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ARTIFICIAL INTELLIGENCE IN DRUG DISCOVERY AND DEVELOPMENT

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Abstract: Artificial intelligence (AI) has become more prevalent in a number of societal fields, most notably the pharmaceutical industry. In this review, we focus on how AI is being used in a variety of pharmaceutical industry fields, such as drug discovery and development, drug repurposing, increasing pharmaceutical productivity, and clinical trials, among others. This use of AI lessens the workload of human workers while also achieving goals quickly. A interesting and expanding field is artificial intelligence (AI). Because of the large and growing volume of data, AI techniques are becoming indispensable for the full evaluation of information underlying data. AI is being used to accelerate progress and improve decision making in various sectors and disciplines of drug discovery and development, including medicinal chemistry, upscaling, molecular and cell biology, pharmacology, pharmacokinetics, formulation development, and toxicity. In clinical testing, AI plays a critical role in raising success rates by improving trial design (biomarkers, efficacy parameters, dose selection, trial duration), target patient population selection, patient stratification, and patient sample evaluation. We also explore crosstalk between AI tools and methodologies, current issues and solutions, and the future of AI in the pharma industry.

Index Terms **- Artificial Intelligence (AI), Pharmaceutical, Development.**

1. Introduction

In the pharmaceutical market, data digitization has increased dramatically in recent years. However, the challenge of gathering, evaluating, and utilizing knowledge to solve complicated clinical problems arises with digitalization [1]. This encourages the adoption of AI, which can manage massive amounts of data with greater automation [2]. AI is a technology-based system that use a variety of advanced tools and networks to simulate human intelligence. At the same time, it does not threaten to totally replace human physical presence [3][4]. AI employs systems and software that can read and learn from input data in order to make independent judgments for achieving certain goals. As stated in this review, its applications in the pharmaceutical industry are constantly being expanded. According to the McKinsey Global Institute, rapid breakthroughs in AI-guided automation are likely to totally transform society's work culture [5][6].

2. Artificial Intelligence In Life Cycle Product

AI can be imagined assisting in the development of a pharmaceutical product from the bench to the bedside because it can aid in rational drug design [7], decision making, determining the right therapy for a patient, including personalised medicines, and managing clinical data generated and using it for future drug development [8].

E-VAI is an analytical and decision-making AI platform developed by Eularis that uses machine learning (ML) algorithms and an easy-to-use user interface to create analytical roadmaps based on competitors, key stakeholders, and currently held market share to predict key drivers in pharmaceutical sales [9], allowing marketing executives to allocate resources for maximum market share gain, reversing poor sales, and anticipating where to make investments. Figure 1 summaries many AI uses in drug research and development.

