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Artificial Intelligence In Drug Discovery And Development

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❖ **Abstract –**

Artificial intelligence (AI) focuses on creating intelligent modeling that helps process information, solve problems and make decisions. Artificial intelligence has recently played an important role in several fields of pharmaceuticals such as drug discovery, drug development, polypharmacology, hospital pharmacy, etc. When deep neural networks (DNN) or recurrent neural networks (RNN) are used. Currently, several drug development applications have been analyzed and supported technological performance in quantitative structure-property relationship (QSPR) or Quantitative structure-activity relationship (QSAR). In addition, de novo design significantly contributes to the invention of newer drug molecules with desired/optimal properties. This review article discusses the use of artificial intelligence in pharmacy, particularly in drug discovery, drug product development, polypharmacology and hospital pharmacy.

❖ **Introduction –**

Artificial Intelligence (AI) "is the science and engineering of creating intelligent machines, especially intelligent computer programs. It is about the use of computers as a means to understand intelligence, but artificial intelligence should not be limited to methods that are biologically observable".[1,2] in 1956 Allen Newell\and his colleagues created Logic Theorist, the first\portable software of artificial intelligence.[3] Although the original\goals of artificial intelligence have not yet been fully realized , many AI technologies have become\unaffordable and their use\increases over time. Artificial intelligence technologies are very popular today due to various forms of artificial intelligence various fields, from robotics, speech interpretation, image analysis, etc. A number of innovative\techniques have been developed in the computer. Scientific researchers are trying to make computers intelligent, which some have proven useful in chemistry, biology and medicine. Artificial intelligence is used to design new organic synthetic systems, to understand complex biological systems, to design new APIs or to develop new analytical/ diagnostic devices or methods. AI techniques also apply to drug discovery, drug development, drug reprocessing, drug metabolism prediction, drug toxicity analysis, pharmaceutical productivity improvement, clinical trials, and almost all medical fields. [4] All these technologies are \ listed together below In IDD (Artificial Intelligence Drug Discovery). These

AI techniques are not yet routinely practical for computer aided drug design (CADD), but they are still used to solve complex drug discovery problems. Compared with ligand-based drug design (LBDD) and structure-based drug design (SBDD), AIDS appears. Some books are available that include a discussion of AIDD. [5,6] Initially, AI was used to develop logic programming. Platforms (Prolog[7] LISP[8]) with standard programming languages. Later as part of Machine Learning (ML)[5,9,10] many new methods Knowledge Base Systems (KBS)\such as Artificial Neural Networks (ANN), Support Vector Machines (SVM), Genetic Algorithms (GA), Deep Learning\ n(DL) Fuzzy Systems (FS), pattern recognizers, classifiers, etc. Have been introduced and all have found applications in IDD. [11,12] In the current scenario, AI methods are evolving in addition to the molecular modeling methods of CADD scientists. It seems currently, AIDD-based operations differ from the atomic-level operations provided by molecular modeling methods, but the overlap between these operations increases exponentially. Due to ML Contribution to Drug Discovery (MLDD) [5, 9,10 ,13] increases, the terms AIDD and MLDD\ are not considered synonymous. Machine learning and data mining can be applied to provide many solutions such as –classification, regression, clustering, dimension reduction, learning, deep learning, outlier detection and many others. In addition, several sub-topics of machine Learning are ANN, DNN (Deep Neural Networks), RNN (Recurrent Neural Networks), CNN (Convolutional Neural Networks), GA, SVM, Bayesian Networks, DT (Decision Trees), LR (Logistic Regression), k-NN (k-nearest neighbours'), NB (marine Bayesian) \techniques are also important in CADD.

