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INTEGRATION OF ARTIFICIAL INTELLIGENCE IN DRUG DISCOVERY AND DEVELOPMENT

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Abstract:This study compares the drug development process with non-integrated AI drug discovery, concentrating on medications such as Bexion, Halicin, and DSP-1181. The study analyzes 500 academic publications on AI-enabled medication development and discovery using VOSviewer. The findings demonstrate the superiority of AI over non-integrated techniques in terms of finding novel therapeutic targets, cutting costs and development time, and increasing the effectiveness of clinical trials. The study is published under the Creative Commons Attribution-NonCommercial-Share Alike 4.0 License and is available to the public.

The process of developing new drugs is costly, time-consuming, and fraught with failure. Artificial intelligence (AI) has become a game-changing technology in drug discovery in recent years, providing creative answers to challenging problems facing the pharmaceutical industry. This book addresses the various aspects of AI's involvement in drug discovery, including the creation of new AI approaches, the identification of new medications, and AI-assisted drug delivery design. We examine several AI methodologies, such as deep learning and machine learning, and their uses in drug development, virtual screening, and target identification. This essay also explores the evolution of AI in medicine throughout history, highlighting the technology's significant influence on healthcare. It also discusses AI's function in the representative drug delivery systems.

IndexTerms **- Artificial intelligence, Drug discovery, Drug development, Deep learning, Machine learning**

INTRODUCTION

First, we define some terms related to drug discovery, primarily those related to small molecule design and screening. It should be noted that AI-powered medication repositioning is excluded. This method repurposes current medications or prescription combinations for novel indications. Additionally, target identification i.e, using omics data to determine if a target can be treated is outside the purview and is not included. Instead, we direct the readers to earlier works on target identification using omics data and medication repositioning.

The lack of available medications or the extreme toxicity and/or limited efficacy of currently available medications serve as the driving forces behind the drug discovery endeavor. It is first necessary to generate an underlying hypothesis—which entails target identification and validation that the disease can be treated by activating or inhibiting a target (such as an enzyme, receptor, ion channel, etc). As part of the hit-to-lead phase, lead optimization, and hit discovery processes, comprehensive assays will be carried out for the chosen target in order to identify the hits and eventually the leads (i.e., drug candidates). Clinical trials and preclinical research are subsequently undertaken on the medication candidates. If the medication candidate is approved, it can be introduced to the market as a disease-treating medication.

High-throughput screening (HTS), a hit-finding strategy supported by the advancement of automation and the accessibility of huge chemical libraries, has been suggested since the 1980s to boost the discovery efficiency and speed up the search for small-molecule drugs. Large-scale structure-activity relationship (SAR) datasets, which help build chemical databases like ZINC and PubChem, are a notable product of HTS. Virtual screening, or virtual screening (VS), is the process of searching through huge chemical libraries using a variety of computational algorithms to find potentially active chemicals to test in further in vitro and in vivo studies. Stated differently, structure-based VS aims to identify active compounds by computational methods, leveraging target knowledge (structure-based target) or known active ligands (ligand-based VS) to enhance the likelihood of identifying active molecules.[1]

HISTORY OF AI :

Figure 1: History of AI [5]

RESOURCES AND METHODS FOR AI-BASED DRUG DISCOVERY:

Sources for data

Applying AI to drug discovery requires a high-quality dataset. Technological and high-throughput sequencing advances have accelerated the creation of a number of open-access, free drug discovery databases. These databases speed up the drug discovery process and allow it to move into the big data era. A list of representative databases is provided, together with web links, summaries, and references. Due to lack of space, their applications are not covered in this study. [2]

