Advances of AI-driven Drug Design and Discovery in Pharmaceuticals - Review

Dev Ras Pandey [1*], Sushree Sasmita Dash [1], Akanksha Mishra [1]

Abstract

The field of drug design and discovery is undergoing a transformative shift, leveraging Artificial Intelligence (AI) and Machine Learning (ML) techniques to expedite and optimize the drug development process. Traditional methods are often costly and time-consuming, involving extensive testing and sequential stages. However, contemporary drug development integrates AI, particularly in drug identification and preclinical studies, resulting in significant resource and time savings. AI is utilized for bioactivity and physicochemical forecasting, de novo molecule design, synthesis prediction, and drug-target profile representation. This review introduces the AI-based Drug Design and Discovery System (AI-D3S), a comprehensive approach utilizing serialization, de-serialization, Particle Swarm Optimization (PSO), and Support Vector Machine (SVM). The system demonstrates superior accuracy, precision, sensitivity, and specificity compared to conventional methods, showcasing an average improvement of 8.7%. Our review study evaluates the system on two chemical databases, MAO and Biodegradation, and illustrates its efficacy in predicting drug-annotation combinations. The potential of AI in pharmaceuticals extends from drug design to personalized therapies, decision-making, and efficient resource allocation in marketing. The research envisions AI as an indispensable tool in the pharmaceutical sector, driving innovation, reducing costs, and ensuring the production of higher-quality products. The AI-D3S model presented in this study sets the stage for future advancements in drug design and discovery, offering a promising avenue for the integration of AI in revolutionizing the pharmaceutical industry.

Keywords: Drug Design, Artificial Intelligence, Machine Learning, AI-Driven, Drug Development, Pharmaceuticals

Significance | The application of AI in pharmaceuticals holds the promise of personalized therapies, streamlined production, and improved market strategies, making it an indispensable tool for the future of drug development.

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1. Introduction

The process of medication development is costly and time-consuming, including testing hundreds of substances and conducting tests to identify safe and productive pharmaceuticals (Caban, Stepnowski, 2021). Developing drugs typically consists of the sequential stages depicted in Figure 1. Contemporary drug creation aims to accelerate the intermediate phases, minimizing expenses through utilizing Machine Learning (ML) techniques in creating drugs, primarily during the drug identification and preclinical study phases Kolluri et al. (2022). Essentially, molecules undergo sequential tests to ascertain their characteristics, efficacy, and safety for subsequent phases McComb et al. (2022). ML is becoming more prevalent in accurately forecasting molecular features during the first phases, substantially alleviating the burden of following procedures (such as clinical trials) and resulting in considerable savings of resources and time Sun et al. (2022).

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The present-day uses of Artificial Intelligence (AI) in drug development encompass various areas, such as bioactivity or physicochemical forecasting using numerical structure-activity (property) connection designs, anticipating relationships among drug-protein and drug-drug groups, de novo molecule design for generating molecular frameworks with desired pharmacological characteristics, and synthesis forecasting for forecasting products in reactions during synthesis Kolluri et al. (2022). Conventional AI algorithms have a limitation in handling inputs of fixed sizes. Therefore, early drug discovery efforts have relied on feature engineering, which involves constructing and utilizing problem-specific biochemical descriptions Duch et al. (2007) Vora et al. (2023).

AI is now increasingly utilized in numerous areas, with the pharmaceutical business being a prominent benefactor (Kulkov, 2021). Various tools have been created using the networks that are the fundamental structure of AI platforms. Its purpose was to aid in examining a patient's healthcare records and connection to an extensive database, proposing treatment approaches for the disease. This approach is utilized for the expeditious identification of illnesses Mirmozaffari et al. (2022).

The contribution of AI in creating pharmaceutical products, from initial research to patient utilization, is envisioned Paul et al. (2021). AI can help design drugs, aid decision-making processes, find personalized therapies for patients, and handle the clinical information produced for future medication development. E-VAI, an AI platform, utilizes ML methods and a user-friendly interface to create logical directions based on opponents, essential stakeholders, and market penetration (Mehta) Brown et al. (2020). This platform predicts the primary trends in pharmaceutical sales, enabling marketing managers to distribute resources effectively, improve sales performance, and make informed investment decisions Hessler et al. (2018). Various use cases for AI in the research and development of drugs are illustrated in Figure 2.