❖ **Classification of AI –**

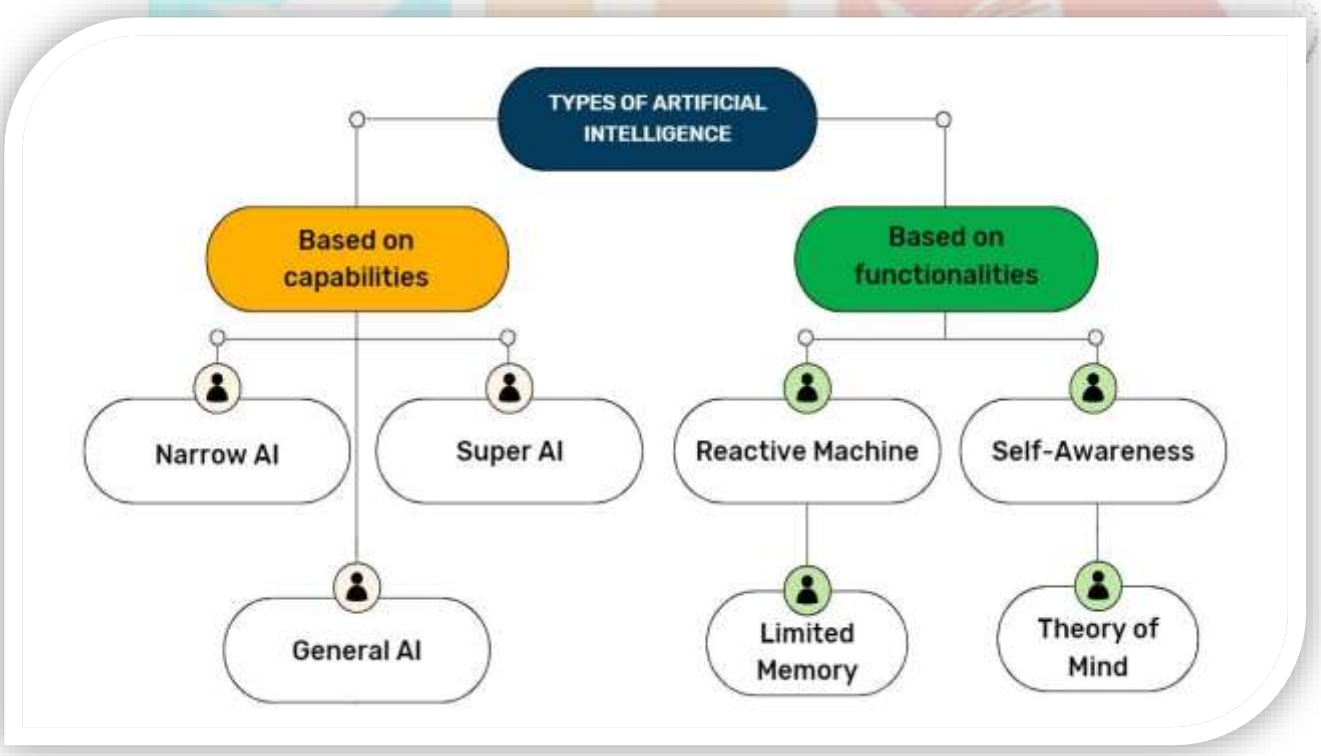

Figure no 1. Types of AI

❖ **Artificial intelligence in Drug Discovery –**

The vast chemical space containing more than 1060 compounds facilitates the synthesis of a large number of pharmacological molecules. On the other hand, the lack of new technology delays the drug development process, making it a time-consuming and expensive task that can be handled by artificial intelligence [14]. AI can identify hit and lead compounds and provide faster drug target validation and drug design optimization [15] Figure illustrates the many uses of artificial intelligence in drug discovery. Despite the benefits, AI has significant data challenges such as data volume, growth, diversity and uncertainty. Conventional algorithms may not be able to handle data sets available to pharmaceutical organizations for drug development, which can include millions of molecules. A computer model based on quantitative structure-activity relationship (QSAR) can quickly predict a large number of chemicals or simple physicochemical properties such as log P or log D. However, these models cannot predict complex biological characteristics such as chemical activity. And side effects. In addition, QSAR-based models face problems such as short training sets, experimental data errors in the training sets, and lack of experimental validations. To address these issues, newly emerging AI tools such as deep learning (DL) and related modeling studies can be used to Ax the safety and efficacy of medicinal compounds using big data modeling and analysis. Merck sponsored the QSAR ML 2012 competition. To explore the benefits of DL in the pharmaceutical drug development process. In an Absorption, Distribution, Metabolism, Excretion and Toxicity (ADMET) dataset of 15 drug candidates, DL models outperformed classical ML predictability. [16] [17]. Describing the distribution of molecules and their properties, a virtual chemical space resembles a geographical map of molecules. The purpose of chemical spatial imaging is to collect spatial information about molecules in space to search for bioactive compounds; therefore, virtual screening (VS) helps select relevant molecules for subsequent \testing. Several chemical facilities including PubChem, ChemBank, DrugBank and ChemDB are open to the public. Many in silico methods for virtual screening of compounds from virtual chemical plants and structure- and ligand-based methodologies enable better profiling and faster elimination. Lead-free compounds and the choice of therapeutic molecules with lower costs. Use drug design techniques such as coulomb arrays and molecular fingerprinting to select a lead ingredient, \study physical, chemical and toxicological profiles [18]. To predict the target chemical structure of a substance, multiple features such as predictive models and molecules. Similarity, molecular formation process and use of in silico methods [15] [16]. Pereira et al. Presented DeepVS, a new docking method for 40 receptors and 2950 ligands, which showed remarkable performance when 95,000 decoys were tested against these receptors [20]. Another study used a multi-objective automatic substitution algorithm to improve the potency profile of a cyclin-dependent kinase-2 inhibitor \by examining its conformational similarity, biochemical activity, and physicochemical properties [21]. The use of QSAR modeling tools led to the development of AI -based QSAR techniques including decision trees, support vector machines, random forests and linear discriminant analysis (LDA) that can be used to speed up QSAR analysis [22] [23] [24]. While King Et al. Evaluated the ability of six artificial intelligence algorithms to classify anonymous substances based on biological activity with conventional techniques [25], they found a minimal statistical difference.

