



# African Journal of Biological Sciences



## The Evolution of Modern-day Drug Discovery and Development Processes: Current Understanding and Future Perspectives

Sanjoy Majumder<sup>1</sup> and Gagan Kumar Panigrahi<sup>1\*</sup>

School of Applied Sciences, Centurion University of Technology and Management, Odisha, India

\*Corresponding Author's Email: [gagan.panigrahi@cutm.ac.in](mailto:gagan.panigrahi@cutm.ac.in)

### Abstract

Developing a new drug and bringing it to the market is a complex and time-consuming process that involves multiple phases of drug discovery and development. However, recent advancements in various technologies, such as multi-omics, genome editing, Artificial Intelligence (AI), and Machine Learning (ML), have significantly improved this process. These technologies have made the process more accurate, less time-consuming, and cost-effective compared to the conventional methods of drug discovery and development. In the current age, discovering and developing drugs is a collaborative effort that involves scientific breakthroughs, technological advancements, and regulatory oversight. The pharmaceutical industry is constantly innovating new techniques, fostering interdisciplinary collaboration, and prioritizing patient-centered approaches. In this review, we explore the latest and most updated information about using advanced technologies in drug discovery. The review begins by briefly explaining the conventional drug discovery and development process, then delves into the applications of multi-omics, genome editing technology, systems biology, artificial intelligence, and machine learning.

**Keywords:** Drugs, Multi-omics, Artificial intelligence, Machine learning, Genome-editing, Systems biology

Article History

Volume 6, Issue 5, Apr 2024

Received: 15 Apr 2024

Accepted: 21 Apr 2024

doi: [10.33472/AFJBS.6.5.2024.1211-1234](https://doi.org/10.33472/AFJBS.6.5.2024.1211-1234)

## Introduction

Since the beginning of humanity, humans have always tried to alleviate the suffering from illnesses. In ancient times chance discoveries or observing natural processes were the usual ways of finding treatments for sufferings, often using ingredients from plants or animals especially crude extracts (Dias et al., 2012; Panigrahi et al., 2021). Historically, drug discovery has been a product of trial and error. Before the pharmaceutical industry came into existence, most of the drug discoveries were by chance. Knowledge of traditional medicines or ethno-medical information passed from one generation to another makes the basis for current advanced research on drug discovery from natural resources. Until the mid nineteenth century natural medications was the only way of relieving suffering. Choral hydrate, a sedative was the first synthetic drug discovered in 1869 (Jones AW, 2011) Modern drug discovery research started around the beginning of 1900AD. The Modern drug discovery process needs a very long period of time to bring a new drug into the market and also huge amount of budget is needed in this process (Singh et al., 2023). Identifying a biological target, such as a receptor, enzyme, protein or gene that is believed to be the primary cause of a disease is the first step in drug discovery. Majority of drug targets are proteins (Hopkins and Groom et al., 2002; Xu et al., 2007; Patro et al., 2023). Focus of the researchers is on discovering and developing new drugs with a distinct mode of action from those already approved drugs.

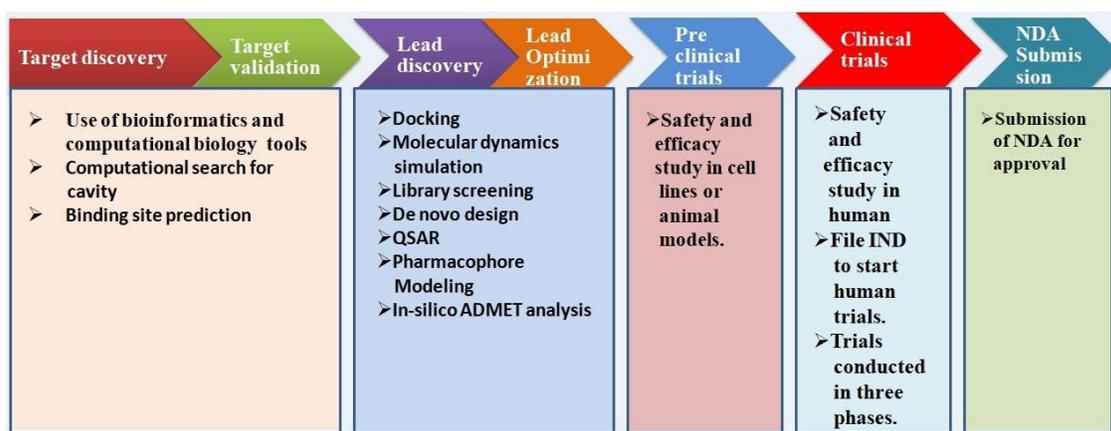
The initial stage of drug discovery is target identification, which involves identifying a biological element or mechanism that plays a role in a particular disease (Sakharkar et al., 2019). The cause of a disease can be any biological mechanism that is essential to its development, such as a gene, enzyme, protein, or any other. Researchers use genetic and biochemical approaches to describe the molecular pathways involved in a specific disease, including genes that are over expressed or altered in the disease, as well as proteins and enzymes that are crucial for the disease's development. They may also screen large chemical databases to find molecules that interact with the target. In epidemiological studies, researchers analyze vast datasets to identify factors, such as environmental exposures or genetic risk factors, that are linked to a specific disease. To validate targets, researchers use advanced techniques and tools, such as disease association, cell-based models, protein interactions, signaling pathways analysis, functional analysis of genes, in vitro genetic manipulation, antibodies and chemical genomics (Emmerich et al., 2021; Ikeda et al., 2023). Traditionally, the process of drug discovery and development mainly involves searching for candidates that are highly potent and selective towards a specific biological target. However, recent evidence

indicates that many therapeutic agents affect several targets. Polypharmacology refers to the nature of ligand binding to multiple targets or we can say one drug many targets (Chaudhari et al., 2020; Kabir et al, 2022). Computer aided drug design (CADD) can be defined as a method of drug designing using computational tools (Hassan-Baig et al., 2016; Gurung et al., 2021). CADD methods are largely dependent on bioinformatics tools and databases. Uses of CADD methods have accelerated the drug discovery process (Giordano et al., 2022; Alhaji et al., 2019). Drug-target interaction is an important area of research in drug discovery. It involves identifying the interactions between chemical compounds and protein targets (Katsila et al., 2016). Recently, the use of artificial intelligence (AI) has opened up new possibilities in this field. AI has the potential to improve the efficiency and success rate of drug development by allowing researchers to reach the more upstream stage of drug discovery (Blanco-González et al., 2023). Multi-omics data including genomics, proteomics and transcriptomics, has also seen contributing significantly in the progress. There is a vast amount of biomedical information available in each field, covering drugs, proteins, diseases, side effects, biological processes, molecular functions, cellular components, biological enzymes and ion channels. Such information is stored in specialized databanks, which helps researchers in the drug discovery process. Developing a new drug is a very lengthy and multi-step process, mainly focusing on transforming a lead compound into a drug molecule (Kiriiri et al., 2020). The high failure rate of this process is the primary cause of the significant increase in the cost of developing new drugs. It is crucial to have a thorough understanding of the drug discovery process in order to overcome the obstacles encountered by the pharmaceutical industry when developing new drugs (Karmakar et al., 2020). The standard procedure for drug discovery consists of identifying the drug target, which may be a protein or another target related to a specific disease, validating the target, screening potential lead compounds, and optimizing those compounds. Following preclinical testing, a clinical trial is conducted on humans. If the trials are successful, an application for drug approval is submitted (Figure1). This process requires a significant amount of time and budget, with a high risk of failure. In general, developing a new drug is a time-consuming that can take 10-17 years and cost between 1 and 2 billion USD (Leelananda and Lindert, 2016). Finding active compounds from existing chemicals is usually the first step in a drug discovery and development project. Nowadays, high-throughput screening (HTS) automates the screening of thousands of compounds against a molecular target or cellular assay in a short time, improving the discovery process (Maia et al., 2020). Although HTS allows screening of large number of compounds, but it is very expensive, time consuming and also not all targets suitable for HTS. Virtual screening gave the advantage to select a

smaller number of compounds for biological testing from a very large number of compounds in a short period of time (Damm-Ganamet et al., 2019). While many pharmaceutical companies have their own libraries with millions of compounds, it is expensive to maintain and perform high-throughput screening. Virtual screening offers an alternative approach to screen millions of compounds within a few days, making it a cost-effective solution (Lavecchia and Di, 2013; Liu et al., 2022). Molecular docking is a widely used virtual screening method, particularly when the three dimensional (3D) structure of the target protein is known (Ibrahim et al., 2022; Zhang et al., 2023; Anand, R., 2018). Obtaining the 3D structure of a protein-ligand complex is crucial in learning about the binding mechanism between the ligand and target protein at an atomic level (Bagherian et al., 2021; Burley et al., 2021; Jadaun et al., 2017). This information is especially vital for lead optimization purposes. It can predict the binding affinity between the ligand and protein also the interactions between them. Due to this molecular docking has been in use for many decades and has led to the discovery and development of numerous new drugs (Sethi et al., 2020; Halder et al., 2023; Shah et al., 2024; Matter and Sottriffer, 2011).