The subsequent parts are arranged in the specified fashion: Section 2 focuses on the literature survey and analysis Arabi et al. (2021). Section 3 introduces the AI-based Drug Design and Discovery System (AI-D3S), a system for designing and discovering drugs using artificial intelligence. The simulation results and findings are found in section 4. Section 5 addresses the last remarks and potential areas for future exploration.

2. Literature Survey and Analysis

Emerging fields such as molecular biology, genomics, and high-throughput screenings are anticipated to lead to the discovery of several novel medications in the present decade. Medications' efficacy largely depends on the precise interaction between their molecules and complimentary structures or biological receptors.

Graph Neural Networks (GNNs) are specific neural networks that directly process data organized as graphs. They have garnered significant interest and attention Xiong et al. (2021). This paper presents the uses of GNNs in de novo drug development, focusing on three key areas: molecule scoring, molecular creation and optimization, and synthesis scheduling. The research also analyzes the present obstacles and prospective pathways of GNNs in de novo drug creation.

This study outlines the recent advancements made by the PROTAC method for drug development and exploration Guedeney et al. (2023). It will present the latest findings from research and offer recommendations for pharmacists in designing new PROTACs as a successful therapy. Expanding the scope of the functional space allows us to produce a wider variety of potential therapeutic candidates.

Three alkaloid substances, namely lycorine, emetine, and cephaeline, were discovered to be potent inhibitors of SARS-CoV-2 Ren et al. (2022). These compounds effectively target the possible sites concurrently. To do that, a thorough process was devised using mathematical methods and experimental procedures to develop a novel strategy for building anti-virus inhibitors targeting multiple sites.

The research has created a novel set of scoring systems called DockTScore, which incorporates physics-based factors with ML techniques Guedes et al. (2021). Scoring algorithms were specifically designed for two significant therapeutic targets, proteases and protein-protein bonds, which belong to a unique category of molecules used in drug development.

OpenChem is a PyTorch-based ML toolset for mathematical chemistry and drug development Korshunova et al. (2021). OpenChem provides a user-friendly and efficient approach to creating models with a software architecture organized into separate modules. It includes many modules for preparing data. The GitHub repository offers unrestricted access to it. OpenChem is a software program that is constructed using the PyTorch framework. It is specifically designed to perform efficiently on Graphics Processing Units (GPUs) and handle extensive data collection.

The research wants to explore drug relationships by examining the connections between proteins targeted by two medicines (Mei, Zhang, 2021). The research suggests a straightforward drug target profile representation to illustrate medicines and drug combinations to achieve this objective. The study constructs an l2-regularized logistical regression algorithm to forecast drug-drug associations. The deciphered processes might offer biological understanding into possible negative pharmacological interactions of concurrently given medications.

This study comprehensively overviews traditional and recently developed AI methods Zeng et al. (2022). It is a current and easily

understandable resource for the drug industry's wide-ranging computational research and development. The research gives many perspectives on deep-generating modeling and outlines the mathematical frameworks used to depict biochemical and biological frameworks and their practical applications.

The paper primarily examines Multi-Objective Optimization (MOO) approaches, including their comparability, benefits, and constraints, after briefly discussing Single-Objective Optimization (SOO) and methods for incorporating several criteria into it (Lambrinidis, Tsantili-Kakoulidou, 2021). Utilizing a combination of MOO methodologies, either in addition to AI or as a supplement to SOO, significantly enhances the efficiency of drug creation. This approach aids in decision-making and improves the likelihood of success.

Based on the preceding discourse, a novel AI-driven medication design and development approach is necessary. Utilizing various AI techniques can boost the outcomes and increase precision.

3. Proposed AI-based Drug Design and Discovery System

Serialization and de-serialization are employed to circumvent the need for retraining the model with the training dataset whenever a new testing set is provided to the web application.

As seen in Figure 3, the initial stage involves training the model using the provided training datasets. The model is stored in a file in Hierarchy Data Type 5 (HDF5). The act of saving the model is referred to as serializing, and it is accomplished utilizing the built-in component "save" in Keras. The model's components are stored in one serialization document, including its architecture, measurements, learning setup (loss and optimizer), and optimization states.