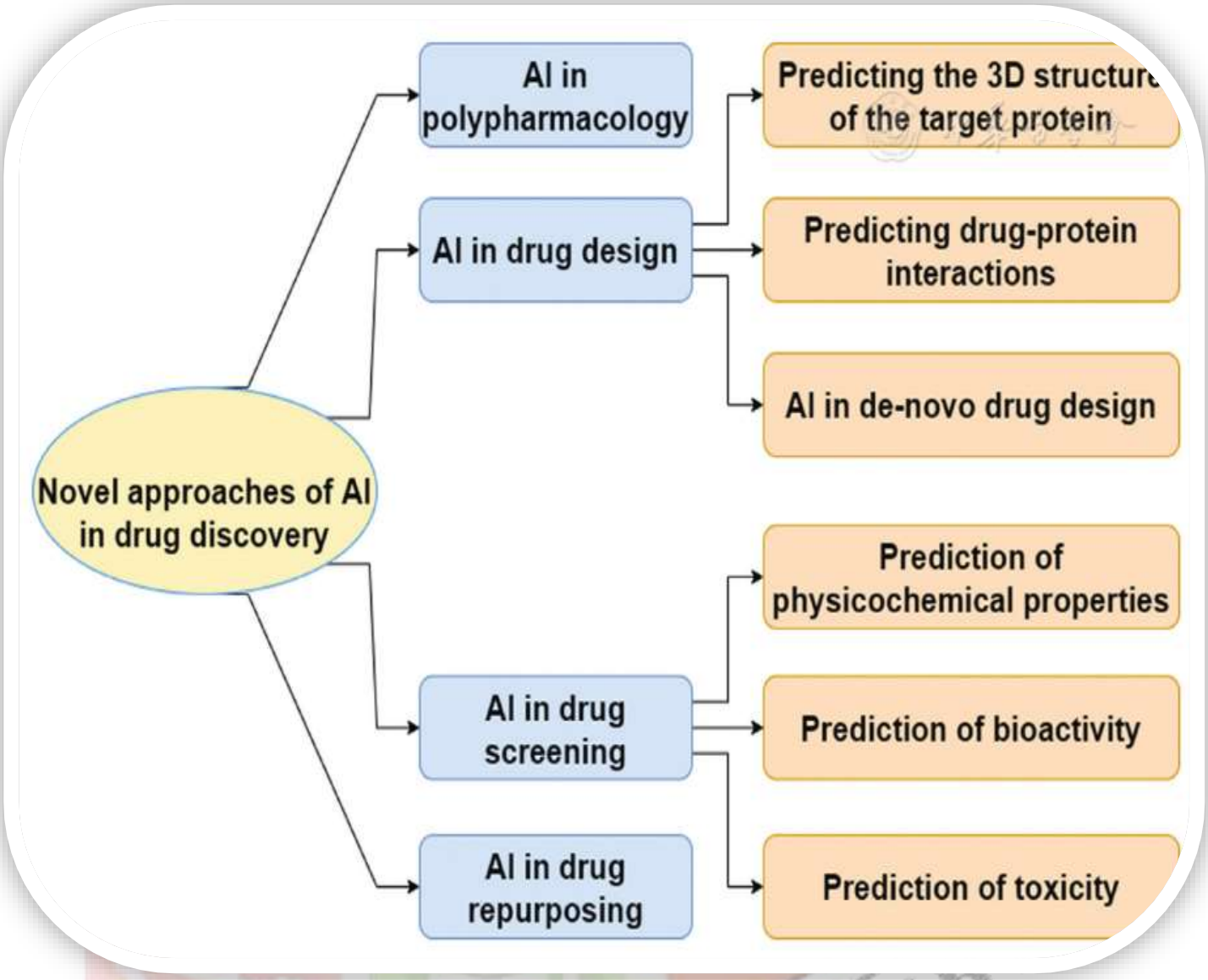

Figure no 2: Artificial intelligence (AI) in drug discovery AI has the potential to help in several areas of drug discovery, including Drug design, drug screening, polypharmacology, and drug repurposing.

❖ **Artificial Intelligence in designing drug molecule –**

1. Predicting the structure of the target protein –

To effectively treat patients, it is important to choose an appropriate target during the development of a therapeutic molecule. Several overexpressed proteins are involved in the development of the disease. Therefore, to specifically target a disease, it is necessary to predict the structure of the target protein when creating a drug molecule. AI can aid structure-based drug design by predicting the 3D protein structure because the design matches the chemical environment of the target protein site. This facilitates the target effect and safety aspects of the compound before its synthesis or manufacture. [26]. AlphaFold, an artificial intelligence tool based on DNN networks', was used to predict the 3D structure of the target protein by comparing the distances of adjacent amino acids and the corresponding angles of peptide bonds. This method gave excellent results when 25 out of 43 structures were correctly predicted. RNN was used for protein structure prediction in AI Qureshi's study. The author discussed recurrent geometric network (RGN), \which consists of three stages: computation, geometry and estimation. In that case, the basic protein sequence was encoded and the torsion angles of a given residue and the partially completed framework derived from that upstream geometric unit were taken as input and provided the new framework as output. The final unit resulted

in a 3D structure. The root mean square deviation (dRMSD) of the distance was used to evaluate the difference between the expected and experimental structure. RGN configurations were tuned to minimize dRMSD between predicted and experimental structures [27]. Al Qurashi predicted that his AI method will predict protein structure faster than AlphaFold. Although AlphaFold predicts