Drug discovery can be classified into three main periods (Pina et al., 2010). The first period dates back to the nineteenth century when drug discovery was mostly based on serendipity (Doytchinova, 2022). The second period began in the early twentieth century with the discovery of new drug structures which played a role in a new era of antibiotic discovery. The end of the 20<sup>th</sup> century saw significant advances in drug discovery, mainly because of technological advancements such like molecular modeling, combinatorial chemistry and automated high-throughput screening, based on known structures (Mohs and Greig, 2017). The emergence of recombinant DNA technology also revolutionized the process and made it easier to determine potential drug target candidates. The onset of the “Omics” and AI revolution in the twenty-first century marked the beginning of the third period, which has seen a surge in biopharmaceutical drugs approved by FDA/EMA for therapeutic use (Pina et al., 2010). In recent past with the development of new technologies, the process of drug discovery also changed. Nowadays drug discovery process can be defined as the process in which potential drug candidates are identified using computational, experimental and AI models. The use of AI and computational tools in the drug discovery process helps to minimize the time and cost of the process as it offers the advantage of delivering a potential new drug candidate much faster than conventional methods (Qi et al., 2023; Zhao et al., 2023). The most important computational tools in drug discovery are used for virtual screening, ADMET prediction, and prediction of protein-ligand binding, denovo design etc. (Nisha et al., 2016). ML enhances the potential of VS by enabling faster and more precise tracking of forecasted hits, as opposed to

conducting computationally intensive simulations or exhaustive similarity searches ( Dara et al., 2022). The application of ML is widespread, encompassing the discovery of novel drugs, repositioning of compounds, the anticipation of ligand-protein interactions, assessment of drug efficacy, identification of safety biomarkers, and optimization of molecule bioactivity (Carpenter and Huang, 2018; Oliveira et al., 2023). With the help of genomic research, target-based drug discovery has become more efficient by adopting systematic and knowledge-driven approaches. This approach starts with the identification of genes that can be altered to achieve a desirable phenotype and then searches for or develops compounds that can selectively interact with the products of these genes to improve the disease state or alleviate symptoms. Currently, Artificial intelligence (AI) and machine learning (ML) technologies are gaining much more attention in the field of drug designing process (Gupta et al., 2021). In this review, we will elaborate on how advanced multiomics technology, chemoinformatic tools, genome editing technology, AI technology, machine learning algorithms and access to medical big data transformed the recent drug discovery process (Niazi and Mariam, 2023).

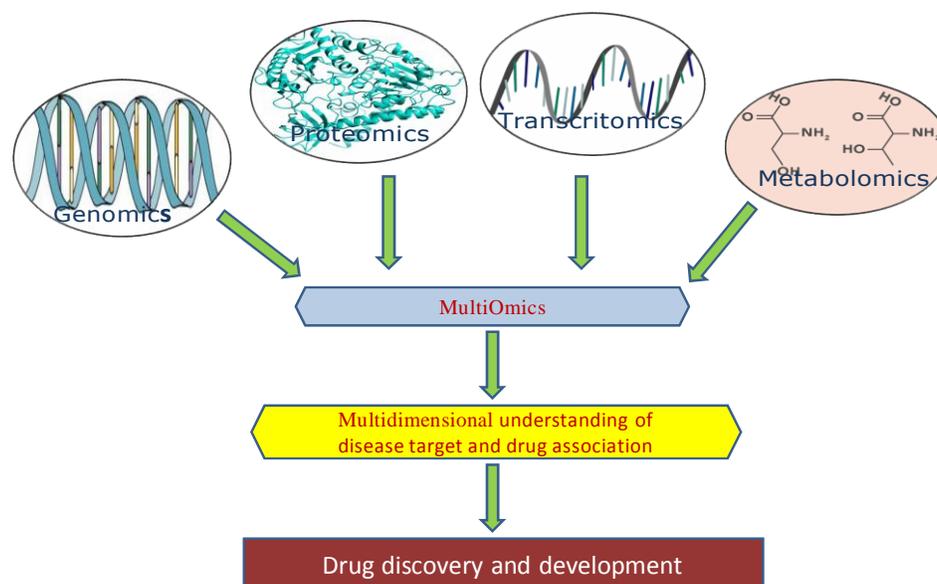


**Figure1: Schematic diagram of different stages of drug discovery process.**

## Multi-Omics Technologies in Drug Discovery and Drug Development

With the successful completion of the human genome project, there has been a significant increase in genomic, transcriptomic, proteomic and structural data. By utilizing these multi-omics data by bioinformatics and data analytics techniques, the process of identifying effective drug targets has become much faster and less expensive, resulting in the discovery of numerous excellent drug targets (Batoool et al., 2019; Gibbs RA, 2020; Wang et al., 2015). Bioinformatics aims to uncover insights from biological data, including amino acid sequences, protein

structures, and biomedical text. These insights lead to important applications such as drug design, and novel therapy discovery. Data generated from the nucleotide and protein sequencing technologies helps in the understanding of various pathophysiological conditions which can further aid in the process of drug discovery. These data are the basis for genomics, transcriptomics, proteomics, epigenetics and metabolomics too (somda et al., 2023; Wingert and Camacho et al., 2018). These are together commonly referred as multi-omics. The use of bioinformatics analysis can accelerate the identification of potential drug targets, the screening and refining of drug candidates, as well as help in the characterization of adverse effects and the prediction of drug resistance (Paananen and Fortino, 2020; Xia X., 2017). The integration of genomics, proteomics and other omics has led to the development of effective strategies for solving a wide range of biochemical problems and creating novel methodologies that have resulted in the production of innovative biomedical products. Consequently, the scientific community has witnessed a growing trend in research aimed at elucidating the mechanism of therapeutic action, predicting drug resistance and identifying biomarkers for different disorders. The process of developing novel medications is a complex one. For the development of drugs, understanding protein structure and function is crucial. Bioinformatics tools helps in understanding the protein structure and also interactions between protein-protein, protein-ligand, protein-DNA and protein-RNA (Wooller et al., 2017). Drug discovery process is multidisciplinary in nature. To make a effective drug discovery process a combinatorial approach is needed with genomics, transcriptomics, proteomics, metabolomics, bioinformatics, molecular docking and mass spectrometry (Aggarwal et al., 2023). The process of identifying and isolating potential drug candidates is challenging in cases, where information about the structural specificity and physiological pathways is not available. Molecular techniques like whole-genome sequencing and cellular protein expression profiling are crucial tools in drug discovery for analyzing large datasets (Qin D. 2019). In targeted drug discovery, OMICs, such as genomics, proteomics, and metabolomics, are frequently utilized (Russell et al., 2013; De Oliveria et al., 2018) (Figure 2). To improve drug discovery and development, a multidisciplinary approach is required that employs novel molecular tools to identify and isolate active compounds, in conjunction with all available computational tools (Shicheng et al., 2023; Zhang et al., 2022). A major portion of drug targets are proteins and 3D structures of those proteins are very important for testing and identification of the hit. If the 3D structure is not available with the database, 3D structure can be determine using bioinformatics techniques like homology modeling (Li et al., 2020).



