsmedchemlett.8b00437.

(33) Narayanan, R. R.; Durga, N.; Nagalakshmi, S. Impact of Artificial Intelligence (AI) on Drug Discovery and Product Development. Ind. J. Pharm. Edu. Res 2022, 56 (3s), s387–s397. https://doi.org/10.5530/ijper.56.3s.146.

(34) J. Michael Dunn on Information Based Logics; Bimbó, K., Ed.; Outstanding Contributions to Logic; Springer International Publishing: Cham, 2016; Vol. 8. https://doi.org/10.1007/978-3-319-29300-4.

(35) Baek, M.; DiMaio, F.; Anishchenko, I.; Dauparas, J.; Ovchinnikov, S.; Lee, G. R.; Wang, J.; Cong, Q.; Kinch, L. N.; Schaeffer, R. D.; Millán, C.; Park, H.; Adams, C.; Glassman, C. R.; DeGiovanni, A.; Pereira, J. H.; Rodrigues, A. V.; Van Dijk, A. A.; Ebrecht, A. C.; Opperman, D. J.; Sagmeister, T.; Buhlheller, C.; Pavkov-Keller, T.; Rathinaswamy, M. K.; Dalwadi, U.; Yip, C. K.; Burke, J. E.; Garcia, K. C.; Grishin, N. V.; Adams, P. D.; Read, R. J.; Baker, D. Accurate Prediction of Protein Structures and Interactions Using a Three-Track Neural Network. Science 2021, 373 (6557), 871–876. https://doi.org/10.1126/science.abj8754.

(36) Gaudelet, T.; Day, B.; Jamasb, A. R.; Soman, J.; Regep, C.; Liu, G.; Hayter, J. B. R.; Vickers, R.; Roberts, C.; Tang, J.; Roblin, D.; Blundell, T. L.; Bronstein, M. M.; Taylor-King, J. P. Utilizing Graph Machine Learning within Drug Discovery and Development. Briefings in Bioinformatics 2021, 22 (6), bbab159. https://doi.org/10.1093/bib/bbab159.

(37) Baltrusaitis, T.; Ahuja, C.; Morency, L.-P. Multimodal Machine Learning: A Survey and Taxonomy. IEEE Trans. Pattern Anal. Mach. Intell. 2019, 41 (2), 423–443. https://doi.org/10.1109/TPAMI.2018.2798607.

(38) Brown, K. A.; Joh, E.; Buchan, S. A.; Daneman, N.; Mishra, S.; Patel, S.; Day, T. Inflection in Prevalence of SARS-CoV-2 Infections Missing the N501Y Mutation as a Marker of Rapid Delta (B.1.617.2) Lineage Expansion in Ontario, Canada. June 25, 2021. https://doi.org/10.1101/2021.06.22.21259349

(39) Huang, T.; Mi, H.; Lin, C.; Zhao, L.; Zhong, L. L. D.; Liu, F.; Zhang, G.; Lu, A.; Bian, Z. MOST: Most-Similar Ligand Based Approach to Target Prediction. BMC Bioinformatics 2017, 18 (1), 165. https://doi.org/10.1186/s12859-017-1586-z.

(40) Yu, Y.; Yu, Q.; Zhang, X. Allosteric Inhibition of HIF-2α as a Novel Therapy for Clear Cell Renal Cell Carcinoma. Drug Discovery Today 2019, 24 (12), 2332–2340. https://doi.org/10.1016/j.drudis.2019.09.008.

(41) Dhakal, A.; McKay, C.; Tanner, J. J.; Cheng, J. Artificial Intelligence in the Prediction of Protein–Ligand Interactions: Recent Advances and Future Directions. Briefings in Bioinformatics 2022, 23 (1), bbab476. https://doi.org/10.1093/bib/bbab476.

(42) Qiu, X.; Li, H.; Ver Steeg, G.; Godzik, A. Advances in AI for Protein Structure Prediction: Implications for Cancer Drug Discovery and Development. Biomolecules 2024, 14 (3), 339. https://doi.org/10.3390/biom14030339.