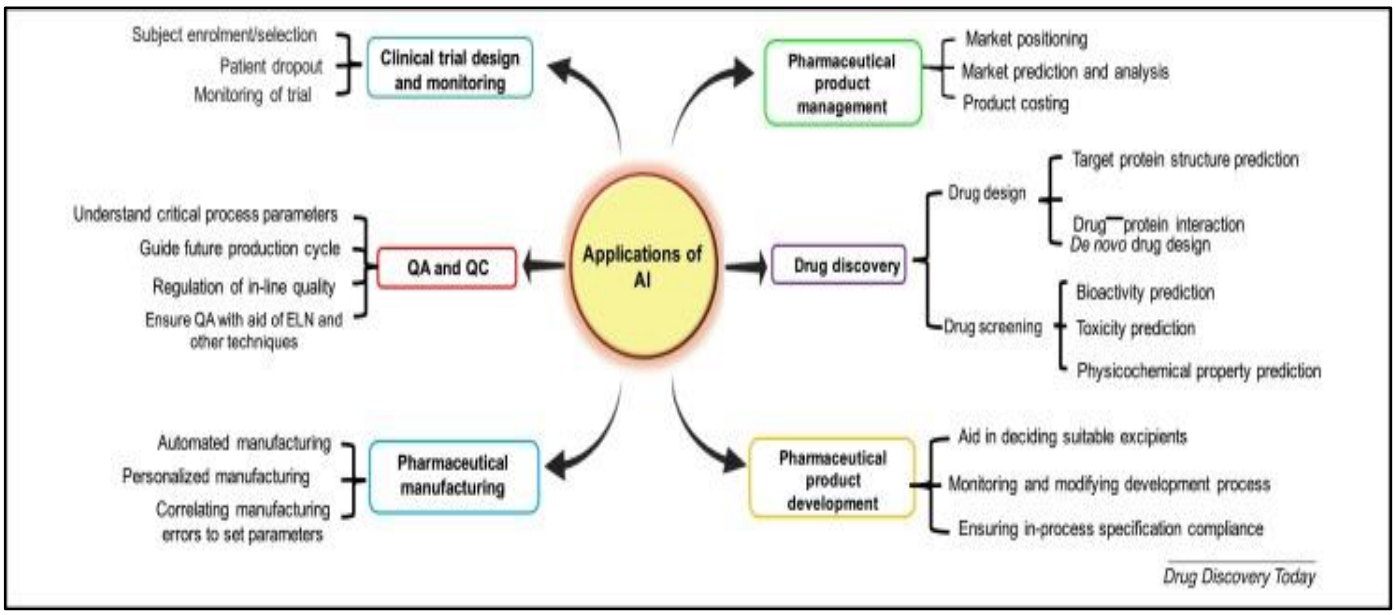

figure no 1 : artificial intelligence (ai) is being used in various areas of the pharmaceutical sector, ranging from drug discovery to pharmaceutical product management.

3. Artificial Intelligence In Drug Discovery

The enormous chemical space, which contains $>10^{60}$ compounds, encourages the synthesis of a huge number of pharmacological molecules [10]. The lack of new technology, on the other hand, delays the medication development process, making it a time-consuming and expensive task that can be handled by applying AI [11]. AI can identify hit and lead compounds, as well as provide faster validation of the drug target and optimization of drug structure design [10]. [12] Figure 2 illustrates many AI uses in drug discovery.