**Figure 2: Multiomics' role in drug discovery and development**

Due to the fast-paced production of large amounts of data produced by omics technologies, effective management of these data has become a challenge. Omics data, when integrated, can provide in-depth molecular insights that can help in save time and resources in drug discovery research and streamline the process, and enhances prediction of drug efficacy and safety at a quicker pace (Koromina et al., 2019). There are two traditional methods, namely, structure-based and ligand-based design, which rely on the properties of the biological target's active site or its known active binders, respectively.

### Genome Editing in Drug Development Process

The manipulation of genomes is crucial in the preclinical stage of drug discovery. Through modifications in gene expression or sequence, scientists can create various assays to detect disease targets and evaluate the effectiveness of treatments. Genome editing technologies which include CRISPR/Cas systems, TALENS and Zinc finger nucleases have facilitated drug discovery process (Chakraborty et al., 2017). CRISPR, a revolutionary genome editing tool which works with Cas proteins especially Cas9 protein is ubiquitously used (Zhang et al., 2018). In combination with advanced multiomics technologies gene editing has greatly transformed the drug discovery process. Essentially the process of drug discovery starts with the identification of a target. The use of CRISPR/Cas9 accelerated the identification of new drug targets more effectively and also increases the success rate in drug discovery. Researchers

of drug discovery field are exploiting CRISPR/Cas to knock out or switch off a particular gene or a set of genes to understand the functions of those genes. Genome editing technology such as CRISPR based screening method can be used to systematically knockout, inhibit or activate large numbers of candidate genes to find potential drug targets (Chanchal et al., 2024). Using the CRISPR technology functional information of the target can be collected. CRISPR is accelerating all stages of drug discovery process (Liu et al., 2021). Prior to the creation or identification of a drug identifying a specific protein as the target involved in the disease is a crucial step in the drug discovery process. Exploring gene function and selecting specific targets can be achieved using CRISPR screening techniques. Knockouts can also be utilized to detect genes or gene pathways that govern the target protein, influencing diseases and becoming a target for therapeutic agents (Fellmann C. et al., 2017). Once target is found and validated, the next step is finding a hit. In recent years CRISPR based genome editing techniques can facilitate the generation of mutant cell lines that mimic disease phenotypes. These cell lines are then used for high throughput screening of millions of compounds resulting in identification of hundreds of hits (Chan et al., 2022). At this stage after validation of hits few are selected as lead. Then these leads are optimized and tested for safety. The lead optimization process includes the characterization of adsorption, distribution, metabolism and excretion (ADME) and toxicity testing. In preclinical settings, by developing cell based or animal models by CRISPR the process of safety and efficacy testing has been accelerated ( Li et al., 2020).

### **Systems Biology Techniques for Advancing Drug Discovery**

In recent decades, significant progress has been made in biological sciences, resulting in the accumulation of a vast amount of molecular data at the genome, transcriptome, proteome and metabolome levels. While the complete identification of genes and proteins provides a comprehensive list of individual molecular components, it is insufficient to fully understand the complexity inherent in biological systems (Zou et al., 2013; Yue and Dutta , 2022). Pharmacology has been utilizing systems biology techniques to gain insight into the mechanism of drug action. Systems biology research focuses on molecular interactions between drugs and their targets within human cells. Notable advancements in this field include the emergence of drug-target networks, the ability to predict drug-target interactions, exploration of drug-related adverse effects, drug repositioning and the predictions of drug combinations (Ebrahimi and Roshani, 2024). In the long run, advances in the field of systems pharmacology will help in developing more effective therapies and new drugs for patient

treatment management. Systems biology approaches play a crucial role in several clinically significant applications in drug discovery.

Complex diseases such as cancer are caused by multiple molecular abnormalities, which need a network perspective to better understand (Leung et al., 2013). The clinical phases of many drug candidates have failed due to incomplete understanding of the cellular pathways they target. Therefore, instead of targeting single proteins, entire cellular pathways must be considered in drug discovery (Chua and Roth, 2011). This will enable the translation of preclinical discoveries into clinical benefits. Rather than studying individual genes, systems biology research focuses on understanding the complex interplay of cellular pathways in explaining these diseases (Jun et al., 2013). It believes that multiple interconnected cellular pathways are involved in the underlying complex diseases. As a result, biological network analysis and dynamical modeling have become more usual in understanding the relationship between genotype and phenotype in human disease.

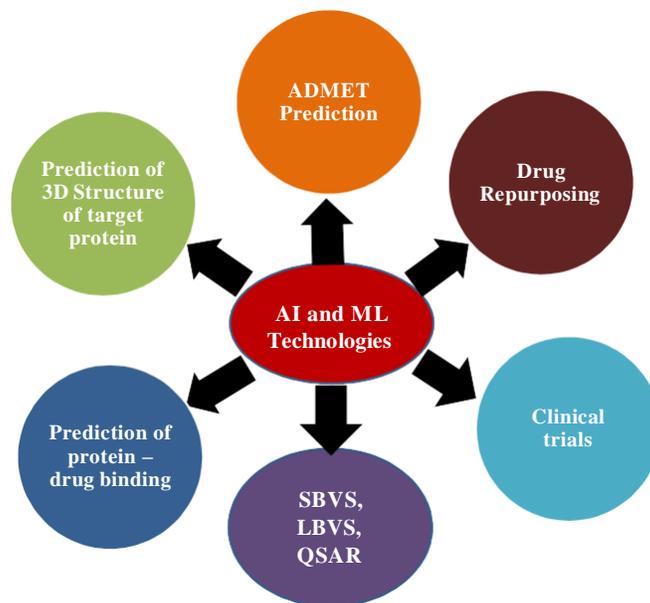
## **Artificial Intelligence and Machine Learning Revolutionizing Drug Discovery**

Working with high-dimensional multi-omics data can be difficult, especially when it comes to integrating and analyzing it. Artificial Intelligence (AI) and Machine Learning (ML) techniques can be employed to identify patterns in this intricate data, which can aid in predicting gene function or phenotypic traits (Liu et al., 2022; Miller and Riley, 2021; Chan et al., 2019; Deng et al., 2020). These advanced techniques of AI and ML make the task of recognizing patterns within complex data relatively easier. Drug discovery and development process faces the challenges such as low efficacy, time consuming, high cost. Artificial intelligence (AI) and Machine Learning (ML) technology has significantly accelerated the process of drug discovery and development, making the process more time and cost effective (Tripathi et al., 2021; Mak and Pichika, 2019). The machine learning process involves creating a model based on past data to make predictions on future data (Cruz and Wishart, 2007).

Drug development process can be greatly benefitted from the already available vast chemical space, which comprises more than  $10^{60}$  unique molecules which are potential pharmacologically active molecules. This abundance of molecules provides an extensive resource to explore and utilize for finding potential drug candidates. Use of this resource in conventional way for drug development will take huge time and also there are chances of high failure. To use such huge resource there is a need of some advance technology which can use

such large amount of data to find potential drug candidate in a time effective manner and fortunately AI/ML are such technologies (Paul et al., 2021; Selvaraj et al., 2022; Kumar et al., 2023). In the drug discovery process, AI/ML has opened up new opportunities for researchers to quickly identify the most promising candidates (Han et al., 2023; Machancoses and Martínez, 2019; Bess et al., 2022). AI includes various methods such as reasoning, knowledge representation, solution search and machine learning (ML), which is a fundamental paradigm. Deep learning (DL) methods recognize patterns within classified data, which is a subfield of ML that uses artificial neural networks (ANNs) (Visan and Negut, 2024).