(43) Ribeiro, A. J. M.; Tyzack, J. D.; Borkakoti, N.; Holliday, G. L.; Thornton, J. M. A Global Analysis of Function and Conservation of Catalytic Residues in Enzymes. Journal of Biological Chemistry 2020, 295 (2), 314–324. https://doi.org/10.1074/jbc.REV119.006289.

(44) Kumar, D.; Yadav, A.; Ahmad, R.; Dwivedi, U. N.; Yadav, K. CRISPR-Based Genome Editing for Nutrient Enrichment in Crops: A Promising Approach Toward Global Food Security. Front. Genet. 2022, 13, 932859. https://doi.org/10.3389/fgene.2022.932859.

(45) Avorn, J. The $2.6 Billion Pill — Methodologic and Policy Considerations. N Engl J Med 2015, 372 (20), 1877–1879. https://doi.org/10.1056/NEJMp1500848.

(46) Gao, K. Y.; Fokoue, A.; Luo, H.; Iyengar, A.; Dey, S.; Zhang, P. Interpretable Drug

Target Prediction Using Deep Neural Representation. In Proceedings of the Twenty-Seventh International Joint Conference on Artificial Intelligence; International Joint Conferences on Artificial Intelligence Organization: Stockholm, Sweden, 2018; pp 3371–3377. https://doi.org/10.24963/ijcai.2018/468.

(47) Tian, K.; Shao, M.; Wang, Y.; Guan, J.; Zhou, S. Boosting Compound-Protein Interaction Prediction by Deep Learning. Methods 2016, 110, 64–72. https://doi.org/10.1016/j.ymeth.2016.06.024..

(48) Sun, S.; Wang, J.; Liu, W.; Chen, J.; Zhou, L.; Wu, C.; Yu, H.; Hu, J. Regulatory Roles of Bxy-Laf-1 in Reproductive Behaviour of Bursaphelenchus Xylophilus. Front. Physiol. 2022, 13, 1024409. https://doi.org/10.3389/fphys.2022.1024409.

(49) Mayr, A.; Klambauer, G.; Unterthiner, T.; Steijaert, M.; Wegner, J. K.; Ceulemans, H.; Clevert, D.-A.; Hochreiter, S. Large-Scale Comparison of Machine Learning Methods for Drug Target Prediction on ChEMBL. Chem. Sci. 2018, 9 (24), 5441–5451. https://doi.org/10.1039/C8SC00148K.

(50) Cichońska, A.; Ravikumar, B.; Rahman, R. AI for Targeted Polypharmacology: The next Frontier in Drug Discovery. Current Opinion in Structural Biology 2024, 84, 102771. https://doi.org/10.1016/j.sbi.2023.102771.

(51) Reddy, A. S.; Zhang, S. Polypharmacology: Drug Discovery for the Future. Expert Review of Clinical Pharmacology 2013, 6 (1), 41–47. https://doi.org/10.1586/ecp.12.74.

(52) Blaschke, T.; Arús-Pous, J.; Chen, H.; Margreitter, C.; Tyrchan, C.; Engkvist, O.; Papadopoulos, K.; Patronov, A. REINVENT 2.0: An AI Tool for De Novo Drug Design. J. Chem. Inf. Model. 2020, 60 (12), 5918–5922. https://doi.org/10.1021/acs.jcim.0c00915.

(53) Jiménez-Luna, J.; Grisoni, F.; Weskamp, N.; Schneider, G. Artificial Intelligence in Drug Discovery: Recent Advances and Future Perspectives. Expert Opinion on Drug Discovery 2021, 16 (9), 949–959. https://doi.org/10.1080/17460441.2021.1909567.

(54) Dobson, C. M. Chemical Space and Biology. Nature 2004, 432 (7019), 824–828. https://doi.org/10.1038/nature03192.

(55) De Gonzalo, G. Correction: De Gonzalo, G. Lipase Catalysed Kinetic Resolution of Racemic 1,2-Diols Containing a Chiral Quaternary Center. Molecules 2018, 23, 1585. Molecules 2018, 23 (10), 2503. https://doi.org/10.3390/molecules23102503.