Representative databases for drug discovery

Database	Website URL	Description	Reference
ChEMBL	https://www.ebi.ac.uk/chembl/	A manually curated database of bioactive molecules with drug-like properties. It gathers chemical, bioactivity, and genomic data to aid the translation of genomic information into effective new drugs.	Mendez et al.
ChemDB	http://cdb.ics.uci.edu	A chemical database that contains nearly 5 million commercially available small molecules, along with their predicted or experimentally determined physicochemical properties.	Chen et al.
COCONUT	https://coconut.naturalproducts.net/	A database that contains 407,270 unique natural products, along with information about their molecular properties and molecular descriptors.	Sorokina et al.
DGIdb	http://www.dgidb.org	A database that provides information on DTI & druggable genomes from over 30 trusted sources.	Freshour et al.
DrugBank	http://www.drugbank.ca	A database of drugs, their targets, 3D structures, and other useful information.	Wishart et al.
DTC	http://drugtargetcommons.fimm.fi/	A crowd-sourcing platform that provides drug-target bioactivity data and classification of targets.	Tang et al.
INPUT	http://cbcb.cdutcm.edu.cn/INPUT/	A network pharmacology platform for traditional Chinese medicine. It contains 29,812 compounds isolated from 4,716 Chinese herbs.	Li et al.
PubChem	https://pubchem.ncbi.nlm.nih.gov/	An open chemistry database that provides information about molecules, such as chemical structures, identifiers, chemical and physical properties, and biological activities.	Kim et al.
SIDER	http://sideeffects.embl.de	A database that provides information on marketed medicines and their recorded adverse reactions.	Campillos et al.
STITCH	http://stitch.embl.de/	A database of known and predicted interactions between chemicals and proteins, including 9,643,763 proteins from 2,031 organisms.	Szklarczyk et al.

Over 2 million compounds with drug-like characteristics are now found in the manually curated database ChEMBL. ChEMBL collects data on the deposited substances' molecular characteristics, toxicity, therapeutic indications, metabolism, excretion, absorption, distribution, and target interactions.[3]

Nearly 5 million commercially available small molecules and their physical characteristics, such as molecular weight, solubility, and rotatable bonds, are listed in the publicly available database ChemDB. Moreover, ChemDB has a number of cheminformatics tools integrated into it, including Smi2Depict, MOLpro, AquaSol, and Reaction Predictor, which make the database easy to utilize for drug development.[4]

A platform specifically designed for online analysis specifically for traditional Chinese medicine is called the Intelligent Network Pharmacology Unique for Traditional Chinese Medicine (INPUT).13 Currently gathered from open databases and scholarly sources, INPUT comprises 4,716 plants, 29,812 herbal compounds, and 9,847 illnesses. The network of herbs, chemicals, genes, and diseases in INPUT makes them cross-linked, making it easier to identify medications with a herb focus and to understand traditional Chinese medicine from a scientific standpoint.[2]

Chemical information about molecules, including their properties, properties in the biological, chemical, and hazardous domains, can be found freely on PubChem. These are all collected information from over 850 sources. Molecular formula, structure, and other identifiers can be entered as keywords to conduct a chemical search in PubChem. Nowadays, one of the most important databases for computational drug design and discovery is PubChem.

Machine learning methods to drug discovery

Using ML techniques to their full potential and gathering pharmacological data, AI innovation is given top attention in drug discovery. Artificial intelligence (AI) is primarily useful in turning medical data into research like reusable techniques; it does not depend on any hypothetical advancements. Generally speaking, ML is related to various methodologies such as Random Forest, Naive Bayesian Classification (NBC), Multiple Linear Regression (MLR), Logistic Regression (LR), Linear Discriminant Analysis (LDA), Probabilistic Neural Networks (PNN), Multi-Layer Perceptron (MLP), Support Vector Machine (SVM), etc (Lavecchia and Di Giovanni 2013). Specifically, AI breakthroughs are applied as a deep learning technique towards medication creation to gain proficiency in feature extraction and feature generalization.[7]