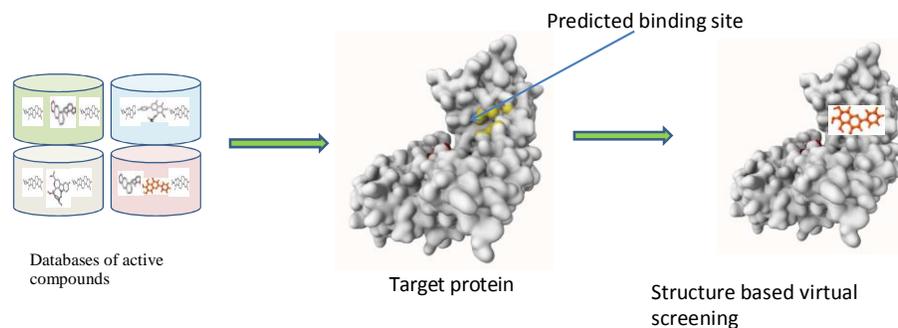
AI-powered techniques have the potential to be employed in various stages of drug discovery and development process, including discovering new targets, assessing the interactions between drugs and targets, exploring the mechanisms of diseases, and enhancing the design and optimization of small molecule compounds (Jeon et al., 2014; Vamathevan et al., 2019; Lee et al., 2019; Bender and Ciriano, 2021) (Figure 3). ML techniques offer a range of capabilities that can enhance the process of discovering and making decisions for well-defined questions that have huge amount of top-quality data. The goal of drug discovery's target identification phase is to pinpoint proteins or other molecules that could modify a disease's course if their behavior was changed. ML are used to analyze diverse forms of data, such as gene expression profiles, protein-protein interaction networks, and genomic and proteomic data, to pinpoint possible targets that are likely to be involved in disease processes (Bagherian et al., 2021; Sliwoski et al., 2013). Extracting information on target association with disease is mainly done through reviewing the literature. As a complementary approach, Natural Language Processing (NLP) and text mining can be utilized to identify relevant target-disease pairs from the literature and create databases for target identification (Khan et al., 2020). To extract drug-disease, gene-disease, and target-drug associations from articles, deep learning-based tools such as BeFree and PKDE4J can be utilized (Bravo et al., 2015; Song et al., 2018; Alam and Schmeier, 2021). Drug discovery often requires the three-dimensional structures of potential target proteins. If the 3D structure of the target protein is not available the prediction of the structure can be solely done from their amino acid sequence. Recently, AI systems achieved a significant breakthrough in this field with AlphaFold2 (Sebastian et al., 2021; Jumper et al., 2021; Bhatarai et al., 2019; Panigrahi et al., 2021; Panigrahi et al., 2021a).



**Figure 3: Graphical representation of multifaceted function of AI and ML technologies in the drug discovery and development processes.**

### **AI/ML in Structure-Based Virtual Screening (SBVS)**

Structure-based virtual screening (SBVS), also known as target-based virtual screening, is a method used to predict the formation of a stable complex between a ligand and a molecular target by determining their interaction (Panigrahi et al., 2020; Sahoo and Satpathy, 2021; Panigrahi and Satapathy, 2020a; Panigrahi and Satapathy, 2020b; Shin et al., 2017; McGibbon et al., 2022 (Figure 4). It requires the 3D structure of the target protein to perform the screening process. The virtual screening process selects compounds based on how well they interact with the target protein. In recent years, researchers have been utilizing machine learning (ML)-based algorithms to enhance the precision of scoring functions, conformational sampling, and other aspects of structure-based virtual screening (SBVS) (Singh et al., 2024; Scantlebury et al., 2023). These methods are becoming more popular because they can provide reliable predictions and better generalization in models.



**Figure 4: Schematic diagram of Structure-based screening.**

### AI/ML in Ligand-Based Virtual Screening (LBVS)

Identifying lead compounds through experimental methods like high-throughput screening can prove to be a costly and time-consuming process (Hughes et al., 2011; ). The main objective of LBVS is to discover novel molecules by utilizing ligands that have already demonstrated biological activity (Berrhail et al., 2022). This method focuses on identifying compounds with comparable structures from virtual libraries without taking into account the molecular target structure. The underlying principle behind this approach is that molecules that share similar structures may exhibit similar biological activity. Consequently, LBVS endeavors to identify biologically active compounds by pinpointing those with matching molecular scaffolds or pharmacophore moieties (Bustamam et al., 2021). Quantitative structure-activity relationships (QSAR) models are regression or classification models, used to predict physicochemical properties and biological activities of unknown chemical entities (Kim and Cho, 2019; Mu et al., 2011). QSARs are widely used in the drug discovery process to reduce the cost of laboratory testing and achieve high throughput prediction and screening. Nowadays, advanced machine learning algorithms are used to establish QSAR models, making more efficient prediction (Soares et al., 2022; Prabha et al., 2021).

### AI/ML in ADMET Predictions

ADMET analysis is a crucial aspect of drug design and screening that involves studying five key properties - adsorption, distribution, metabolism, excretion, and toxicity (Guan et al., 2018). Poor ADMET properties are responsible for about half of clinical trial failures. The utilization of chemo informatics tools has brought about a significant change in the process of drug development by enabling the faster prediction of the absorption, distribution, metabolism, excretion, and toxicity (ADMET) profiles of newly designed drugs (Yang et al., 2018). The

development of ADMET prediction models has progressed significantly. The field of prediction of ADMET properties has been broadened with the inclusion of ML algorithms, high-throughput assay development, structure-based modeling and data mining (Sahu et al., 2022; Gu et al., 2024). Many studies have provided evidence of the importance of machine learning in ADMET prediction, which helps to speed up the identification of small molecules. Prediction models use molecular features to establish correlations with ADMET properties. These features may include properties of substructures, atom counts, partial charges, Van der Waals volume, and surface area. Toxicity can be detected in small molecules by identifying pre-defined substructures that contribute to it, and can be used to predict toxicity. The use of AI and ML has made it possible to predict patient response to specific drugs, which in turn has facilitated the design and monitoring of clinical trials (Kashyap and Siddiqi, 2021; Chopra et al., 2023; Panigrahi and Satapathy, 2021; Sahoo et al., 2023).

### **AI/ML in De Novo Drug Design**

De novo drug design uses computational approach to create/design new molecular structures from molecular units (Moret et al., 2023; Jung et al., 2020; Sahoo et al., 2023a; Panigrahi et al., 2024; Das et al., 2024). The search for effective treatments for both existing and novel diseases requires a huge amount of resources, capital, and time. De novo drug design mostly relied on structure-based drug design techniques for developing ligands that fit the binding pocket of the target protein (Tiago et al., 2021; Xiaochu Tong, 2021). However, ligand-based approaches are also used which data-driven and do not depend on predefined rules. De novo drug design has employed various deep learning architectures, such as generative adversarial networks (GANs), recurrent neural networks (RNNs), reinforcement learning (RL), and variational autoencoders (VAEs). Out of these, RNNs are the most commonly used deep learning architecture in de novo design (Mouchlis et al., 2021; Dominic D. Martinelli, 2022). It is also the most widely used application in de novo drug design. The drug discovery process has been positively impacted by artificial intelligence, particularly machine learning.

### **Conclusion and Future Perspectives**

Novel bioinformatics approaches and latest advanced genome editing tools has opened the door for more effective drug discovery and development. Artificial intelligence has the potential of greatly transforming the overall drug discovery and development process. Although systems biology research is going on for many decade but the full potential of this field has been seen only after completion of human genome project and availability of multi

omics technologies. The potential of integrated omics data for accelerating drug development can be unlocked by effectively managing the challenges with strategic planning and expert guidance. The combination of the CRISPR-Cas9 system with multi-omic platforms and AI represents a dynamic field expected to advance drug discovery and development process. Several methods to improve the efficiency of drug discovery and development have been suggested, adopted, and implemented to varying degrees in pharmaceutical research and development projects. These include utilizing multiomics techniques, the combination of phenotypic and target-based screening, the use of current drug molecules through repurposing and repositioning, and implementing pharmaceutical modeling and artificial intelligence. With the ongoing advancement in the field of AI, ML and OMICs technologies, the drug discovery and development process is taking a new shape which will enhance the productivity of the pharmaceutical industry; in general it will make the medicines more affordable.

