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AI ASSISTS IN DRUG DISCOVERY AND DRUG DELIVERY SYSTEMS.

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Abstract:

Artificial Intelligence (AI) has emerged as a powerful tool in various domains, and the field of drug discovery and drug delivery is no exception. This review article aims to provide an overview of the applications of AI in drug discovery and delivery and explore its future prospects. The article begins by introducing the fundamental concepts of AI. Furthermore, the article discusses the AI-powered software or tools including for drug discovery, in nanotechnology and in drug formulation and delivery. Finally, the article presents the future prospects of AI in drug discovery and drug delivery systems.

Keywords: AI in drug discovery, AI in drug delivery systems, and AI-powered software or tools.

Introduction:

Artificial intelligence is a discipline of computer science that focuses primarily on creating machines capable of doing activities that would otherwise require human expertise and input. The rapidly expanding subject of artificial intelligence (AI) is revolutionizing several industries, including healthcare. In recent years, the use of artificial intelligence (AI) in medicine delivery systems has yielded promising outcomes. The term "A.I." was initially coined by John McCarthy in 1956. Artificial intelligence can be utilized to develop innovative medications. The application of artificial intelligence in formulation development is critical. In the field of medication administration, a range of artificial network types, including deep and neural networks, are used.[1] Artificial intelligence (AI) is a branch of computer science that is only focused on developing machines capable of executing tasks. AI has streamlined and impacted the pharmaceutical sector in a various ways, including the development of new and improved therapies as well as the fight against rapidly spreading diseases.

The algorithms, which are a collection of rules to follow when using computing equipment to perform computations or solve issues, are critical in developing the AI architecture.[2] AI applications in the drug development pipeline include drug development methods and processes, pharmaceutical R&D efficiency and

attrition, and collaborations between AI and pharmaceutical companies.[3] Although there are many advantages to using AI in drug discovery, there are drawbacks as well.[4] Among the algorithms utilized in the drug design and discovery process are artificial neural networks, deep neural networks, support vector algorithms for classification and regression, generative adversarial networks, symbolic learning, and meta-learning. The classification of active and inactive, drug release monitoring, pre-clinical and clinical development, primary and secondary drug screening, biomarker development, pharmaceutical manufacturing, physiochemical property and bioactivity identification, toxicity prediction, mode of action identification, and drug formulation development have all benefited from the application of artificial intelligence principles.[5]

AI in drug discovery:

The average cost of the medication discovery and development process is US$2.8 billion, and it can take more than ten years. Despite this, nine out of ten medicinal compounds do not pass regulatory approval or Phase II clinical trials. algorithms like extreme learning machines, and nearest-neighbour classifiers. A number of biopharmaceutical firms, including Bayer, Roche, and Pfizer, have partnered with IT firms to create a platform for the development of treatments in fields including cardiology and immuno-oncology. Furthermore, in order to find novel pathways and predictive biomarkers for personalized medical methods, AI algorithms can handle not only traditional biological data but other aspects like electronic health records, patient demographics, and clinical trial data. It offers a cohesive and all-encompassing therapeutic approach that helps address missed goals that can be achieved by conventional means and provides patients with individualized treatments based on their unique genetic composition and other disease-affecting elements.[4,6]