The file undergoes deserialization and is sent to the Flask website. Converting serialized data back into its original form is known as de-serialization. In Keras, this is accomplished through the built-in component "load_model." By utilizing the serialization file for storing the pre-trained modeling's arrangement, it is possible to circumvent the need to refine the framework with the trained database each time a new tested database is submitted to the web page.

The Particle Swarm Optimisation (PSO) method is combined with Support Vector Machine (SVM) to achieve categorization and optimize characteristics, including choosing features and optimizing parameters. In the PSO, the optimal placement of the rabbit, denoted as X, is determined by using SVM settings in the selected set of characteristics for all cross-validation cycles. The flowchart depicting the AI-D3S technique is presented in Figure 4. It showcases the three stages of the method: (1) Preprocessing, (2) selecting features and optimizing, and (3) categorization and verification.

3.1 Data description

The research conducted experimental assessments using two chemical substance databases for the suggested technique. The initial database is the monoamine oxidase, accessible on the IAPR-TC15 website. It comprises 65 components and is categorized into two distinct groups. Of the total number of molecules, 32 can specifically inhibit PSO, commonly used as an antidepressant medication. On the other hand, the remaining 35 compounds do not possess this inhibitory effect. Each of the 65 compounds has an average size of 15.2 elements. The intermediate level of molecules in this collection is 3.2 edges. The compound with the fewest atoms consists of 12, whereas the compound with the most significant number of atoms consists of 28. Each row in the dataset represents a molecule; every compound has 1600 characteristics. The second database, biological degradation, is derived from the Acquired Immunodeficiency Syndrome (AIDS) and an antiviral screening database of active drugs. It comprises 1000 substances, 42 structural descriptions, and one experimental category.

The results have been utilized to construct quantitative structure-activity relationship algorithms for investigating the correlations among chemical composition and biodegradation of compounds. The biodegradation test outcomes of 1000 compounds were gathered from the National Institution of Technologies and Examination (NITE) website.

3.2 Data preprocessing

This section explains transitioning from Monoamine Oxidase (MAO) to the characteristics that characterize chemical data. The cheminformatics information that was previously utilized has been converted into a simplified molecular input line entry systems file utilizing the OpenTable program. The research computes the cellular description using E-dragon. Complex molecules can be characterized by several qualities, including topological indexes defining three-dimensional molecules, quantum mechanical descriptions, and molecule field variables. These properties can amount to hundreds of millions. The indicators can be categorized as either structure or physiological. Structural descriptions include molecular mass, volume, rotatable securities, interatomic lengths, atom categories, molecule walk matters, and atom dispersion. Physicochemical descriptions encompass electronegativity, fragrance, and solvation characteristics.

A comprehensive examination of this dataset and the employed approach has been presented in a prior publication. Initially, the provided database is partitioned into the training and testing databases. Moreover, the training and testing databases have been partitioned into the characteristics of the database and the desired database.

Both the training characteristics database and the training targeting database comprise 23000 training specimens. The testing characteristics and targeting databases include 3000 testing specimens. During the information pre-processing step, the