## References

Aggarwal, S., Karmakar, A., Krishnakumar, S., Paul, U., Singh, A., Banerjee, N., ... & Srivastava, S. (2023). Advances in drug discovery based on genomics, proteomics and bioinformatics in malaria. *Current Topics in Medicinal Chemistry*, 23(7), 551-578.

Alam, T., & Schmeier, S. (2021). Deep learning in biomedical text mining: contributions and challenges. In *Multiple Perspectives on Artificial Intelligence in Healthcare: Opportunities and Challenges* (pp. 169-184). Cham: Springer International Publishing.

Alhaji Isa, M., & Singh Majumdar, R. (2019). Computer-aided drug design based on comparative modeling, molecular docking and molecular dynamic simulation of Polyphosphate kinase (PPK) from *Mycobacterium tuberculosis*. *Journal of Proteins and Proteomics*, 10, 55-68.

Álvarez-Machancoses, Ó., & Fernández-Martínez, J. L. (2019). Using artificial intelligence methods to speed up drug discovery. *Expert opinion on drug discovery*, 14(8), 769-777.

Anand, R. (2018). Identification of potential antituberculosis drugs through docking and virtual screening. *Interdisciplinary Sciences: Computational Life Sciences*, 10, 419-429.

Bagherian, M., Sabeti, E., Wang, K., Sartor, M. A., Nikolovska-Coleska, Z., & Najarian, K. (2021). Machine learning approaches and databases for prediction of drug-target interaction: a survey paper. *Briefings in bioinformatics*, 22(1), 247-269.

Batool, M., Ahmad, B., & Choi, S. (2019). A structure-based drug discovery paradigm. *International journal of molecular sciences*, 20(11), 2783.

Berrhail, F., Belhadef, H., & Haddad, M. (2022). Deep Convolutional Neural Network to improve the performances of screening process in LBVS. *Expert Systems with Applications*, 203, 117287.

Bender, A., & Cortés-Ciriano, I. (2021). Artificial intelligence in drug discovery: what is realistic, what are illusions? Part 1: Ways to make an impact, and why we are not there yet. *Drug discovery today*, 26(2), 511-524.

Bess, A., Berglind, F., Mukhopadhyay, S., Brylinski, M., Griggs, N., Cho, T., ... & Wasan, K. M. (2022). Artificial intelligence for the discovery of novel antimicrobial agents for emerging infectious diseases. *Drug discovery today*, 27(4), 1099-1107.

Bhatarai, B., Walters, W. P., Hop, C. E., Lanza, G., & Ekins, S. (2019). Opportunities and challenges using artificial intelligence in ADME/Tox. *Nature materials*, 18(5), 418-422.

Blanco-Gonzalez, A., Cabezon, A., Seco-Gonzalez, A., Conde-Torres, D., Antelo-Riveiro, P., Pineiro, A., & Garcia-Fandino, R. (2023). The role of ai in drug discovery: challenges, opportunities, and strategies. *Pharmaceuticals*, 16(6), 891.

Bravo Serrano, À., Piñero González, J., Queralt Rosinach, N., Rautschka, M., & Furlong, L. I. (2015). Extraction of relations between genes and diseases from text and large-scale data analysis: implications for translational research. *BMC Bioinformatics*. 2015 Feb 21; 16 (1): 55.

Burley, S. K., Bhikadiya, C., Bi, C., Bittrich, S., Chen, L., Crichlow, G. V., ... & Zhuravleva, M. (2021). RCSB Protein Data Bank: powerful new tools for exploring 3D structures of biological macromolecules for basic and applied research and education in fundamental biology, biomedicine, biotechnology, bioengineering and energy sciences. *Nucleic acids research*, 49(D1), D437-D451.

Bustamam, A., Hamzah, H., Husna, N. A., Syarofina, S., Dwimantara, N., Yanuar, A., & Sarwinda, D. (2021). Artificial intelligence paradigm for ligand-based virtual screening on the drug discovery of type 2 diabetes mellitus. *Journal of Big Data*, 8(1), 74.

Chanchal, D. K., Chaudhary, J. S., Kumar, P., Agnihotri, N., & Porwal, P. (2024). CRISPR-Based Therapies: Revolutionizing Drug Development and Precision Medicine. *Current Gene Therapy*, 24(3), 193-207.

Chakraborty, C., Teoh, S. L., & Das, S. (2017). The smart programmable CRISPR technology: a next generation genome editing tool for investigators. *Current drug targets*, 18(14), 1653-1663.

Chan, H. S., Shan, H., Dahoun, T., Vogel, H., & Yuan, S. (2019). Advancing drug discovery via artificial intelligence. *Trends in pharmacological sciences*, 40(8), 592-604.

Chan, Y. T., Lu, Y., Wu, J., Zhang, C., Tan, H. Y., Bian, Z. X., ... & Feng, Y. (2022). CRISPR-Cas9 library screening approach for anti-cancer drug discovery: overview and perspectives. *Theranostics*, 12(7), 3329.

Chaudhari, R., Fong, L. W., Tan, Z., Huang, B., & Zhang, S. (2020). An up-to-date overview of computational polypharmacology in modern drug discovery. *Expert opinion on drug discovery*, 15(9), 1025-1044.

Chopra, H., Shin, D. K., Munjal, K., Dhama, K., & Emran, T. B. (2023). Revolutionizing clinical trials: the role of AI in accelerating medical breakthroughs. *International Journal of Surgery*, 109(12), 4211-4220.

Chua HN, Roth FP. (2011). Discovering the targets of drugs via computational systems biology. *J Biol Chem*. Jul 8;286(27):23653-8. doi: 10.1074/jbc.R110.174797.

Carpenter, K. A., & Huang, X. (2018). Machine learning-based virtual screening and its applications to Alzheimer's drug discovery: a review. *Current pharmaceutical design*, 24(28), 3347-3358.

Cruz, J. A., & Wishart, D. S. (2006). Applications of machine learning in cancer prediction and prognosis. *Cancer informatics*, 2, 117693510600200030.

Damm-Ganamet, K. L., Arora, N., Becart, S., Edwards, J. P., Lebsack, A. D., McAllister, H. M., ... & Mirzadegan, T. (2019). Accelerating lead identification by high Throughput virtual screening: prospective case studies from the pharmaceutical industry. *Journal of Chemical Information and Modeling*, 59(5), 2046-2062.

Dara, S., Dhamecherla, S., Jadav, S. S., Babu, C. M., & Ahsan, M. J. (2022). Machine learning in drug discovery: a review. *Artificial Intelligence Review*, 55(3), 1947-1999.