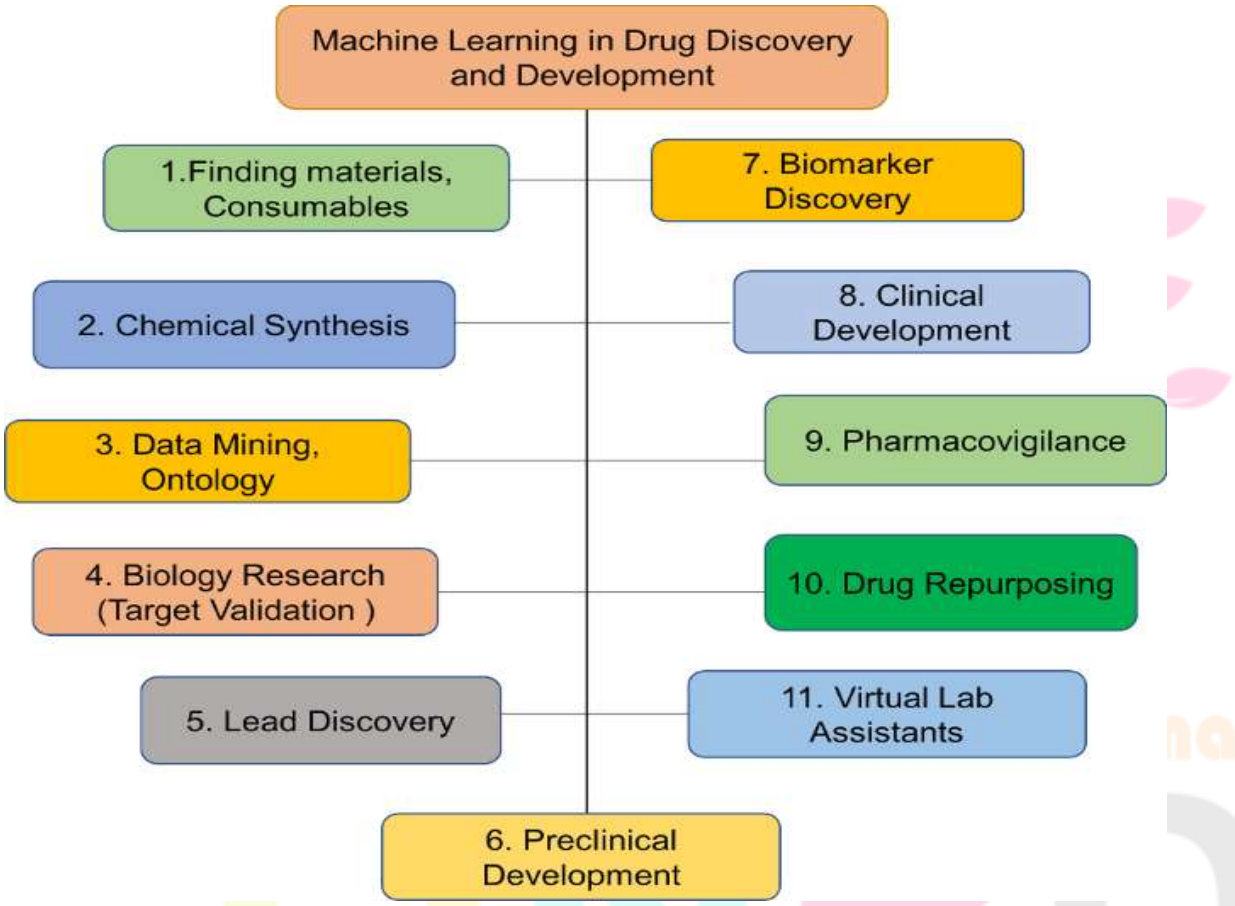

Figure 2: ML in Drug Discovery & Development [8]

Deep Learning (DL) Methods

In almost every scientific and technological discipline, deep learning algorithms are regarded as one of the most innovative topics for research and development. One of the main pillars of deep learning (DL) and the ongoing success that AI-based integration of conventional approaches brings is the rebirth of artificial neural networks (ANNs) into viable algorithms from their previous postulated and expected applications, initially conceived in the 1950s. Computational models can learn an abstraction of multidimensional data with DL methods.[6]

In order to build systems that are capable of completing sophisticated data recognition, interpretation, and production, the foundations of deep learning are frequently involved with neural networks (NNs). Three primary artificial neural network subsets are now being employed in drug discovery: convolutional neural networks (CNNs), recurrent neural networks (RNNs), and deep neural networks (DNNs).