(56) Olmedo, D. A.; Durant-Archibold, A. A.; López-Pérez, J. L.; Medina-Franco, J. L. Design and Diversity Analysis of Chemical Libraries in Drug Discovery. CCHTS 2024, 27 (4), 502–515. https://doi.org/10.2174/1386207326666230705150110.

(57) Chen, H.; Engkvist, O.; Wang, Y.; Olivecrona, M.; Blaschke, T. The Rise of Deep Learning in Drug Discovery. Drug Discovery Today 2018, 23 (6), 1241–1250. https://doi.org/10.1016/j.drudis.2018.01.039.

(58) Agu, P. C.; Obulose, C. N. Piquing Artificial Intelligence towards Drug Discovery: Tools, Techniques, and Applications. Drug Development Research 2024, 85 (2), e22159. https://doi.org/10.1002/ddr.22159.

(59) Gómez-Bombarelli, R.; Wei, J. N.; Duvenaud, D.; Hernández-Lobato, J. M.; Sánchez-Lengeling, B.; Sheberla, D.; Aguilera-Iparraguirre, J.; Hirzel, T. D.; Adams, R. P.; Aspuru-Guzik, A. Automatic Chemical Design Using a Data-Driven Continuous Representation of Molecules. ACS Cent. Sci. 2018, 4 (2), 268–276. https://doi.org/10.1021/acscentsci.7b00572.

(60) Merk, D.; Friedrich, L.; Grisoni, F.; Schneider, G. De Novo Design of Bioactive Small Molecules by Artificial Intelligence. Molecular Informatics 2018, 37 (1–2), 1700153. https://doi.org/10.1002/minf.201700153.

(61) Segler, M. H. S.; Kogej, T.; Tyrchan, C.; Waller, M. P. Generating Focused Molecule Libraries for Drug Discovery with

Recurrent Neural Networks. ACS Cent. Sci. 2018, 4 (1), 120–131. https://doi.org/10.1021/acscentsci.7b00512.T.

(62) Wei, Y.; Shan, L.; Qiu, T.; Lu, D.; Liu, Z. Machine Learning-Assisted Retrosynthesis Planning: Current Status and Future Prospects. Chinese Journal of Chemical Engineering 2025, 77, 273–292. https://doi.org/10.1016/j.cjche.2024.10.014.

(63) Segler, M. H. S.; Preuss, M.; Waller, M. P. Planning Chemical Syntheses with Deep Neural Networks and Symbolic AI. Nature 2018, 555 (7698), 604–610. https://doi.org/10.1038/nature25978.

(64) .Schneider, G.; Clark, D. E. Automated De Novo Drug Design: Are We Nearly There Yet? Angew Chem Int Ed 2019, 58 (32), 10792–10803. https://doi.org/10.1002/anie.201814681

(65) Popova, M.; Isayev, O.; Tropsha, A. Deep Reinforcement Learning for de Novo Drug Design. Sci. Adv. 2018, 4 (7), eaap7885. https://doi.org/10.1126/sciadv.aap7885.

(66) Gómez-Bombarelli, R.; Wei, J. N.; Duvenaud, D.; Hernández-Lobato, J. M.; Sánchez-Lengeling, B.; Sheberla, D.; Aguilera-Iparraguirre, J.; Hirzel, T. D.; Adams, R. P.; Aspuru-Guzik, A. Automatic Chemical Design Using a Data-Driven Continuous Representation of Molecules. ACS Cent. Sci. 2018, 4 (2), 268–276.

(67) https://doi.org/10.1021/acscentsci.7b00572.

(68) Chaudhari, R.; Fong, L. W.; Tan, Z.; Huang, B.; Zhang, S. An Up-to-Date Overview of Computational Polypharmacology in Modern Drug Discovery. Expert Opinion on Drug Discovery 2020, 15 (9), 1025–1044. https://doi.org/10.1080/17460441.2020.1767063.

(69) Mak, K.-K.; Pichika, M. R. Artificial Intelligence in Drug Development: Present Status and Future Prospects. Drug Discovery Today 2019, 24 (3), 773–780. https://doi.org/10.1016/j.drudis.2018.11.014.