- Das, R and Panigrahi, G.K. (2024). Messenger RNA surveillance: current understanding, regulatory mechanisms and future implications. *Molecular Biotechnology*: 1-18.
- de Oliveira Viana, J., Scotti, M. T., & Scotti, L. (2019). Molecular docking studies in multitarget antitubercular drug discovery. *Multi-Target Drug Design Using Chem-Bioinformatic Approaches*, 107-154.
- Deng, L., Zhong, W., Zhao, L., He, X., Lian, Z., Jiang, S., & Chen, C. Y. C. (2020). Artificial intelligence-based application to explore inhibitors of neurodegenerative diseases. *Frontiers in Neurorobotics*, 14, 617327.
- Dias, D. A., Urban, S., & Roessner, U. (2012). A historical overview of natural products in drug discovery. *Metabolites*, 2(2), 303-336.
- Doytchinova, I. (2022). Drug design—past, present, future. *Molecules*, 27(5), 1496.
- Ebrahimi, A., & Roshani, F. (2024). Systems biology approaches to identify driver genes and drug combinations for treating COVID-19. *Scientific Reports*, 14(1), 2257.
- Emmerich, C. H., Gamboa, L. M., Hofmann, M. C., Bonin-Andresen, M., Arbach, O., Schendel, P., ... & Parnham, M. J. (2021). Improving target assessment in biomedical research: the GOT-IT recommendations. *Nature reviews Drug discovery*, 20(1), 64-81.
- Fellmann, C., Gowen, B. G., Lin, P. C., Doudna, J. A., & Corn, J. E. (2017). Cornerstones of CRISPR–Cas in drug discovery and therapy. *Nature reviews Drug discovery*, 16(2), 89-100.
- Gibbs, R. A. (2020). The human genome project changed everything. *Nature Reviews Genetics*, 21(10), 575-576.
- Giordano, D., Biancaniello, C., Argenio, M. A., & Facchiano, A. (2022). Drug design by pharmacophore and virtual screening approach. *Pharmaceuticals*, 15(5), 646.
- Guan, L., Yang, H., Cai, Y., Sun, L., Di, P., Li, W., ... & Tang, Y. (2019). ADMET-score—a comprehensive scoring function for evaluation of chemical drug-likeness. *Medchemcomm*, 10(1), 148-157.
- Guo, S., Zhang, D., Wang, H., An, Q., Yu, G., Han, J., ... & Huang, J. (2023). Computational and systematic analysis of multi-omics data for drug discovery and development. *Frontiers in Medicine*, 10, 1146896.
- Gupta, R., Srivastava, D., Sahu, M., Tiwari, S., Ambasta, R. K., & Kumar, P. (2021). Artificial intelligence to deep learning: machine intelligence approach for drug discovery. *Molecular diversity*, 25, 1315-1360.
- Gurung, A. B., Ali, M. A., Lee, J., Farah, M. A., & Al-Anazi, K. M. (2021). An updated review of computer-aided drug design and its application to COVID-19. *BioMed research international*, 2021.
- Gu, Y., Wang, Y., Zhu, K., Li, W., Liu, G., & Tang, Y. (2024). DBPP-Predictor: a novel strategy for prediction of chemical drug-likeness based on property profiles. *Journal of Cheminformatics*, 16(1), 4.

Halder D, Das S, Jeyaprakash RS. (2023). Identification of natural product as selective PI3K $\alpha$  inhibitor against NSCLC: multi-ligand pharmacophore modeling, molecular docking, ADME, DFT, and MD simulations. *Mol Divers*. Sep 15. doi: 10.1007/s11030-023-10727-2.

Han, R., Yoon, H., Kim, G., Lee, H., & Lee, Y. (2023). Revolutionizing medicinal chemistry: the application of artificial intelligence (AI) in early drug discovery. *Pharmaceuticals*, 16(9), 1259.

Hassan Baig, M., Ahmad, K., Roy, S., Mohammad Ashraf, J., Adil, M., Haris Siddiqui, M., & Choi, I. (2016). Computer aided drug design: success and limitations. *Current pharmaceutical design*, 22(5), 572-581.

Hopkins, A. L., & Groom, C. R. (2002). The druggable genome. *Nature reviews Drug discovery*, 1(9), 727-730.

Hughes JP, Rees S, Kalindjian SB, Philpott KL. (2011). Principles of early drug discovery. *Br J Pharmacol*. Mar;162(6):1239-49. doi: 10.1111/j.1476-5381.2010.01127.x.

Ibrahim, M. A., Abdeljawaad, K. A., Abdelrahman, A. H., Jaragh-Alhadad, L. A., Oraby, H. F., Elkaeed, E. B., ... & Hegazy, M. E. F. (2022). Exploring natural product activity and species source candidates for hunting ABCB1 transporter inhibitors: An in silico drug discovery study. *Molecules*, 27(10), 3104.

Ikeda, K., Maezawa, Y., Yonezawa, T., Shimizu, Y., Tashiro, T., Kanai, S., ... & Osawa, M. (2023). DLiP-PPI library: An integrated chemical database of small-to-medium-sized molecules targeting protein–protein interactions. *Frontiers in Chemistry*, 10, 1090643.

Jadaun, A., Subbarao, N., & Dixit, A. (2017). Allosteric inhibition of topoisomerase I by pinostrobin: Molecular docking, spectroscopic and topoisomerase I activity studies. *Journal of Photochemistry and Photobiology B: Biology*, 167, 299-308.

Jeon, J., Nim, S., Teyra, J., Datti, A., Wrana, J. L., Sidhu, S. S., ... & Kim, P. M. (2014). A systematic approach to identify novel cancer drug targets using machine learning, inhibitor design and high-throughput screening. *Genome medicine*, 6, 1-18.

Jones AW. (2011). Early drug discovery and the rise of pharmaceutical chemistry. *Drug Test Anal*. Jun;3(6):337-44. doi: 10.1002/dta.301.

Jumper, J., Evans, R., Pritzel, A., Green, T., Figurnov, M., Ronneberger, O., ... & Hassabis, D. (2021). Highly accurate protein structure prediction with AlphaFold. *Nature*, 596(7873), 583-589.

Jung, H.W., Panigrahi, G.K., Jung, G-Y., Lee, Y.J., Shin, K.H., Sahoo, A., Choi, E.S., Lee, E., Kim, K.M., Yang, S.H., Jeon, J.S., Lee, S.C., and Kim, S.H. (2020). PAMP-triggered immunity involves proteolytic degradation of core nonsense-mediated mRNA decay factors during early defense response. *The Plant Cell* 32(4): 1081-1101.

Jussi Paananen, Vittorio Fortino (2020). An omics perspective on drug target discovery platforms, *Briefings in Bioinformatics*, Volume 21, Issue 6, November, doi.org/10.1093/bib/bbz122 .

- Kabir A, Muth A. (2022). Polypharmacology: The science of multi-targeting molecules. *Pharmacol Res.* Feb;176:106055. doi: 10.1016/j.phrs.2021.106055.
- Karmakar, P., Trivedi, A., & Gaitonde, V. (2020). Introductory chapter: The modern-day drug discovery. *Drug Discovery and Development-New Advances.*
- Kashyap K. and Siddiqi MI. (2021). Recent trends in artificial intelligence-driven identification and development of anti-neurodegenerative therapeutic agents. *Mol Divers,* Aug;25(3):1517-1539. doi: 10.1007/s11030-021-10274-8.
- Katsila, T., Spyroulias, G. A., Patrinos, G. P., & Matsoukas, M. T. (2016). Computational approaches in target identification and drug discovery. *Computational and structural biotechnology journal*, 14, 177-184.
- Khan, O., Badhiwala, J. H., Grasso, G., & Fehlings, M. G. (2020). Use of machine learning and artificial intelligence to drive personalized medicine approaches for spine care. *World neurosurgery*, 140, 512-518.
- Kim, S., & Cho, K. H. (2019). PyQSAR: a fast QSAR modeling platform using machine learning and jupyter notebook. *Bulletin of the Korean Chemical Society*, 40(1), 39-44.
- Kiriiri, G.K., Njogu, P.M. & Mwangi, A.N. (2020). Exploring different approaches to improve the success of drug discovery and development projects: a review. *Futur J Pharm Sci* 6, doi: org/10.1186/s43094-020-00047-9.
- Koromina M, Pandi MT, Patrinos GP. (2019). Rethinking Drug Repositioning and Development with Artificial Intelligence, Machine Learning, and Omics. *OMICS*, Nov;23(11):539-548. doi: 10.1089/omi.2019.0151.
- Kumar, M., Nguyen, T. N., Kaur, J., Singh, T. G., Soni, D., Singh, R., & Kumar, P. (2023). Opportunities and challenges in application of artificial intelligence in pharmacology. *Pharmacological Reports*, 75(1), 3-18.
- Lavecchia A, Di Giovanni C. (2013). Virtual screening strategies in drug discovery: a critical review. *Curr. Med. Chem.* 20(23), 2839–2860.
- Lee I, Keum J, and Nam H. (2019). DeepConv-DTI: Prediction of drug-target interactions via deep learning with convolution on protein sequences. *PLoS Comput Biol.*, Jun 14;15(6):e1007129. doi: 10.1371/journal.pcbi.1007129.
- Leelananda, S. P., & Lindert, S. (2016). Computational methods in drug discovery. *Beilstein journal of organic chemistry*, 12(1), 2694-2718.
- Leung, E. L., Cao, Z. W., Jiang, Z. H., Zhou, H., & Liu, L. (2013). Network-based drug discovery by integrating systems biology and computational technologies. *Briefings in bioinformatics*, 14(4), 491-505.
- Li, H., Yang, Y., Hong, W., Huang, M., Wu, M., & Zhao, X. (2020). Applications of genome editing technology in the targeted therapy of human diseases: mechanisms, advances and prospects. *Signal transduction and targeted therapy*, 5(1), 1.