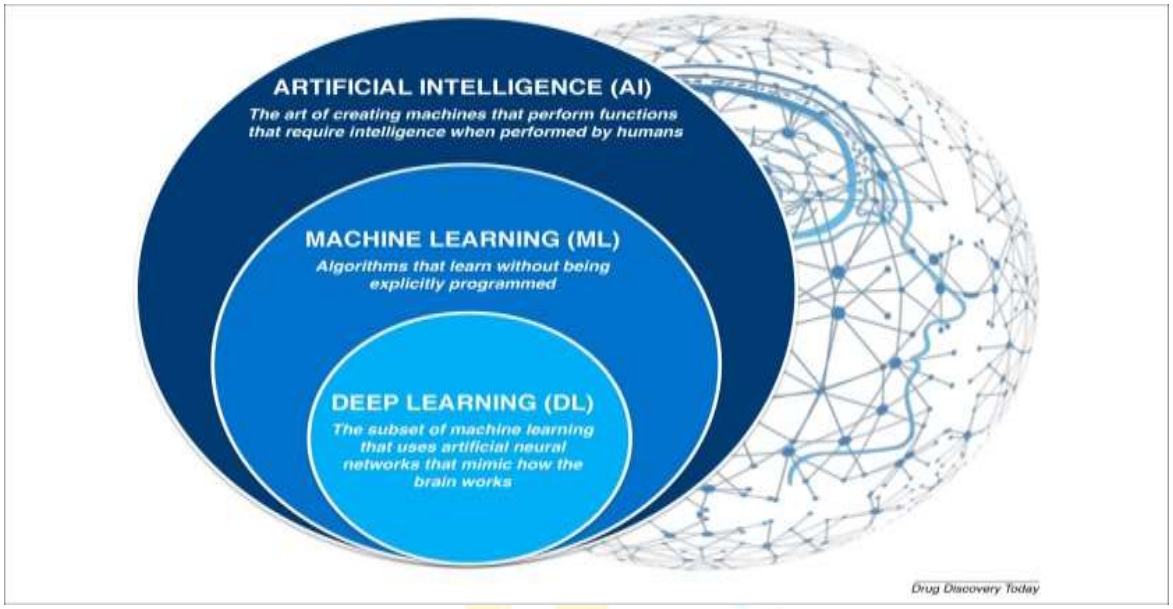

Figure 3: DL in Drug Discovery & Development [9]

AI IN DRUG DEVELOPMENT:

Pre-clinical testing through clinical trials is the first of two main stages in the development of new drugs; the second is submitting the product for regulatory approval. Artificial Intelligence has been incorporated into the development stages more recently. Its main purpose is to facilitate the gathering, organizing, and analyzing of "big data" in order to enhance trial performance and gain regulatory approval. In order to conduct clinical trials, test sites and staff must be identified and evaluated. These criteria include having access to a sufficient number of trial participants, clinical competency, administrative and technical support that can meet performance standards, and the ability to identify potential trial participants from clinical records.

Artificial intelligence (AI) techniques are being used to screen possible sites for their past compliance with enrollment requirements, evaluate electronic health records to find possible participants who fit the trial's inclusion/exclusion requirements, and integrate real-world data that might enhance trial performance. Machine learning technologies have been necessary more recently due to the integration of digital health monitoring into clinical trial protocols and the requirement for sophisticated data processing. AI is also able to recognize early warning signs of possible unfavorable events and dynamically indicate participant status. Submission of data to regulatory bodies is subject to stringent rules and procedures that are constantly being updated to incorporate real-world facts and data from digital monitoring systems.