protein structures with sequences comparable to the reference structures, it is likely to be more accurate [28]. One study had a nonlinear triple NN tool based on forward learning and a backpropagation error algorithm used with MATLAB to predict the 2D structure of a protein. The input and output datasets were trained in MATLAB and NNs served as learning algorithms and performance evaluators. The 2D structure prediction was 62.72% [29].

2.Prediction of Drug-Protein Interactions –

Drug-protein interactions are critical for therapeutic efficacy. Predicting how a drug interacts with a receptor or protein is critical to understanding drug efficacy and effectiveness [26]. It also allows drug reuse and avoids polypharmacology. Imprecise prediction of ligand-protein interactions enabled by various artificial intelligence techniques has improved therapeutic efficacy [26, 30]. Wang et al. to discover nine new compounds and their interactions with four important targets. described a model using an SVM approach based on primary protein sequences and structural features of small molecules and trained on 15,000 protein-ligand interactions [31]. Yu et al. used two RF models to predict potential drug-protein interactions by combining pharmacological and chemical data and validating them against known platforms such as SVM with excellent sensitivity and specificity. In addition, these states can predict drug-target associations, which can then be extended to predict target-disease and target-target associations, thus accelerating the drug discovery process [32]. Xiao et al. used the neighbourhood sweep rule and synthetic minority oversampling techniques. Create an DrugTarget for optimal data collection. It is a mixture of four extra-terrestrial predictors (iDrug-GPCR, iDrug-Chl, iDrug-Enz and iDrug-NR) to determine how the drug interacts with G protein-coupled receptors (GPCR), ion channels, enzymes. , and nuclear receptors, here in order. Target knife tests were used to compare this predictor with \other predictors, with the former outperforming the latter in terms of consistency and predictive accuracy [33].