- Li, K., Du, Y., Li, L., & Wei, D. Q. (2020). Bioinformatics approaches for anti-cancer drug discovery. *Current drug targets*, 21(1), 3-17.
- Liu, S. H., Xiao, Z., Mishra, S. K., Mitchell, J. C., Smith, J. C., Quarles, L. D., & Petridis, L. (2022). Identification of small-molecule inhibitors of fibroblast growth factor 23 signaling via in silico hot spot prediction and molecular docking to  $\alpha$ -Klotho. *Journal of chemical information and modeling*, 62(15), 3627-3637.
- Liu, X., Yi, W., Xi, B., & Dai, Q. (2022). Identification of Drug-Disease Associations Using a Random Walk with Restart Method and Supervised Learning. *Computational and Mathematical Methods in Medicine*.
- Liu, W., Li, L., Jiang, J., Wu, M., & Lin, P. (2021). Applications and challenges of CRISPR-Cas gene-editing to disease treatment in clinics. *Precision clinical medicine*, 4(3), 179-191.
- Lv, Q., Zhou, F., Liu, X., & Zhi, L. (2023). Artificial intelligence in small molecule drug discovery from 2018 to 2023: Does it really work?. *Bioorganic Chemistry*, 106894.
- Maia, E. H. B., Assis, L. C., De Oliveira, T. A., Da Silva, A. M., & Taranto, A. G. (2020). Structure-based virtual screening: from classical to artificial intelligence. *Frontiers in chemistry*, 8, 343.
- Mak, K. K., & Pichika, M. R. (2019). Artificial intelligence in drug development: present status and future prospects. *Drug discovery today*, 24(3), 773-780.
- Malandraki-Miller S, Riley PR. (2021 ). Use of artificial intelligence to enhance phenotypic drug discovery. *Drug Discov Today*. Apr;26(4):887-901. doi: 10.1016/j.drudis.2021.01.013.
- Manan Shah, Maanit Patel, Monit Shah, Monali Patel, Mitul Prajapati (2024). Computational transformation in drug discovery: A comprehensive study on molecular docking and quantitative structure activity relationship (QSAR). *Intelligent Pharmacy*, doi.org/10.1016/j.ipha.2024.03.001.
- Martinelli, D. D. (2022). Generative machine learning for de novo drug discovery: A systematic review. *Computers in Biology and Medicine*, 145, 105403.
- Matter H, Sotriffer C. (2011). Applications and success stories in virtual screening. In: *Virtual screening: principles, challenges, and practical guidelines*. Sotriffer C (Ed.). Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany, 319–358.
- McGibbon, M., Money-Kyrle, S., Blay, V., & Houston, D. R. (2023). SCORCH: improving structure-based virtual screening with machine learning classifiers, data augmentation, and uncertainty estimation. *Journal of Advanced Research*, 46, 135-147.
- Mohs RC, Greig NH. (2017). Drug discovery and development: Role of basic biological research. *Alzheimers Dement (N Y)*, Nov 11;3(4):651-657. doi: 10.1016/j.trci.2017.10.005.
- Moret, M., Pachon Angona, I., Cotos, L., Yan, S., Atz, K., Brunner, C., ... & Schneider, G. (2023). Leveraging molecular structure and bioactivity with chemical language models for de novo drug design. *Nature Communications*, 14(1), 114.

Mouchlis, V. D., Afantitis, A., Serra, A., Fratello, M., Papadiamantis, A. G., Aidinis, V., ... & Melagraki, G. (2021). Advances in de novo drug design: from conventional to machine learning methods. *International journal of molecular sciences*, 22(4), 1676.

Mu, G., Liu, H., Wen, Y., & Luan, F. (2011). Quantitative structure–property relationship study for the prediction of characteristic infrared absorption of carbonyl group of commonly used carbonyl compounds. *Vibrational Spectroscopy*, 55(1), 49-57.

Niazi SK. and Mariam Z. (2023). Recent Advances in Machine-Learning-Based Chemoinformatics: A Comprehensive Review. *Int J Mol Sci.*, Jul 15;24(14):11488. doi: 10.3390/ijms241411488.

Nisha, C. M., Kumar, A., Nair, P., Gupta, N., Silakari, C., Tripathi, T., & Kumar, A. (2016). Molecular docking and in silico ADMET study reveals acylguanidine 7a as a potential inhibitor of  $\beta$ -secretase. *Advances in bioinformatics*, 2016.

Oliveira, T. A. D., Silva, M. P. D., Maia, E. H. B., Silva, A. M. D., & Taranto, A. G. (2023). Virtual screening algorithms in drug discovery: A review focused on machine and deep learning methods. *Drugs and Drug Candidates*, 2(2), 311-334.

Panigrahi, G.K., Sahoo, A and Satapathy, K.B. (2024). The processing body component varicose plays a multilayer role towards stress management in Arabidopsis. *Plant Physiology Reports*: 1-10. <https://doi.org/10.1007/s40502-023-00778-w>.

Panigrahi, G. K., & Satapathy, K. B. (2020). Arabidopsis DCP5, a decapping complex protein interacts with ubiquitin-5 in the processing bodies.

Panigrahi, G. K., & Satapathy, K. B. (2020a). Formation of Arabidopsis Poly (A)-Specific Ribonuclease associated processing bodies in response to pathogenic infection. *Plant Archives*, 20(2), 4907-12.

Panigrahi, G.K., and Satapathy, K.B. (2021). *Pseudomonas syringae* pv. *syringae* Infection Orchestrates the Fate of the Arabidopsis J Domain Containing Cochaperone and Decapping Protein Factor 5. *Physiological and Molecular Plant Pathology* 113(101598): 1-9.

Panigrahi, G. K., Sahoo, S. K., Sahoo, A., Behera, S., Sahu, S., Dash, A., & Satapathy, K. B. (2023). Bioactive molecules from plants: a prospective approach to combat SARS-CoV-2. *Advances in Traditional Medicine*, 23(3), 617-630.

Panigrahi, G. K., Sahoo, A., & Satapathy, K. B. (2021). Insights to plant immunity: Defense signaling to epigenetics. *Physiological and Molecular Plant Pathology*, 113, 101568.

Panigrahi, G. K., Sahoo, A., & Satapathy, K. B. (2021a). Differential expression of selected Arabidopsis resistant genes under abiotic stress conditions. *Plant Science Today*, 8(4), 859-864.

Panigrahi, G. K., & Satapathy, K. B. (2020b). Sacrificed surveillance process favours plant defense: a review. *Plant Archives* (09725210), 20(2).

Patro, I., Sahoo, A., Nayak, B. R., Das, R., Majumder, S., & Panigrahi, G. K. (2023). Nonsense-mediated mRNA decay: Mechanistic insights and physiological significance. *Molecular Biotechnology*, 1-15.

Paul, D., Sanap, G., Shenoy, S., Kalyane, D., Kalia, K., & Tekade, R. K. (2021). Artificial intelligence in drug discovery and development. *Drug discovery today*, 26(1), 80–93. <https://doi.org/10.1016/j.drudis.2020.10.010> .

Pereira, T., Abbasi, M., Ribeiro, B., & Arrais, J. P. (2021). Diversity oriented deep reinforcement learning for targeted molecule generation. *Journal of cheminformatics*, 13(1), 21.