Adhering to stringent protocols and procedures, regulatory submissions are incorporating real-world evidence and data from digital monitoring systems. As previously said in this article, the usage of real-world data may also need the integration of various data sources with ontologies or knowledge graphs.[10]

FUTURE SCOPE OF AI IN DRUG DISCOVERY & DEVELOPMENT:

AI in research and science

In science, artificial intelligence is advancing rapidly. Compared to human thinking, artificial intelligence is capable of handling enormous amounts of data and processing it more quickly. Because of this, it is ideal for research involving sources with large amounts of data. In this area, AI is already making strides.

AI in cybersecurity

Another industry that is gaining from AI is cyber security. The risk posed by hackers is growing as more businesses move their data to cloud and IT networks.

AI in data analysis

AI and ML have a lot to offer data analysis. AI algorithms have the capacity to get better through repetition, which increases their accuracy and precision. Large dataset handling and processing can be aided by AI for data analysts.

AI in transport

AI has been used in the transportation industry for many years. Since 1912, autopilot has been used to guide aircraft in the air. Although autopilots are only used in airplanes, they can also be used in other types of vehicles. Autopilot is another tool used by spaceships and ships to assist them stay on course.

AI in home

AI has made a unique home in people's homes thanks to Smart Home Assistants. Two well-known smart home appliances that allow you to complete a variety of tasks with voice commands are Google Home and Amazon Echo.

AI in health care

The benefits of this technology are also being utilized by the medical industry. Medical professionals and researchers are benefiting greatly from AI.

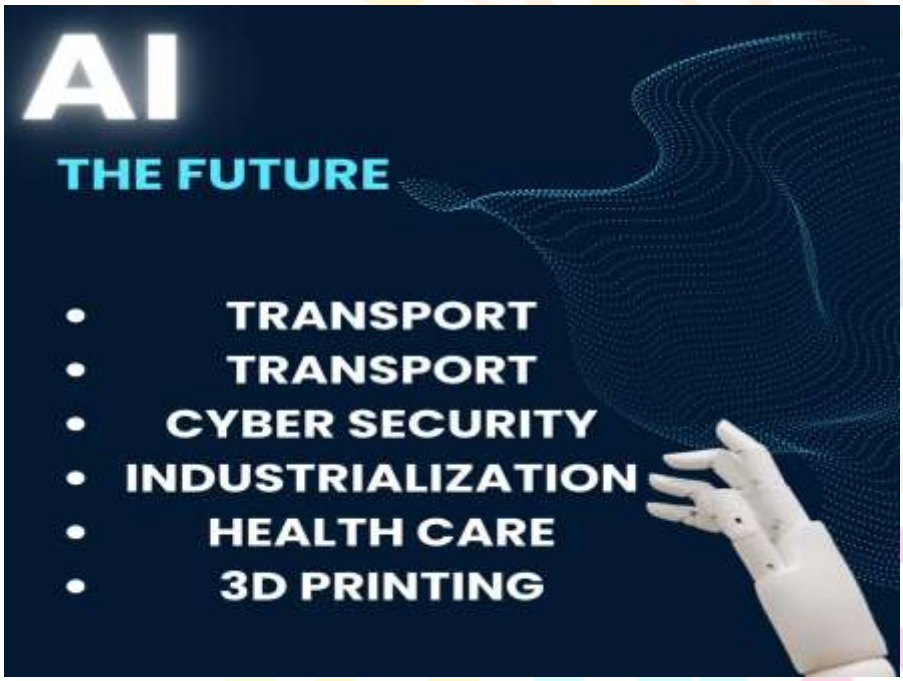

Figure 4: Future of AI[22]

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LIMITATIONS OF AI IN DRUG DISCOVERY & DEVELOPMENT:

Obtaining vast amounts of high-quality data is unquestionably necessary for the successful application of AI techniques in drug research and development. It's possible that the results of AI-derived analysis from inconsistently-quality data won't be repeatable or accurately applicable in clinical settings. Furthermore, information on pharmaceutical companies' drug products including those that fail to receive approval is not generally disclosed. Instead, it is not transparent and full of details. This limits AI's capacity to discover and foresee new innovative agents and targets for medical treatments.