AI was also used to repurpose already approved drugs and avoid polypharmacology. its potential to predict drug target interactions. The recycled drug is immediately suitable for phase II clinical trials. Releasing an expired drug results in financial savings as it costs only $8.4 million, while releasing a completely new pharmacological entity costs $41.3 million [34]. A new association between a drug and a disease can be predicted using an "association fault" strategy that can be knowledge-based or computational [35]. ML methodology using techniques such as SVM, NN, logistic regression and DL is widely used for computationally driven networks. Logistic regression platforms \such as PREDICT, SPACE, and other ML techniques consider drug-drug, disease-disease, target molecule, chemical structure, and \gene expression profiles for drug reuse. Drug-protein interactions can also predict the likelihood of polypharmacology or propensity to drugs interact with many receptors and cause unwanted side effects [38]. To create safer drug compounds, AI can design a new molecule using the principles of polypharmacology [39]. Using artificial intelligence systems like SOM and the huge databases already available, multiple agents can be linked to multiple targets and extra-targets. Pharmacological properties of drugs and potential targets can be combined with Bayesian classifiers and SEA algorithms [37].

De Novo Drug Design with Artificial Intelligence De Novo drug design has been popular in recent years as a method to create therapeutic compounds. De Novo drug design has been replaced by new DL approaches, as the former has disadvantages such as complex synthetic routes and problematic prediction of the bioactivity of a new molecule. For every million structures that can be generated by computational

synthetic design, thousands of different synthetic pathways can be predicted. Due to its many advantages, including online learning, optimization of previously learned data and suggestions for possible synthetics. pathways for compounds, the use of artificial intelligence in the de novo design of molecules can be useful for the pharmaceutical industry and lead to rapid control design and development [40,41].