Figure 1. Drug development process

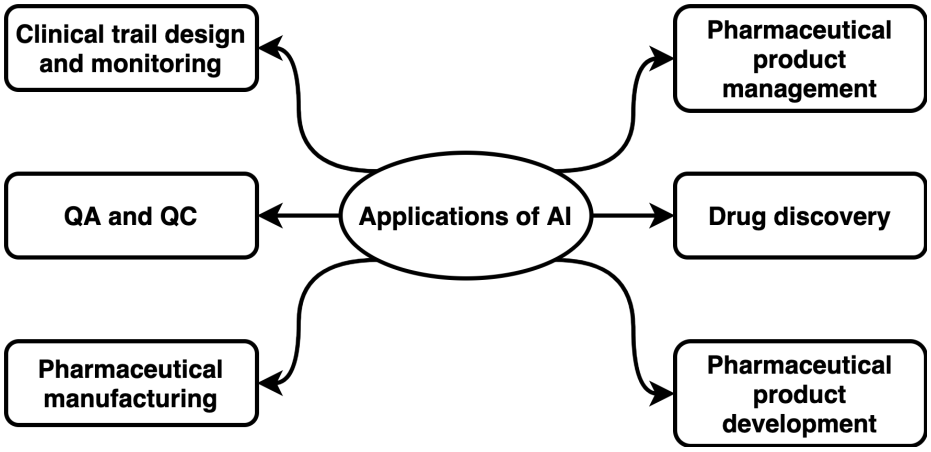

Figure 2. Applications of AI

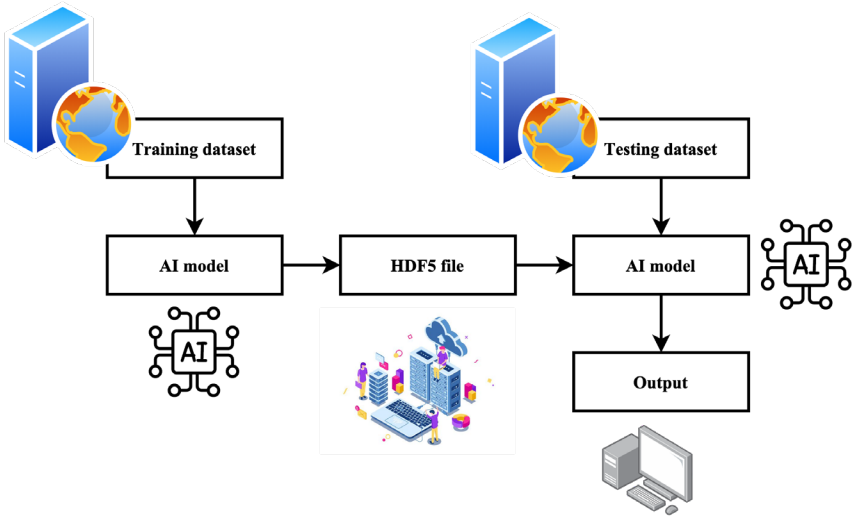

Figure 3. AI-based drug design process

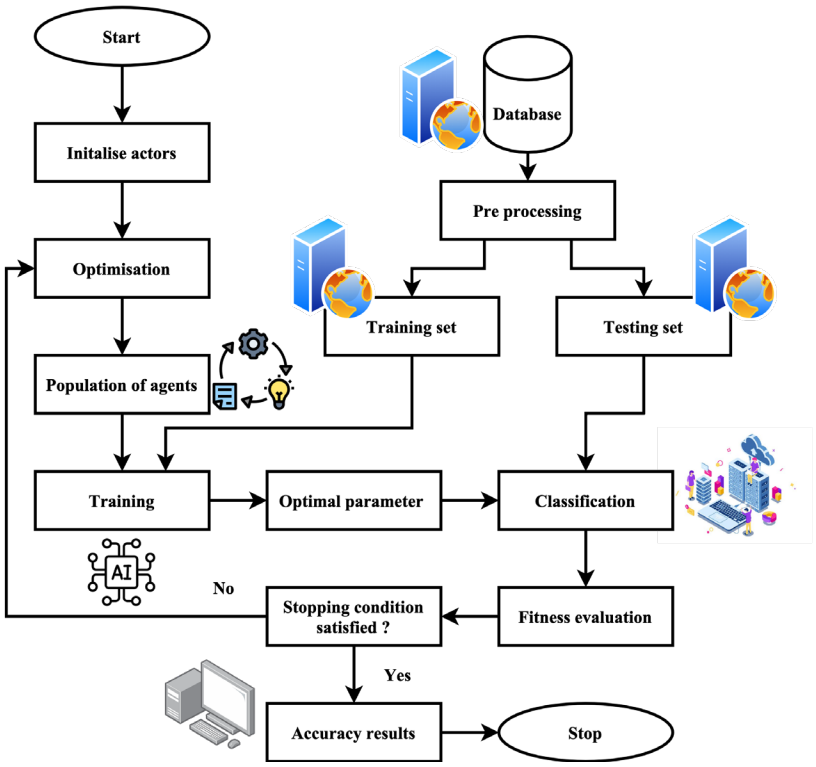

Figure 4. The drug discovery process based on AI

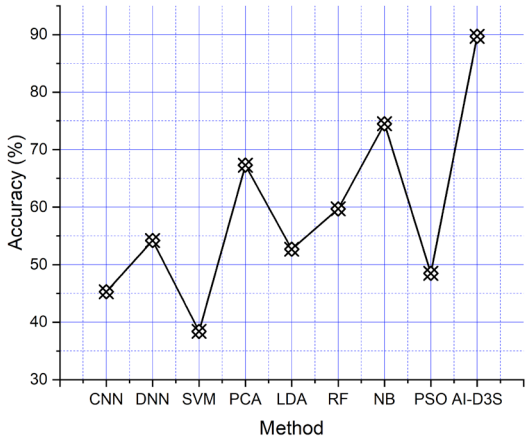

Figure 5. Accuracy analysis of drug design and discovery systems

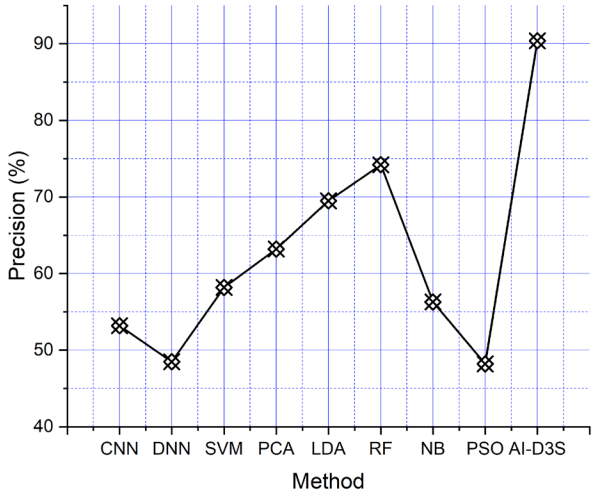

Figure 6. Precision analysis of drug design and discovery systems

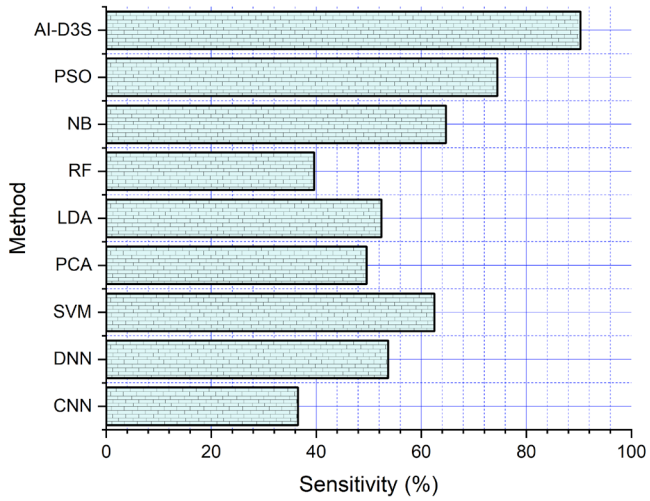

Figure 7. Sensitivity analysis of drug design and discovery systems

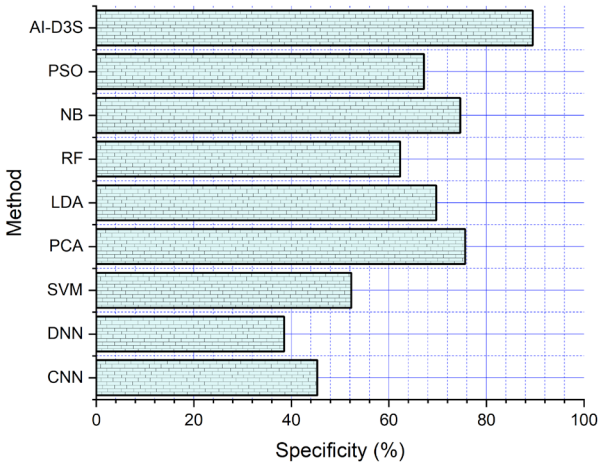

Figure 8. Specificity analysis of drug design and discovery systems

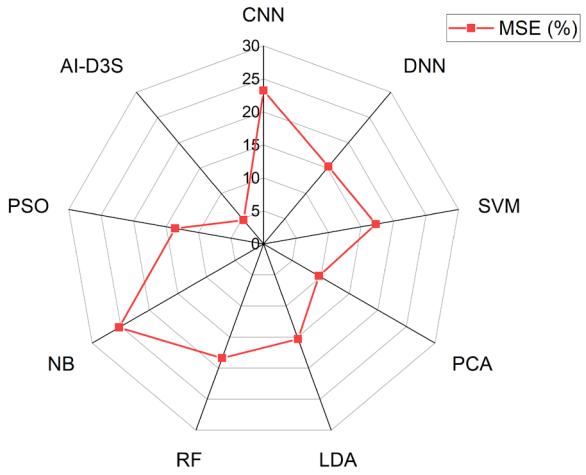

Figure 9. MSE analysis of drug design and discovery systems

definite information of the traits is converted into numerical figures using mapping. The remedies developed by PSO must be examined throughout the iterative procedure to validate their efficacy. The fitness function (ff_o) utilized by the PSO is explicitly specified as

$$ff_o = k_1 + k_2\frac{E}{D} - G \quad (1)$$

$$k_2 = k_1 \quad (2)$$

$$ff_o = k_3 \quad (3)$$

The categorization error rate, denoted as E, is determined by the overall amount of characteristics in the data set, represented by D. There are two variables, k_1 and k_2, which separately measure the significance of categorization quality (as determined by the classifications) and the total size of the subgroup. $k_1$is determined within the interval [0, 1]. G denotes the grouping column for the classification algorithm, while k_3 indicates the requirement that every method be contrasted with the fitness function. To optimize the outcome, the value of ff_o must be more significant than T.