(70) Ryu, J. Y.; Kim, H. U.; Lee, S. Y. Deep Learning Improves Prediction of Drug–Drug and Drug–Food Interactions. Proc. Natl. Acad. Sci. U.S.A. 2018, 115 (18). https://doi.org/10.1073/pnas.1803294115.

(71) Struble, T. J.; Alvarez, J. C.; Brown, S. P.; Chytil, M.; Cisar, J.; DesJarlais, R. L.; Engkvist, O.; Frank, S. A.; Greve, D. R.; Griffin, D. J.; Hou, X.; Johannes, J. W.; Kreatsoulas, C.; Lahue, B.; Mathea, M.; Mogk, G.; Nicolaou, C. A.; Palmer, A. D.; Price, D. J.; Robinson, R. I.; Salentin, S.; Xing, L.; Jaakkola, T.; Green, William. H.; Barzilay, R.; Coley, C. W.; Jensen, K. F. Current and Future Roles of Artificial Intelligence in Medicinal Chemistry Synthesis. J. Med. Chem. 2020, 63 (16), 8667–8682. https://doi.org/10.1021/acs.jmedchem.9b02120.

(72) Singh, A. V.; Bansod, G.; Mahajan, M.; Dietrich, P.; Singh, S. P.; Rav, K.; Thissen, A.; Bharde, A. M.; Rothenstein, D.; Kulkarni, S.; Bill, J. Digital Transformation in Toxicology: Improving Communication and Efficiency in Risk Assessment. ACS Omega 2023, 8 (24), 21377–21390. https://doi.org/10.1021/acsomega.3c00596.

(73) Rai, M.; Paudel, N.; Sakhrie, M.; Gemmati, D.; Khan, I. A.; Tisato, V.; Kanase, A.; Schulz, A.; Singh, A. V. Perspective on Quantitative Structure–Toxicity Relationship (QSTR) Models to Predict Hepatic Biotransformation of Xenobiotics. Livers 2023, 3 (3), 448–462. https://doi.org/10.3390/livers3030032.N.

(74) Mone, N. S.; Syed, S.; Ravichandiran, P.; Kamble, E. E.; Pardesi, K. R.; Salunke-Gawali, S.; Rai, M.; Vikram Singh, A.; Prasad Dakua, S.; Park, B.; Yoo, D. J.; Satpute, S. K. Synergistic and Additive Effects of Menadione in Combination with Antibiotics on Multidrug-Resistant Staphylococcus Aureus : Insights from Structure-Function Analysis of Naphthoquinones. ChemMedChem 2023, 18 (24), e202300328. https://doi.org/10.1002/cmdc.202300328.Y.

(75) Jiang, Y.; Yu, Y.; Kong, M.; Mei, Y.; Yuan, L.; Huang, Z.; Kuang, K.; Wang, Z.; Yao, H.; Zou, J.; Coley, C. W.; Wei, Y. Artificial

Intelligence for Retrosynthesis Prediction. Engineering 2023, 25, 32–50. https://doi.org/10.1016/j.eng.2022.04.021.

(76) Liu, B.; Ramsundar, B.; Kawthekar, P.; Shi, J.; Gomes, J.; Luu Nguyen, Q.; Ho, S.; Sloane, J.; Wender, P.; Pande, V. Retrosynthetic Reaction Prediction Using Neural Sequence-to-Sequence Models. ACS Cent. Sci. 2017, 3 (10), 1103–1113. https://doi.org/10.1021/acscentsci.7b00303.

(77) Shi, C.; Hu, Y.; Wang, S.; Ma, S.; Zheng, C.; Ma, X.; Luo, Q. RetroLens: A Human-AI Collaborative System for Multi-Step Retrosynthetic Route Planning. In Proceedings of the 2023 CHI Conference on Human Factors in Computing Systems; ACM: Hamburg Germany, 2023; pp 1–20. https://doi.org/10.1145/3544548.3581469.

(78) .Segler, M. H. S.; Waller, M. P. Neural-Symbolic Machine Learning for Retrosynthesis and Reaction Prediction. Chemistry A European J 2017, 23 (25), 5966–5971. https://doi.org/10.1002/chem.201605499.