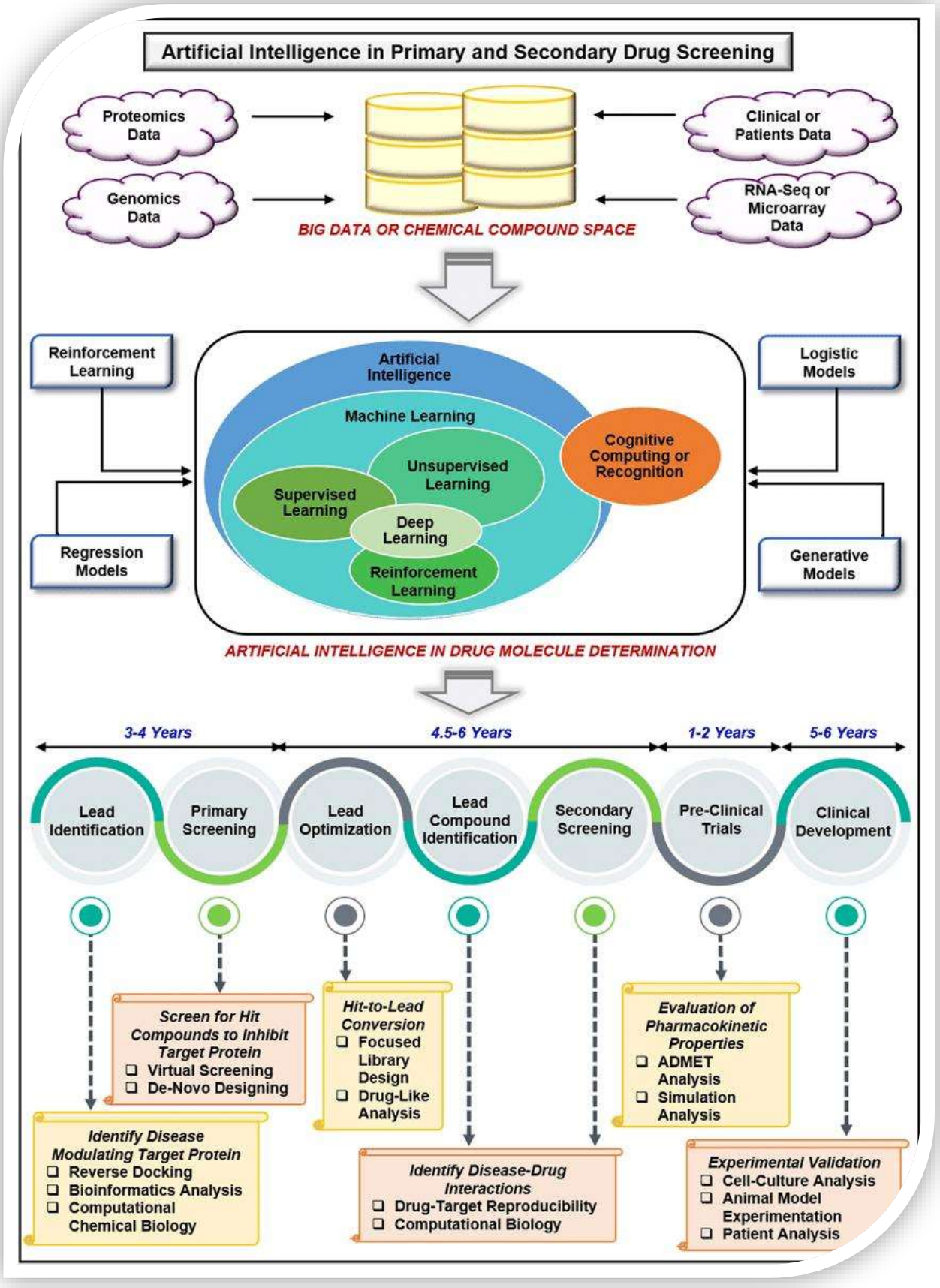

Figure no. 3 AI in Drug Screening

❖ **Artificial Intelligence in Clinical Trial Design –**

Clinical trials take 6-7 years and a significant financial investment to determine the safety and effectiveness of a medicine people for a given disease. However, only one out of ten of the molecules involved in these tests is accepted, resulting in significant losses to the industry [42]. These failures may be due to poor patient selection, lack of technical needs, or lack of infrastructure. However, due to the large amount of digital medical data available, these errors can be reduced by artificial intelligence [43].
The enrollment of participants consumes a third of the clinical trial schedule. Recruitment of eligible patients ensures the success of a clinical trial, which otherwise accounts for 86% of failures [44]. Artificial intelligence can help select a specific affected population for participation in phase II and III clinical trials by applying patient-specific genomic exposure profile analysis that can help select patients almost predict potential therapeutic targets [43]. Preclinical molecular discovery and prediction of lead compounds before entering clinical trials, using other aspects of AI such as predictive ML and other inferential methods, can predict initial lead candidates that will enter clinical trials in a selected patient population [43] . Clinical dropout accounts for 30% of clinical study failures, leading to additional recruitment requirements \to end the trial, resulting in a waste of time and money. This can be avoided by carefully monitoring patients and helping them adhere to the clinical trial protocol [44]. AiCure developed mobile software to track regular medication use in patients with schizophrenia in a phase II trial that improved patient adherence by 25%, ensuring successful completion of the clinical trial.