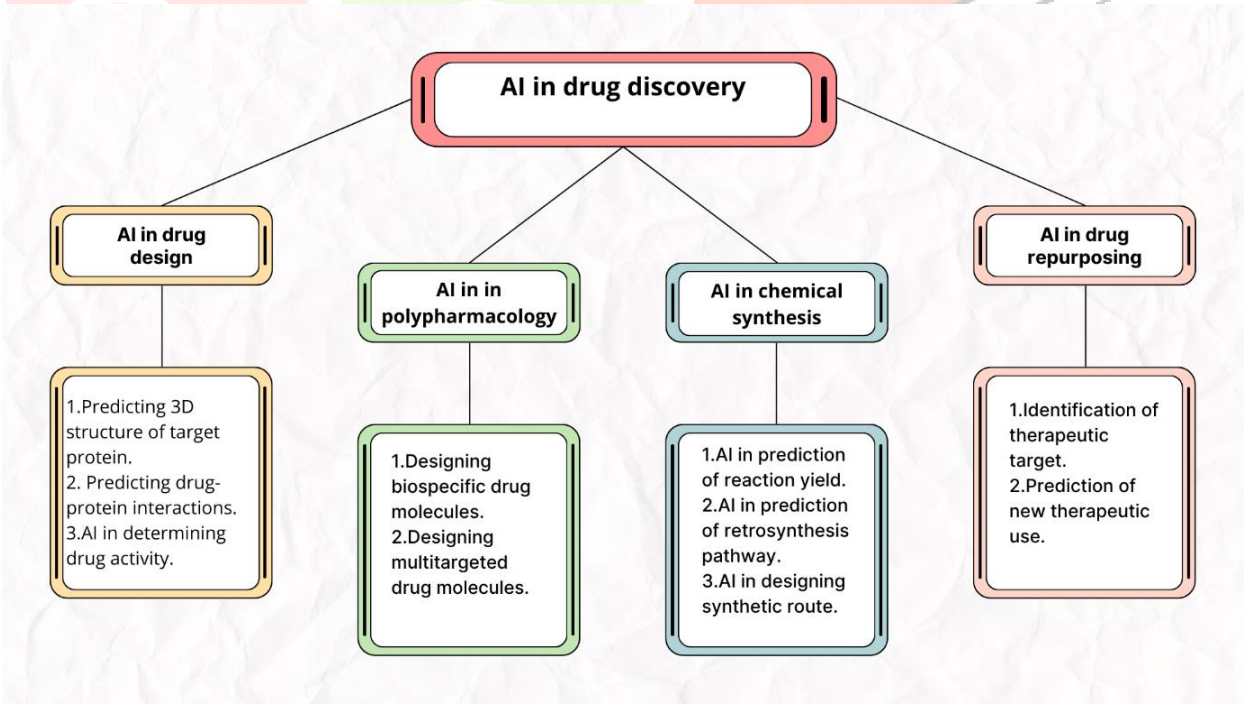

fig.1: AI in drug discovery

AI in designing drug molecules:

Prediction of the target protein structure:

The right target must be chosen when creating a therapeutic molecule in order for treatment to be effective. Numerous proteins are involved in the development of the disease and, in some cases, they are overexpressed. Therefore, in order to create a therapeutic molecule that selectively targets disease, it is essential to anticipate the structure of the target protein. Because the 3D protein structure is designed to fit the target protein site's chemical environment, AI can help with structure-based drug discovery by predicting the compound's effect on the target and safety considerations prior to synthesis or production.[7]

In order to predict the 3D target protein structure, the AI tool AlphaFold—which is based on deep neural networks (DNNs)—analyzed the distance between neighboring amino acids and the related angles of the peptide bonds. It showed great results by correctly predicting 25 out of 43 structures. Recurrent neural networks (RNN) was used to predict the protein structure in a study by AlQurashi. Three stages—computation, geometry, and assessment—were examined by the author and referred to as a recurrent geometric network (RGN). The torsional angles for a specific residue and a partially completed backbone that were obtained from the geometric unit upstream of this were then taken into consideration as input and provided a new backbone as output. In this case, the primary protein sequence was encoded.

The result of the last unit was the 3D structure. The distance-based root mean square deviation (dRMSD) metric was used to evaluate the difference between the experimental and predicted structures. To maintain a low dRMSD between the experimental and predicted structures, the RGN parameters were modified.[8] When it came to protein structure prediction, AlQurashi anticipated that his AI approach would be faster than AlphaFold. When it comes to predicting protein structures with sequences that resemble the reference structures, AlphaFold is probably more accurate. [9]

Predicting drug–protein interactions:

AI's capacity to forecast drug-target interactions has also been applied to help repurpose current medications and get clear of polypharmacology. When an existing medication is repurposed, it becomes eligible for Phase II clinical trials.[10] This also saves money because it costs US$8.4 million to relaunch an existing drug, whereas it costs US$41.3 million to launch a new medicinal entity.[11] The novel relationship between a medicine and an illness, which can be either a knowledge-based or computationally driven network, can be predicted using the "guilt by association" technique.[12] The machine learning (ML) methodology, which makes use of methods like support vector machines (SVM),neural network (NN), logistic regression, and deep learning (DL), is popular in computationally driven networks. When repurposing a medicine, logistic regression platforms like PREDICT, SPACE, and other machine learning techniques take into account factors including drug-drug and disease-disease similarity, target molecule similarity, chemical structure, and gene expression profiles.[13]

In a recent study, deep neural network (DNN) was used to repurpose existing medications with demonstrated effectiveness against SARS-CoV, HIV, influenza virus, and pharmaceuticals that are 3C-like protease inhibitors. The AI platform was trained using extended connectivity fingerprints (ECFP), functional-class fingerprints (FCFPs), and an octanol-water partition coefficient (ALogP_count). Based on their cytotoxicity and viral inhibition, the results showed that 13 of the evaluated medications might move forward with additional research.[14]

AI in drug delivery systems:

AI has been crucial to the advancement and improvement of medication delivery systems. Conventional dosage form-based drug delivery, modified release-based drug delivery, microsystem-based drug delivery, and nanosystem-based drug delivery are among the various types of drug delivery systems covered in this article. conventional drugs delivery methods, such as tablets, capsules, and emulsions. AI applications for matrix tablets, implants, suppositories, and other devices are included in modified release-based drug delivery. Systems like beads, microspheres, and microparticles are examples of AI applications in the field of microsystem-based drug delivery. AI and ML have been used in the field of nanosystem-based drug delivery in the context of nanosuspensions, nanoparticles, and nanorobots. Fig.2 shows several drug delivery systems that make use of machine learning and artificial intelligence.

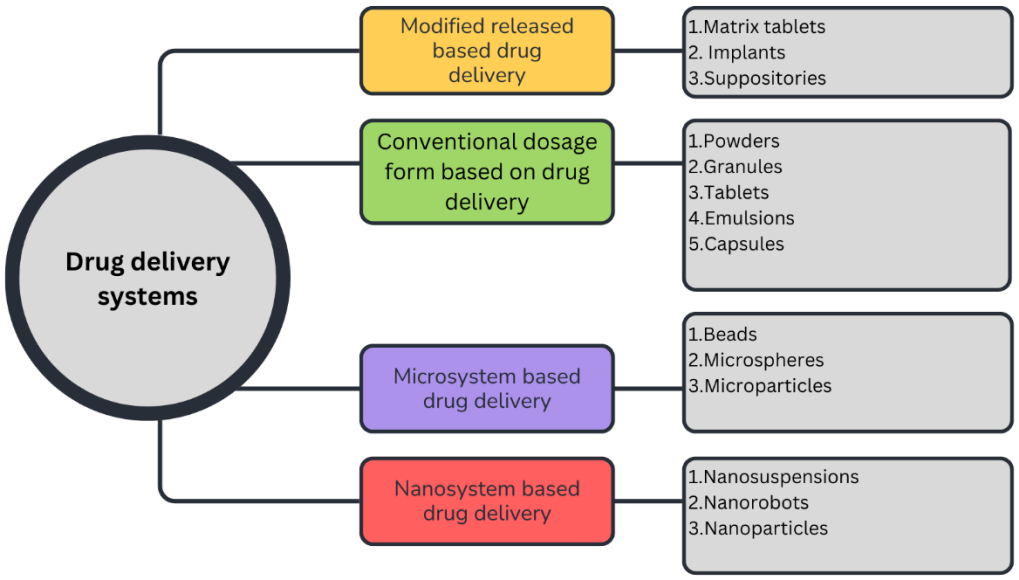

fig.2: AI in drug delivery systems

Modified Release-based Drug Delivery:

Matrix Tablets

In order to model the dissolving profiles of different matrix tablets, both static and dynamic artificial neural networks (ANNs) have been employed in matrix tablet design. In this work, Monte Carlo simulations and the genetic algorithm optimizer tool were used for these ANN-based modelling. To precisely predict the dissolution

properties of hydrophilic and lipid-based matrix tablets with regulated drug release patterns, the researcher used Elman dynamic neural networks and decision trees. Unlike most often used MLP and static networks, the Elman neural networks-based modelling demonstrated the successful modelling of medication releasing patterns by different formulations of hydrophilic as well as lipid-based matrix tablets. [15]

Galata et al. assessed the prediction of the dissolving profiles of hydrophilic matrix sustained-release tablets using three AI systems. In this work, ANN, Ensemble of Regression Trees, and SVM were used for data analysis and dissolution profile prediction. A database for modelling was also created by combining the output data from Process Analytical Technology (PAT) and Critical Material Attributes (CMAs). According to the findings, one of the most crucial elements for the model's prediction was the particle size distribution (PSD). ANN was also found to be the best accurate model out of all of them based on the evaluation metrics.[16]

Implants:

An artificial neural network (ANN) model was used to forecast the formulation parameters and the dexamethasone release profile from the cochlear implant coatings. To produce the best possible medication release profile, the ANN model's capacity to determine the optimal formulation parameter levels was evaluated. In addition to speeding up the formulation design process, the ANN model accurately modelled the drug release profile from the implant device. The results were comparable to those obtained experimentally, indicating the efficacy of the model.[17]

Suppositories

An ANN technique, together with modelling and simulation of the compartment-based models, has been used to assess the differences between the slower and faster release of paracetamol from the layered excipient suppositories. It has been found that the absorption-increasing effect of mono-di-glycerides and the hepatic bypass mechanism combine to boost the degree of medication absorption.[18]

Conventional Dosage form-based Drug Delivery:

Pharmaceutical Powders:

Farizhanidi et al. studied using machine learning (ML) to create an inhalation-based dry powder carrier. 65 datasets, each containing three carriers and three medications, were used for the analysis. Critical Material Attributes (CMAs) and quantitative factors like mean polar facet orientation (FPO), skewness of the assessed profile (Rsk), and root mean square deviation (Rq) were among the scanning electron microscopy (SEM) images used as the database's input variables. The outputs used were the emitted dose (ED) and the fine particle fraction (FPF). For modelling, a feed-forward ANN model was built. Fifty subsets of the database were used for training, and fifteen subsets were used for testing. The accuracy of the model was proved by its R2 values of 0.9820 and 0.9556 for FPF and ED, respectively. This marked a significant improvement over empirical modelling. The feasibility of using AI technologies to develop dry powder inhalation products was demonstrated by this study.[19-29]

Granules:

Zhao et al. examined the assessment and forecasting of drug concentrations in sugar-free granules using AI techniques. This work was the first to demonstrate that the amount of medication in granules could be measured using near-infrared (NIR) spectroscopy. The NIR spectra were then used to anticipate the remaining medication using a number of machine learning approaches. The last three AI techniques that were optimized for modelling development were the evolutionary algorithm, particle swarm optimization (SVM), and backpropagation artificial neural networks (ANN). The results demonstrated that AI models are practical instruments for determining the concentration of medications in granules.[30]

Tablet:

Ma et al. looked into Convolutional neural networks (CNN)s' potential for detecting internal tablet flaws. For this study, different batches of tablets with excipients such mannitol and microcrystalline cellulose were produced. The tablets were then imaged using an X-Ray Computed Tomography (XRCT) machine to process the images. The number of photographs increased from 573 to 43,548 using a picture augmentation technique. Three CNN modules were used for the picture analysis: (1) UNet A, which extracts the tablets from the bottle; (2) Module 2, which does an automated analysis to identify individual tablets; and (3) UNet B, which measures internal cracks in tablets. During the model testing, the UNet neural network showed up to 94% accuracy for seven batches of tablets. Furthermore, this CNN technique could significantly save time, workload, and cost while also aiding in the discovery of defects in other products.[31]

Emulsion:

ANNs have also been employed to develop stable oil-in-water emulsion formulations. The concentrations of lauryl alcohol and time were the unreliable variables (factors) in the optimization of the fatty alcohol concentration to produce oil/water emulsions. The variables that yielded reliable results were droplet size, zeta potential, conductance, and viscosity. Validation testing revealed a significant correlation between the experiment's outcomes and the values predicted by the ANN. An artificial neural network (ANN) model was created to forecast stable microemulsion formulations, such as isoniazid and rifampicin, for oral administration. The ANN model was trained, tested, and validated using data from many pseudo ternary phase triangles that contained a combination of oil and surfactant components.[32,33]

Capsule:

Zhou et al. demonstrated that it is feasible to detect capsule flaws using an enhanced CNN. Handmade capsules with a variety of flaws, including shrivelled, locked, or nested capsules, perforations, concave heads, uncut bodies, and oil stains, were employed in this study. The improved CNN's L2 regularization and Adam optimizer were used to counteract the overfitting of the model. In this work, SVM and K-Nearest Neighbor (KNN) were also employed for comparison. The confusion matrix results showed that our enhanced CNN model could detect capsule flaws with an accuracy of up to 97.56%.[34]

Microsystem-based Drug Delivery:

Microspheres:

ANN and Response Surface Methodology (RSM) were used to optimize alginate-based floating aspirin microspheres, and measurements were made of the excipient ingredient amounts, drug release, and microsphere buoyancy. The in vitro aspirin release pattern was better predicted by the ANN model than by the RSM model.[35]

Microparticles:

A coacervation procedure was used to make benznidazole chitosan microparticles, and an ANN model was used to improve the formulation and go past the dissolution rate-limiting stage. Several optimization strategies were employed in order to attain the maximum yield, best encapsulation efficiency, fastest dissolution rate, and smallest size. There was good agreement between the ANN-predicted optimum values and the experimental outcomes.[36]

Nanosystem-based Drug Delivery:

Nanosuspension:

The process of creating a methotrexate nanosuspension based on acid-base neutralization was examined computationally using the structural and electrical properties of single methotrexate molecules and molecular clusters. Quantum chemistry and molecular frontier orbital calculations are essential for reorganizing the reactivity and transport properties of molecules by identifying the acceptors or donors of their electron area. According to the computational studies, the higher interaction energies between methotrexate molecules are what drive aggregation in the cationic and zwitterionic states of clusters and vice versa.[37]

Nanoparticles:

To produce biodegradable nanoparticles of the triblock poly(lactide)-poly(ethylene glycol)-poly(lactide) copolymer as drug carriers, an artificial neural network (ANN) model has been developed to identify the factors influencing the nanoparticle size. A three-layer feedforward backpropagation artificial neural network (ANN) was utilized to model the formation of nanoparticles.[38]

To investigate the effects of formulation factors and optimize the formulation of polymer-lipid hybrid nanoparticles for controlled administration of verapamil hydro chloride, modelling and optimization were conducted based on the spherical central composite design. By contrasting the predictive performance of ANN models and RSM, it was possible to identify the enhanced generalization and recognition capabilities of ANNs.[39]

Nano Robots:

Computational technologies such as artificial intelligence (AI) maintain the fundamental components of nanorobots, which include integrated circuits, sensors, a power source, and a safe data backup. They are designed to stay out of collisions, recognize objects, locate and cling to them, and ultimately expel them from the body. Advances in nano/microrobot technology allow them to reach the intended location based on physiological characteristics, like pH, increasing efficacy and reducing adverse systemic effects.[40] Developing implantable nanorobots for the controlled delivery of drugs and genes requires taking into account factors like dose adjustment, sustained release, and regulated release. The release of the drugs requires automation controlled by AI tools like ANNs, fuzzy logic, and integrators. AI can affect the movement and behaviour of nanorobots.[41,42]

AI-powered software or tool :