Pina, A. S., Hussain, A., & Roque, A. C. A. (2010). An historical overview of drug discovery. *Ligand-Macromolecular Interactions in Drug Discovery: Methods and Protocols*, 3-12.

Prabha, T., Selvinthanuja, C., Hemalatha, S., Sengottuvelu, S., & Senthil, J. (2021). Machine learning algorithm used to build a QSAR model for pyrazoline scaffold as anti-tubercular agent. *J. Med. Pharm. Allied Sci*, 10, 4024-4030.

Qin D. (2019). Next-generation sequencing and its clinical application. *Cancer Biol Med*. Feb;16(1):4-10. doi: 10.20892/j.issn.2095-3941.2018.0055.

Russell, C., Rahman, A., & Mohammed, A. R. (2013). Application of genomics, proteomics and metabolomics in drug discovery, development and clinic. *Therapeutic delivery*, 4(3), 395-413.

Sahoo, A., Satapathy, K.B and Panigrahi, G.K. (2023). Ectopic expression of disease resistance protein promotes resistance against pathogen infection and drought stress in *Arabidopsis*. *Physiological and Molecular Plant Pathology* 124(101949): 1-7.

Sahoo, A., Satapathy, K.B and Panigrahi, G.K. (2023a). Security check: Plant immunity under temperature surveillance. *Journal of Plant Biochemistry and Biotechnology*: 1-4. <https://doi.org/10.1007/s13562-023-00846-0>.

Sahoo, A., & Satapathy, K. B. (2021). Differential expression of *Arabidopsis* EJC core proteins under short-day and long-day growth conditions. *Plant Science Today*, 8(4), 815-819.

Sahu A, Mishra J, Kushwaha N. (2022). Artificial Intelligence (AI) in Drugs and Pharmaceuticals. *Comb Chem High Throughput Screen.*; 25(11):1818-1837. doi: 10.2174/1386207325666211207153943.

Sakharkar, M. K., Rajamanickam, K., Babu, C. S., Madan, J., Chandra, R., & Yang, J. (2019). Preclinical: drug target identification and validation in human.

Sebastiano, M. R., Ermondi, G., Hadano, S., & Caron, G. (2022). AI-based protein structure databases have the potential to accelerate rare diseases research: AlphaFoldDB and the case of IAHS/Alsin. *Drug Discovery Today*, 27(6), 1652-1660.

Selvaraj, C., Chandra, I., & Singh, S. K. (2021). Artificial intelligence and machine learning approaches for drug design: challenges and opportunities for the pharmaceutical industries. *Molecular diversity*, 1-21.

- Sethi, A., Joshi, K., Sasikala, K., & Alvala, M. (2019). Molecular docking in modern drug discovery: Principles and recent applications. *Drug discovery and development-new advances*, 2, 1-21.
- Singh, N., Vayer, P., Tanwar, S., Poyet, J. L., Tsaïoun, K., & Villoutreix, B. O. (2023). Drug discovery and development: introduction to the general public and patient groups. *Frontiers in Drug Discovery*, 3, 1201419.
- Singh, S., Gupta, H., Sharma, P., & Sahi, S. (2024). Advances in Artificial Intelligence (AI)-assisted approaches in drug screening. *Artificial Intelligence Chemistry*, 2(1), 100039.
- Sliwoski, G., Kothiwale, S., Meiler, J., & Lowe, E. W. (2014). Computational methods in drug discovery. *Pharmacological reviews*, 66(1), 334-395.
- Soares, T. A., Nunes-Alves, A., Mazzolari, A., Ruggiu, F., Wei, G. W., & Merz, K. (2022). The (Re)-Evolution of Quantitative Structure–Activity Relationship (QSAR) studies propelled by the surge of machine learning methods. *Journal of Chemical Information and Modeling*, 62(22), 5317-5320.
- Somda, D., Kpordze, S. W., Jerpkorir, M., Mahora, M. C., Ndungu, J. W., Kamau, S. W., ... & Elbasyouni, A. (2023). The Role of Bioinformatics in Drug Discovery: A Comprehensive Overview.
- Song M., Kim M., Kang K., Kim Y.H., Jeon S. (2018). Application of public knowledge discovery tool (pkde4j) to represent biomedical scientific knowledge. *Front. Res. Metr. Anal.*;3:7.
- Tong, X., Liu, X., Tan, X., Li, X., Jiang, J., Xiong, Z., ... & Zheng, M. (2021). Generative models for de novo drug design. *Journal of Medicinal Chemistry*, 64(19), 14011-14027.
- Tripathi, M. K., Nath, A., Singh, T. P., Ethayathulla, A. S., & Kaur, P. (2021). Evolving scenario of big data and Artificial Intelligence (AI) in drug discovery. *Molecular Diversity*, 25, 1439-1460.
- Vamathevan, J., Clark, D., Czodrowski, P., Dunham, I., Ferran, E., Lee, G., ... & Zhao, S. (2019). Applications of machine learning in drug discovery and development. *Nature reviews Drug discovery*, 18(6), 463-477.
- Visan AI. and Negut I. (2024). Integrating Artificial Intelligence for Drug Discovery in the Context of Revolutionizing Drug Delivery. *Life*, Feb 7;14(2):233. doi: 10.3390/life14020233.
- Wang, C., Hu, G., Wang, K., Brylinski, M., Xie, L., & Kurgan, L. (2016). PDID: database of molecular-level putative protein–drug interactions in the structural human proteome. *Bioinformatics*, 32(4), 579-586.
- Wingert BM. and Camacho CJ. (2018). Improving small molecule virtual screening strategies for the next generation of therapeutics. *Curr Opin Chem Biol*. Jun;44:87-92. doi: 10.1016/j.cbpa.2018.06.006.
- Wooller, S. K., Benstead-Hume, G., Chen, X., Ali, Y., & Pearl, F. M. (2017). Bioinformatics in translational drug discovery. *Bioscience reports*, 37(4), BSR20160180.

Xia X. (2017). *Bioinformatics and Drug Discovery*. *Curr Top Med Chem*. 17(15):1709-1726. doi: 10.2174/1568026617666161116143440.

Xu, H., Xu, H., Lin, M., Wang, W., Li, Z., Huang, J., ... & Chen, X. (2007). Learning the drug target- likeness of a protein. *Proteomics*, 7(23), 4255-4263.

Yang, H., Sun, L., Li, W., Liu, G., & Tang, Y. (2018). In silico prediction of chemical toxicity for drug design using machine learning methods and structural alerts. *Frontiers in chemistry*, 6, 30.

Yue, R. and Dutta, A. (2022). Computational systems biology in disease modeling and control, review and perspectives. *npj Syst Biol Appl* , doi.org/10.1038/s41540-022-00247-4.

Zhang C, Quan R, Wang J. (2018). Development and application of CRISPR/Cas9 technologies in genomic editing. *Hum Mol Genet*. Aug 1;27(R2):R79-R88.

Zhang, Q., Han, J., Zhu, Y., Yu, F., Hu, X., Tong, H. H., & Liu, H. (2023). Discovery of novel and potent InhA direct inhibitors by ensemble docking-based virtual screening and biological assays. *Journal of Computer-Aided Molecular Design*, 37(12), 695-706.

Zhang, Y., Luo, M., Wu, P., Wu, S., Lee, T. Y., & Bai, C. (2022). Application of computational biology and artificial intelligence in drug design. *International journal of molecular sciences*, 23(21), 13568.

Zhao, B. W., Su, X. R., Hu, P. W., Huang, Y. A., You, Z. H., & Hu, L. (2023). iGRLDTI: an improved graph representation learning method for predicting drug–target interactions over heterogeneous biological information network. *Bioinformatics*, 39(8), btad451.

Zou, J., Zheng, M. W., Li, G., & Su, Z. G. (2013). Advanced systems biology methods in drug discovery and translational biomedicine. *BioMed research international*, 2013.