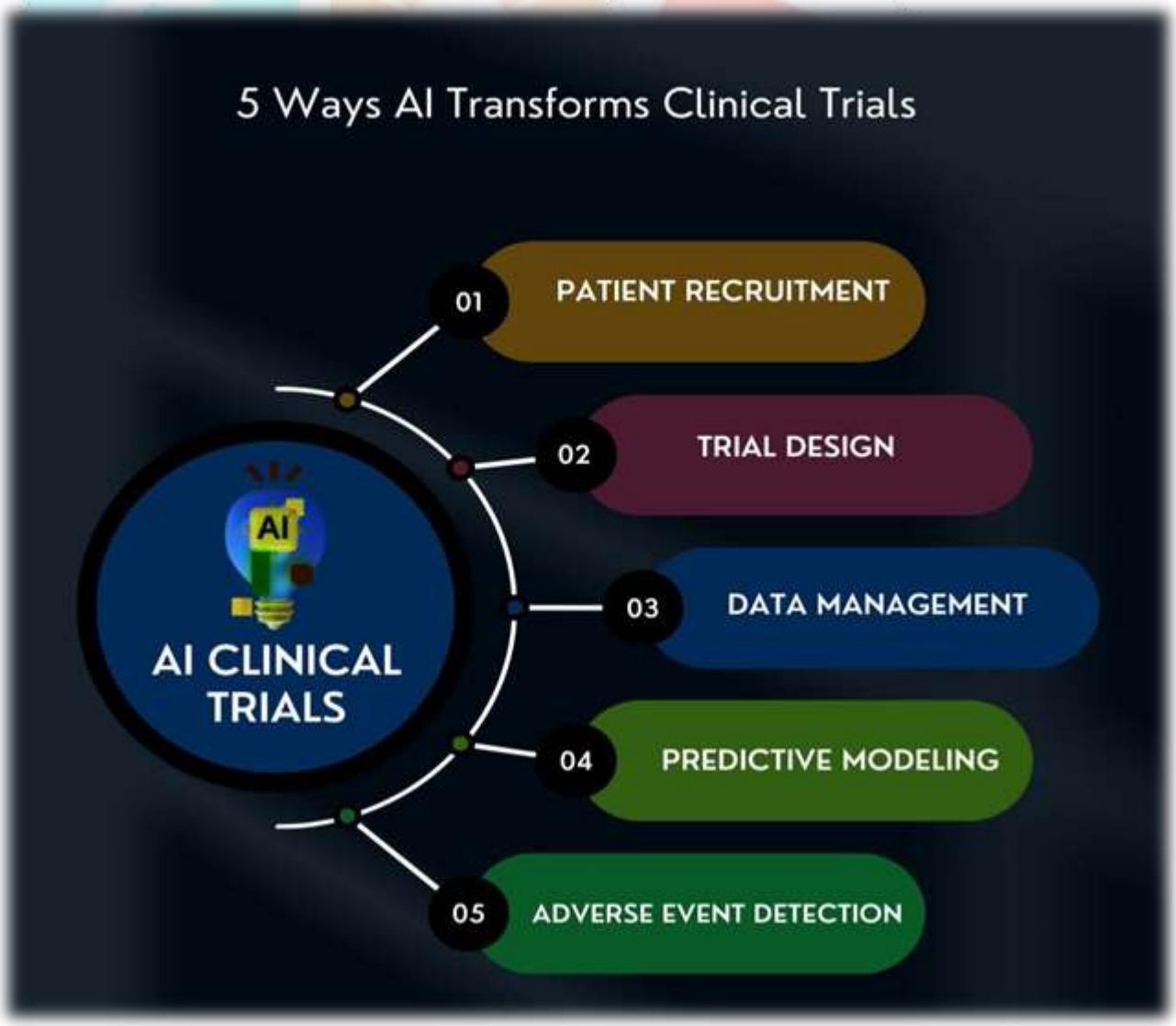

Figure no 4. AI in Clinical Trials

❖ **Artificial Intelligence Approaches in Polypharmacology –**

Today, the concept of "one disease – multiple targets" dominates the concept of "one disease – one target" for an improved realization of the pathological process in diseases on their molecular basis. One-disease-multiple-targets-phenomenon is called polypharmacology.110 There are many useful databases such as PubChem, KEGG, ChEMBL, ZINC, STITCH, Ligand Expo, PDB, Drug Bank, Super Target, Binding DB etc., which are available to provide important and useful information on various crystal structures, chemical properties, biological properties, molecular pathways, binding affinities, diseases, drugs goals etc. AI also helps in finding databases to design poly pharmacological molecules/substances.