3.3 Feature selection process

Feature selection is a preparation procedure frequently employed before ML methods to pick a subset of characteristics that is free from redundancy. It is crucial to prioritize the selection of traits that exhibit strong correlations compared to other characteristics to enhance the precision of predictions and get a more profound comprehension of data in various AI approaches. This suggests that if the two qualities are highly associated, only one adequately and accurately describes the information. The number of individual combinations of features for a feature vector of dimension N is 2^N, representing a vast and challenging space to be thoroughly investigated. Hence, directly assessing becomes difficult as the number of characteristics increases. A vast space for searching significantly challenges the process of feature selection. Metaheuristic methods are extensively employed to address feature choice challenges. PSO is utilized to identify the essential characteristics and dynamically explore a feature space to select the optimal subset of characteristics. The optimal solution should optimize the accuracy of the desired feature while minimizing the categorization error ratio. It should choose the fewest characteristics possible.

3.4 Evaluation of the AI model

The AI algorithm's precision is assessed by applying the logarithmic loss ratio to each drug-annotation combination. The model is evaluated using the average log loss calculated for each column. The task is to forecast the likelihood of a positive reaction for each goal, given the specimen ID. A good response indicates that medicine is classified inside a particular drug class, often known as the target. A lower log loss value suggests more precision.