AI presents a logistical barrier to the healthcare and pharmaceutical industries since it requires pricey software, more modern computers, and staff training or recruitment to get comfortable with AI systems. To increase trust and facilitate the efficient use of computer-based algorithms in the pharmaceutical industry, a multidisciplinary approach to education should include AI professionals, clinical staff, pharmaceutical

management, and patients. To guarantee that AI integration maintains drug discovery standards, new legal and regulatory frameworks must be created. This includes potential ethical problems that could occur when utilizing AI if patient data is disclosed excessively or if the right kind of consent is not obtained. Last but not least, patients with uncommon diseases may be susceptible to treatment bias, a situation in which the subpopulation with the illness has insufficient knowledge to make predictions.[20]

APPLICATIONS OF ARTIFICIAL INTELLIGENCE IN DRUG DISCOVERY & DEVELOPMENT:

A study by José Jiménez-Luna et al. examined the use of AI-assisted computational models in De Novo drug design and ligand-based quantitative structure-activity and property (QSAR/QSPR) drug discovery. Utilizing molecular descriptors to provide machine-readable numbers that are representative of the structural characteristics of molecules, such as functional groups, pharmacophore distribution, and physicochemical properties, has proven successful in the prediction of pharmacokinetic parameters and biological activity in the context of QSAR/QSPR. It is difficult to create novel molecular profiles with appropriate pharmacological potency and attributes using computer-assisted de novo drug design; the most well-known method is ligand and/or structure-based design. With speedier drug target validation, artificial intelligence (AI) can find hit and lead compounds and help forecast the three-dimensional structure of the targeted protein**.**
PDB bind is a database that offers details on the structure of protein-ligand complexes. Combining artificial intelligence (AI) and machine learning (ML) with knowledge of single-cell biology can produce hitherto unheard-of results in drug discovery and development, including improved biomarker prediction and the identification of drug candidates with high-quality and disease-associated targets. Using a unique translational platform of Drug Intelligence Science (DIS) that blends AI/ML with single-cell technologies, HiFiBiO Therapeutics has developed this capability.

AI can improve drug effectiveness and safety by predicting drug metabolism and excretion. This helps in designing novel compounds with enhanced efficacy, pharmacokinetics, and decreased toxicity. AI's utility in predicting medication metabolism and excretion has been demonstrated in recent research, particularly in cancer chemotherapy and infectious illnesses.[11-17]
Ryza Rynazal et al. utilized a local explanatory method to personalize specific bacteria strains as biomarkers for colorectal cancer, suggesting its potential for future personalized treatments.[18]
Sumitomo Dainippon Pharma, in collaboration with ExScientia, developed the first AI-assisted drug molecule, DSP-1181, for obsessive-compulsive disorder in under 12 months, utilizing pharmacology and chemistry expertise for G-PCR drug discovery.[19]

RESULT:

AI, a branch of computer science that focuses on the creation of intelligent machines capable of performing tasks that would typically require human intelligence, has revolutionized various industries. In the field of drug discovery and development, AI has proven to be a valuable tool, enabling scientists to analyze vast amounts of data and make predictions with unprecedented accuracy. One of the most significant contributions of AI in this field is its ability to expedite the process of identifying potential drug targets. Traditionally, this process involved a series of time-consuming experiments and trials. However, with the integration of AI algorithms, researchers can now analyze massive datasets and identify potential drug targets in a fraction of the time. As a result, expenditures are greatly decreased while simultaneously expediting the drug discovery process.

CONCLUSION:

In conclusion, the integration of AI in drug development and discovery has revolutionized the pharmaceutical industry. The ability of AI algorithms to process and analyze vast amounts of data has accelerated the drug discovery process, leading to more efficient and effective treatments. AI can predict drug-drug interactions,

identify potential side effects, and optimize the development of personalized treatments. Furthermore, AI has the potential to reduce costs associated with drug discovery and development. As AI continues to advance, it will undoubtedly play a crucial role in shaping the future of drug development, ultimately benefiting patients worldwide.

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