(79) Segler, M. H. S.; Preuss, M.; Waller, M. P. Planning Chemical Syntheses with Deep Neural Networks and Symbolic AI. Nature 2018, 555 (7698), 604–610. https://doi.org/10.1038/nature25978.

(80) Szymkuć, S.; Gajewska, E. P.; Klucznik, T.; Molga, K.; Dittwald, P.; Startek, M.; Bajczyk, M.; Grzybowski, B. A. Computer-Assisted Synthetic Planning: The End of the Beginning. Angew Chem Int Ed 2016, 55 (20), 5904–5937. https://doi.org/10.1002/anie.201506101

(81) Lotfi Shahreza, M.; Ghadiri, N.; Mousavi, S. R.; Varshosaz, J.; Green, J. R. A Review of Network-Based Approaches to Drug Repositioning. Briefings in Bioinformatics 2018, 19 (5), 878–892. https://doi.org/10.1093/bib/bbx017.

(82) Parvathaneni, V.; Kulkarni, N. S.; Muth, A.; Gupta, V. Drug Repurposing: A Promising Tool to Accelerate the Drug Discovery Process. Drug Discovery Today 2019, 24 (10), 2076–2085. https://doi.org/10.1016/j.drudis.2019.06.014.

(83) Mohanty, S.; Harun Ai Rashid, M.; Mridul, M.; Mohanty, C.; Swayamsiddha, S. Application of Artificial Intelligence in COVID-19 Drug Repurposing. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 2020, 14 (5), 1027–1031. https://doi.org/10.1016/j.dsx.2020.06.068.

(84) Yadav, S.; Singh, A.; Singhal, R.; Yadav, J. P. Revolutionizing Drug Discovery: The Impact of Artificial Intelligence on Advancements in Pharmacology and the Pharmaceutical Industry. Intelligent Pharmacy 2024, 2 (3), 367–380. https://doi.org/10.1016/j.ipha.2024.02.009.

(85) Corsello, S. M.; Bittker, J. A.; Liu, Z.; Gould, J.; McCarren, P.; Hirschman, J. E.; Johnston, S. E.; Vrcic, A.; Wong, B.; Khan, M.; Asiedu, J.; Narayan, R.; Mader, C. C.; Subramanian, A.; Golub, T. R. The Drug Repurposing Hub: A next-Generation Drug Library and Information Resource. Nat Med 2017, 23 (4), 405–408. https://doi.org/10.1038/nm.4306.

(86) Hernandez, J. J.; Pryszlak, M.; Smith, L.; Yanchus, C.; Kurji, N.; Shahani, V. M.; Molinski, S. V. Giving Drugs a Second Chance: Overcoming Regulatory and Financial Hurdles in Repurposing Approved Drugs As Cancer Therapeutics. Front. Oncol. 2017, 7, 273. https://doi.org/10.3389/fonc.2017.00273.

(87) Lozano-Diez, A.; Zazo, R.; Toledano, D. T.; Gonzalez-Rodriguez, J. An Analysis of the Influence of Deep Neural Network (DNN) Topology in Bottleneck Feature Based Language Recognition. PLoS ONE 2017, 12 (8), e0182580. https://doi.org/10.1371/journal.pone.0182580.

(88) Aliper, A.; Plis, S.; Artemov, A.; Ulloa, A.; Mamoshina, P.; Zhavoronkov, A. Deep Learning Applications for Predicting Pharmacological Properties of Drugs and Drug Repurposing Using Transcriptomic Data. Mol. Pharmaceutics 2016, 13 (7), 2524–2530. https://doi.org/10.1021/acs.molpharmaceut.6b00248.

(89) Kadurin, A.; Nikolenko, S.; Khrabrov, K.; Aliper, A.; Zhavoronkov, A. druGAN: An Advanced Generative Adversarial Autoencoder Model for de Novo Generation of New Molecules with Desired Molecular Properties in Silico. Mol. Pharmaceutics 2017, 14 (9), 3098–3104. https://doi.org/10.1021/acs.molpharmaceut.7b00346.