The mathematical expression for assessing the AI system is presented as

$$S = \frac{1}{-N}\sum_{x=0}^{N-1}\frac{1}{M}\sum_{y=0}^{M-1}\left(o_{y,x}\log\left(o_{y,x}\right) + \left(1 - o_{y,x}\right)\log\left(1 - o_{y,x}\right)\right) \quad (4)$$

where: M is the total number of sampling ID occurrences in the test information, denoted by i = 1,2,...,M. N represents the total count of objectives that have been scored, with each target being denoted by a number x ranging from 1 to N. $\hat{o}$ is the estimated likelihood of observing a positive reaction for a given sampling ID. The variable $o_{y,x}$ represents the ground reality, with 1 indicating a positive reaction and 0 indicating otherwise. The log() function represents the logarithm with base e, known as the basic logarithm.

4. Simulation Results and Outcomes

This study used 10-fold cross-validation for SVM and PSO to mitigate any bias in testing and training collections. It is contrasted with eight other widely recognized methods to assess the effectiveness of the suggested AI-D3S method. The procedures were constructed using Matlab, and thoroughly documented research was conducted to provide results. Specifically, the techniques were combined with two widely recognized AI classifications in the field of research, namely PSO and SVM. The study utilized two chemical databases, namely MAO and Biodegradation. Every algorithm was executed 30 times using 30 agents and 100, 500, and 1000 repetitions, respectively.