❖ **Advantages of AI technology –** The potential advantages of AI technology are as follows: [6,15,41]

i) **Minimize Errors:** AI helps reduce errors \and increases accuracy even more accurately. Intelligent robots are made of durable metal bodies and can withstand the aggressive atmosphere ode space, so they are sent to explore space.

ii) **Hard exploration:** AI is useful for exploration. It is also used to search for fuel. AI systems are able to explore the Ookean, overcoming human errors.\iii) Daily application: AI is very useful in our daily activities \and activities. For example, the GPS system is widely used during long journeys. Installing artificial intelligence in Androids enjoys predicting what a person will type. It also helps to correct typos.

iii) **Digital Assistants**: Today, advanced organizations use artificial intelligence systems like avatars (models of digital assistants) to reduce the Inhuman needs. The Avatar is able to follow the right logical decisions because they are completely unemotional. People's emotions and moods interfere with decision-making \and this problem can be solved by \machine intelligence.) Repeated tasks: Generally, people can perform \one task at a time. Unlike humans, machines can multitask and analyze faster than humans. Different parameters of the machine i.e. Speed and time can be adjusted according to their requirements.

vi) Medical use: In general, doctors can assess the condition of patients and analyze side effects \ and other health risks related to drug use. The AI program. Trainee surgeons can collect information using artificial intelligence application programs, such as various artificial surgical simulators (such as gastrointestinal simulations, cardiac stimulations, brain simulations, etc.

vii) No pauses: unlike humans who are able to n8 h/working day with breaks machines are programmed to continuously work long hours without any distraction and boredom.

viii) Increase technological growth: AI technology is widely used in the most advanced technological innovations around the world . It is able to produce \various computer modeling programs and ames for the invention of newer molecules. Artificial intelligence technology is also used in the development of drug dosage forms.

ix) No danger: If you work in danger zones, fire stations, there is a high chance of harming personnel. With machine learning programs problems, the broken \parts can be fixed.

x) Use as help: AI technology had a different function, serving 24x7 both children and parents. It can be a source of teaching and learning for everyone.

xi) Unlimited Features: Machines are not limited by many limitations. Unknown machines can do everything more efficiently and also.

❖ **Disadvantages of AI technology -** The important disadvantages of AI technology are as **follows**:[6,15,41]

i) **Expensive**: Launching AI involves huge expenditure of money. The complex design of the machine, maintenance and repair is very cost-effective. R and D division requires a long time to develop one AI machine. The AI machine needs software updates at regular intervals. Reinstalling and the machine requires longer time and money.

ii) **No Human Copying:** Robots using AI technology relate to the insensitivity of human thinking because they add advantages \to perform a given task more accurately without judgment. When unknown problems occur Ei, robots can make a decision and give a wrong report.

iii) **Experience does not improve**: human resources can be improved by experience. On the other hand, machines equipped with artificial intelligence technology cannot be improved by experience. They cannot recognize what kind of person is hardworking and working.

iv) **Lack of Original Creativity:** Machines equipped with AI technology have no sensitivity or emotional intelligence. Humans have the ability to hear, see, feel and think. They can also use their creativity and thoughts. These functions cannot be achieved using machines.

v) **Unemployment:** Widespread use of AI technology all sectors could lead to widespread unemployment. Unwanted unemployment can cause human workers to lose their work habits and creativity.

❖ **Conclusion –**

Drug design and development continues to be an early adopter of new and growing experimental and computational tools. One of the challenges is deciding whether to use these technologies to improve existing pipeline and processes, or to redesign processes in light of these technologies. Big data, digital health, remote monitoring and genomics increase the need to explore how computational and reasoning methods can be used to improve process in terms of clinical relevance and cost reduction. AI methods have enormous potential to achieve these goals, but their success depends on combining right question with the right technology. During past few years, interest in the use of artificial intelligence technology has been identified in the analysis and interpretation of pharmaceutical critical areas such as drug development, dosage design, polypharmacology, hospital pharmacy, etc.., how technical approaches to AI believe, how a \man imagines information, solves problems \and makes decisions. As a result of the use of artificial intelligence methods, the planning of new hypotheses, strategies, forecasts and the analysis of various related factors were done easily with less time and affordability.

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