(90) Ozerov, I. V.; Lezhnina, K. V.; Izumchenko, E.; Artemov, A. V.; Medintsev, S.; Vanhaelen, Q.; Aliper, A.; Vijg, J.; Osipov, A. N.; Labat, I.; West, M. D.; Buzdin, A.; Cantor, C. R.; Nikolsky, Y.; Borisov, N.; Irincheeva, I.; Khokhlovich, E.; Sidransky, D.; Camargo, M. L.; Zhavoronkov, A. In Silico Pathway Activation Network Decomposition Analysis (iPANDA) as a Method for Biomarker Development. Nat Commun 2016, 7 (1), 13427. https://doi.org/10.1038/ncomms13427.

(91) Li, H.; Sze, K.; Lu, G.; Ballester, P. J. Machine-learning Scoring Functions for Structure-based Drug Lead Optimization. WIREs Comput Mol Sci 2020, 10 (5), e1465. https://doi.org/10.1002/wcms.1465.

(92) Zeng, X.; Xiang, H.; Yu, L.; Wang, J.; Li, K.; Nussinov, R.; Cheng, F. Accurate Prediction of Molecular Properties and Drug Targets Using a Self-Supervised Image Representation Learning Framework. Nat Mach Intell 2022, 4 (11), 1004–1016. https://doi.org/10.1038/s42256-022-00557-6.

(93) Dabhade, P.; Bharadwaj, A.; Bagde, A.; Shende, P. Computational Drug Designing and Drug Discovery Approach in Drug Repositioning: A Review; Nagpur, India, 2024; p 100057. https://doi.org/10.1063/5.0240411.

(94) Gatta, G.; Van Der Zwan, J. M.; Casali, P. G.; Siesling, S.; Dei Tos, A. P.; Kunkler, I.; Otter, R.; Licitra, L.; Mallone, S.; Tavilla, A.; Trama, A.; Capocaccia, R. Rare Cancers Are Not so Rare: The Rare Cancer Burden in Europe. European Journal of Cancer 2011, 47 (17), 2493–2511. https://doi.org/10.1016/j.ejca.2011.08.008.

(95) Padhy, B.; Gupta, Y. Drug Repositioning: Re-Investigating Existing Drugs for New Therapeutic Indications. J Postgrad Med 2011, 57 (2), 153. https://doi.org/10.4103/0022-3859.81870.

(96) Akram, M.; Egbuna, C.; Uche, C. Z.; Chikwendu, C. J.; Zafar, S.; Rudrapal, M.; Munir, N.; Mohiuddin, G.; Hannan, R.; Ahmad, K. S.; Ishfaq, M. A.; Shariati, M. A.; Yessimbekov, Z.; Elbossaty, W. F.; De Andrade Royo, V.; Sahoo, U. K.; David, P.-J.; Aslam, M. M.; Abdellatif, A. A. H.; Singh, A.; Varkey, T. C.; Varkey, P. K.; Tijjani, H.; Adetuyi, B. O.; Merhavy, Z. I.; Patrick-Iwuanyanwu, K. C.; Onodo, U. H.; Shimavallu, C. Trends in Modern Drug Discovery and Development: A Glance in the Present Millennium. In Phytochemistry, Computational Tools and Databases in Drug Discovery; Elsevier, 2023; pp 27–38. https://doi.org/10.1016/B978-0-323-90593-0.00008-3.

(97) Dubey, A. A Review on Current Epidemiology and Molecular Studies of Lumpy Skin Disease Virus-an Emerging Worldwide Threat to Domestic Animals. JMPAS 2023, 12 (1), 5635–5643. https://doi.org/10.55522/jmpas.V12I1.4583

(98) Pal, A.; Curtin, J. F.; Kinsella, G. K. In Silico and in Vitro Screening for Potential Anticancer Candidates Targeting GPR120. Bioorganic & Medicinal Chemistry Letters 2021, 31, 127672. https://doi.org/10.1016/j.bmcl.2020.127672.