Table 1. AI-powered software or tool

For drug discovery	In nanotechnology	For drug formulation and delivery
1.DeepMind's AlphaFold	1. Nanomine	1. Alphafold
2. Insilico Medicine	2.SimuTech Group (AI-Enhanced Simulation Tools)	2.Simulations Plus (ADMET Predictor)
3. Schrödinger	3. Materials Studio (by BIOVIA)	3.Pharmalex
4. Exscientia	4. DeepNano	4.Formulatrix (Formulation and Automation Tools)

For drug discovery:

In a study to develop a medication for the lung disease idiopathic pulmonary fibrosis (IPF), Insilico verified the end-to-end discovery capabilities of its AI platform. In order to predict tissue-specific fibrosis, Insilico trained its deep neural network on omics and clinical datasets, expanding on an initial theory. As a result of this work, targets were found using de novo route reconstruction, causality inference, and deep feature selection using Insilico's PandaOmics target discovery technology. Insilico analyzed data sources such as patents, research articles, and clinical trial databases using a natural language processing engine to evaluate the targets' uniqueness and illness relationship. After 20 targets were identified for validation, Insilico selected the most

promising one. The selected novel intracellular target was subjected to Insilico's generative chemistry drug discovery platform, Chemistry42.

The platform creates hit compounds from scratch using scoring and generative engines. Every molecule produced by Chemistry42 has appropriate physicochemical characteristics and a drug-like molecular structure by default. A library of small compounds was produced as a result of applying Chemistry42 to the unique target identified by PandaOmics.[43] According to reports, DSP-1181 is the first AI-generated medication of this kind to go through clinical trials. In contrast to four years using traditional procedures, Exscientia, which developed DSP-1181 in collaboration with Sumitomo Dainippon Pharma of Japan, reported that it had taken less than 12 months from first screening to the conclusion of preclinical testing (Sumitomo Dainippon Pharma 2020). Optimizing AI in the pharmaceutical business has made a remarkable effect in accelerating the discovery of new drugs. DSP-1181's creators declared that the medication has started a Phase I clinical trial to treat obsessive-compulsive disorder (OCD). Anxiety disorders include OCD.[44]

In nanotechnology:

The ultimate goal should be to create new materials using a material data repository and related analysis and simulation components. A user can do material design to achieve desired nanocomposite qualities and anticipate properties for certain constituent/processing combinations using the database and analysis tools offered by NanoMine. Assume that the user wants to forecast the dielectric permittivity of a nanocomposite material packed with nanosilica and epoxy. Prior to using the embedded heuristic tools of Materials Quantitative Structure-Property Relationship (MQSPR) to predict pertinent surface energies, the first step involves using curated data to query the database for existing data of polymer and particle properties as material property input to the finite element analysis (FEA) model. The data will be processed using the following two subprocesses: (1) microstructure and (2) interphase. The 3D Reconstruction tool is used to create a 3D morphology that is fed to the FEA model after processing parameters from the extrusion processes and the constituent surface energies are associated to descriptors using statistical correlations. Local interphase parameters are obtained for the interphase input using an energy-interphase correlation (Interphase Tool), and these are subsequently entered into the FEA model. The dielectric spectroscopy corresponding to the chosen polymer, particle, and surface treatments is then calculated using the FEA simulation.[45]

For drug formulation and delivery:

By using innovative neural network topologies and training methods based on the geometric, physical, and evolutionary constraints of protein structures, AlphaFold significantly increases the accuracy of structure prediction. Specifically, we provide a novel architecture that allows for accurate end-to-end structure prediction by jointly embedding multiple sequence alignments (MSAs) and pairwise features, as well as a new output format and related loss.[46]

Significance and future outcomes:

The application of artificial intelligence tools and techniques has been examined at every step of the drug development process, from the identification of a novel molecule to the administration of its clinical trials, followed by manufacturing, features of quality control, and product management. Along with playing a significant role in the improvement of the current formulations, AI has also accelerated the development of various drug delivery methods. AI has been taking a promising and well-known approach to formulation development and optimization, even though it has the potential to completely change the drug development process. An AI-based development approach tends to speed up the development process in a relatively efficient, timely, cost-effective, and highly optimized manner, in contrast to the traditional trial-and-error method of drug delivery system development, which consumes a lot of time, money, and effort.[2]

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