The tests are conducted using a computer equipped with an Intel Core i5 CPU running at a clock speed of 2.4 GHz, 6.00 GB of RAM, running on the Windows 10 operating system, and utilizing Matlab 2013a software. The specifications of all evaluated methods have been set in the following order: the number of searching actors is 35, the problem size is 1600, the number of repetitions is 10, and the number of trials is not specified. The fitness algorithm has a parameter k_1 with a value of 0.98 and a parameter k_2 with a value of 0.02. The lower limit of the function is 0, while its maximum value is 1.

Figure 5 displays the accuracy analysis of drug design and discovery methods. The AI-D3S approach has superior accuracy to alternative methods, achieving a result of 89.7%. The AI-driven approach enhances the design and development of pharmaceuticals. It minimizes process errors, resulting in cost reduction for the design process. The AI-D3S approach exhibits an average improvement of 8.7% compared to other methods.

Figure 6 displays the precision analysis of drug design and discovery systems. The AI-D3S findings are compared to current models such as Convolutional Neural Network (CNN), Deep Neural Network (DNN), Support Vector Machine (SVM),

Principal Component Analysis (PCA), Random Forest (RF), Naïve Bayes (NB), and Particle Swarm Optimization (PSO). The AI-D3S model surpasses all other approaches by 7.83% in terms of accuracy, achieving an average accuracy of 90.4% with the assistance of AI techniques.

Figure 7 depicts the sensitivity analysis of drug design and discovery systems. The AI-D3S system surpasses all other approaches by 7.92% in terms of sensitivity for identifying and developing novel pharmaceuticals through AI techniques. The medicine was developed using several machine learning techniques, and the results demonstrate the efficacy of the proposed AI-D3S with a success rate of 90.3%.

Figure 8 demonstrates the specificity analysis of various drug design and discovery systems. The AI-D3S method surpasses all other methods by achieving a specificity of 7.83% in drug discovery and design. On average, the proposed method yields results of 89.5%, reducing overall design expenses and lowering the cost of drugs, making them more accessible to the general population.

Figure 9 compares various approaches to examine Mean Squared Error (MSE) for drug design and discovery systems. The MSE of the proposed AI-D3S is 4.7% lower than previous models. The AI facilitates the discovery and formulation of novel pharmaceutical compounds. Using AI techniques enhances the efficiency of analyzing chemical compounds, hence streamlining the process of developing and finding new chemicals.

5. Conclusion and Future Scope

The progress of AI, accompanied by its impressive tools, consistently strives to diminish the obstacles encountered by pharmaceutical firms, influencing both the medication manufacturing procedure and the entire lifespan. This might elucidate the rise in the number of start-ups in this industry. The healthcare industry is grappling with intricate difficulties, including rising medication and therapy costs. Society requires targeted and substantial reforms in this domain. Incorporating AI into pharmaceutical production makes it possible to produce personalized drugs tailored to meet specific patient requirements, including particular dosages, release variables, and other necessary factors. Employing state-of-the-art AI methods will expedite product development, enhance the safety and quality of goods, optimize the utilization of resources, and reduce costs, thereby elevating the significance of robotics. The research proposes an AI-based Drug Design and Discovery System (AI-D3S) to design and discover the drug process. AI can facilitate the rapid and effortless discovery of hit compounds and provide recommendations for the synthesis pathways of these compounds. AI can anticipate the required chemical composition and enhance the knowledge of drug-target and structure-activity relationships. AI can also significantly contribute to integrating the generated drug into its appropriate dosage form and optimizing it. AI can assist with arriving at quick decisions, resulting in faster production of higher-quality products and ensuring consistency from one batch to another. AI also aids in determining the security and efficacy of the item during research studies, as well as assuring accurate market position and pricing through comprehensive market research and forecasts. While no AI-based pharmaceuticals are available in the marketplace, and some problems need to be addressed to adopt this innovation successfully, AI will grow into an indispensable tool in the pharmaceutical sector in the following years.

Author contribution

D.R.P., S.S.D., A.M. wrote, reviewed and edited the article. All authors read and approved for publication.

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Competing financial interests

The authors have no conflict of interest.

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