(99) Wu, C.; Gao, R.; Zhang, Y.; De Marinis, Y. PTPD: Predicting Therapeutic Peptides by Deep Learning and Word2vec. BMC Bioinformatics 2019, 20 (1), 456. https://doi.org/10.1186/s12859-019-3006-

(100) Dash, S. L.; Gupta, P.; Dubey, A.; Sahu, V. K.; Amit Mishra. An Experimental Models (In-Vivo and In-Vitro) Used for the Study of Antidiabetic Agents. J. Adv. Zool. 2023, 44 (4), 86–95. https://doi.org/10.17762/jaz.v44i4.1461.

(101) Sarker, S. D.; Nahar, L.; Miron, A.; Guo, M. Anticancer Natural Products. In Annual Reports in Medicinal Chemistry; Elsevier, 2020; Vol. 55, pp 45–75. https://doi.org/10.1016/bs.armc.2020.02.001.

(102) Viana, J. D. O.; Félix, M. B.; Maia, M. D. S.; Serafim, V. D. L.; Scotti, L.; Scotti, M. T. Drug Discovery and Computational Strategies in the Multitarget Drugs Era. Braz. J. Pharm. Sci. 2018, 54 (spe). https://doi.org/10.1590/s2175-97902018000001010.

(103) Elbadawi, M.; Li, H.; Basit, A. W.; Gaisford, S. The Role of Artificial Intelligence in Generating Original Scientific Research. International Journal of Pharmaceutics 2024, 652, 123741. https://doi.org/10.1016/j.ijpharm.2023.123741.

(104) Vishnoi, S.; Matre, H.; Garg, P.; Pandey, S. K. Artificial Intelligence and Machine Learning for Protein Toxicity Prediction Using Proteomics Data. Chem Biol Drug Des 2020, 96 (3), 902–920. https://doi.org/10.1111/cbdd.13701.

(105) Zang, Q.; Mansouri, K.; Williams, A. J.; Judson, R. S.; Allen, D. G.; Casey, W. M.; Kleinstreuer, N. C. In Silico Prediction of Physicochemical Properties of Environmental Chemicals Using Molecular Fingerprints and Machine Learning. J. Chem. Inf. Model. 2017, 57 (1), 36–49. https://doi.org/10.1021/acs.jcim.6b00625.

(106) King, J. Michael Philip Schneider 1935–2019. History of Economics Review 2019, 72 (1), 2–3. https://doi.org/10.1080/10370196.2019.1639241.

(107) Basile, A. O.; Yahi, A.; Tatonetti, N. P. Artificial Intelligence for Drug Toxicity and Safety. Trends in Pharmacological Sciences 2019, 40 (9), 624–635.

(108) Rim, K.-T. In Silico Prediction of Toxicity and Its Applications for Chemicals at Work. Toxicol. Environ. Health Sci. 2020, 12 (3), 191–202. https://doi.org/10.1007/s13530-020-00056-4.

(109) Arora, S.; Dubey, A.; Kumari, M. The Role of 3- D Printing Technologies. IJPCA 2024, 11 (2), 112–120. https://doi.org/10.18231/j.ijpca.2024.016.

(110) Kumari, M.; Dubey, A.; Agarwal, S.; Kushwaha, S.; Sachan, A. Kr. Recent Technology and Software for GDP in the Pharmaceutical Industry. Scopus Indexed 2023, 16 (5), 7004–7007. https://doi.org/10.37285/ijpsn.2023.16.5.9.

(111) Kumar, R.; Saha, P.; Nyarko, R. O.; Lokare, P.; Boateng, A. D. E.; Kahwa, I.; Owusu Boateng, P.; Asum, C. Effect of Covid-19 in Management of Lung Cancer Disease: A Review. Asian J Pharm Res Dev 2022, 10 (3), 58–64. https://doi.org/10.22270/ajprd.v10i3.1131.

(112) Mishra, R.; Dwivedi, M.; Dubey, A.; Nyarko, R. O.; Kumari, M.; Tripathi, A. K.; Srivastava, A. Statistical Forecasting Of Drug-Drug Interactions Using Medicines' Physiological Similarity. Asian J Pharm Res Dev 2025, 13, 217-230. https://doi.org/10.22270/ajprd.v13i1.1529