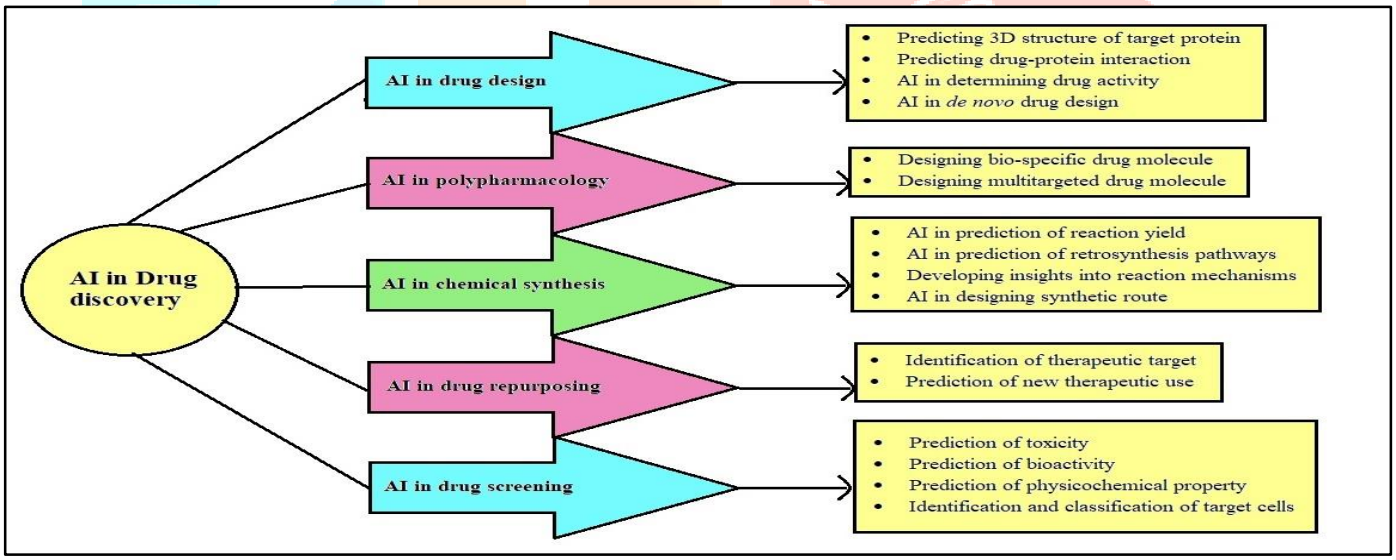

figure no 2: artificial intelligence (ai) in drug discovery ai has the potential to help in several areas of drug discovery, including drug design, chemical synthesis, drug screening, polypharmacology, and drug repurposing.

Despite its benefits, AI has substantial data difficulties, such as data volume, growth, diversity, and uncertainty. Traditional ML algorithms may be unable to deal with the data sets accessible for drug discovery in pharmaceutical organizations, which might include millions of molecules. A computational model based on the quantitative structure-activity relationship (QSAR) can swiftly predict a large number of chemicals or simple physicochemical characteristics like log P or log D. However, these models fall short of predicting complicated biological features such as chemical activity and side effects. Furthermore, QSAR-based models encounter issues such as short training sets, experimental data error in training sets, and a lack of experimental validations. To address these issues, recently emerging AI tools, such as Deep learning (DL) and relevant modelling studies, can be used to evaluate the safety and efficacy of medicinal compounds using big data modelling and analysis. Merck sponsored a QSAR ML competition in 2012 to investigate the benefits of DL in the drug discovery process in the pharmaceutical business. For 15 drug candidate absorption, distribution, metabolism, excretion, and toxicity (ADMET) data sets, DL models outperformed classic ML approaches in terms of predictability. [13] [14].

By depicting the distributions of molecules and their attributes, the virtual chemical space resembles a geographical map of molecules. The goal behind the chemical space visualization is to collect positional information about molecules inside the space in order to search for bioactive compounds; hence, virtual screening (VS) aids in the selection of relevant molecules for subsequent testing. Several chemical spaces, including PubChem, ChemBank, DrugBank, and ChemDB, are open to the public.

Numerous in silico methods for virtual screening compounds from virtual chemical spaces, as well as structure and ligand-based methodologies, allow superior profile analysis, faster elimination of nonlead compounds, and therapeutic molecule selection at a lower cost [10]. To pick a lead ingredient, drug design techniques such as coulomb matrices and molecular fingerprint recognition examine the physical, chemical, and toxicological profiles [15].

To forecast the intended chemical structure of a substance, several characteristics such as predictive models, molecule similarity, the molecule generation process, and the usage of in silico methodologies can be used [12][16]. Pereira et al. presented DeepVS, a new docking method for 40 receptors and 2950 ligands that demonstrated remarkable performance when 95000 decoys were tested against these receptors [17]. A multi-objective automated replacement algorithm was used in another study to enhance the potency profile of a cyclin-dependent kinase-2 inhibitor by examining its form similarity, biochemical activity, and physicochemical features [18].

The use of QSAR modelling tools has led to the development of AI-based QSAR techniques, including decision trees, support vector machines, random forests, and linear discriminant analysis (LDA), which can be used to accelerate QSAR analysis [19][20][21]. When King et al. evaluated the capacity of six AI algorithms to rank anonymous substances in terms of biological activity with that of conventional techniques [22], they discovered a minimal statistical difference.

4. Artificial Intelligence In Drug Screening

4.1 Prediction Of Physicochemical Properties

When developing a new medicine, physicochemical characteristics including solubility, partition coefficient (logP), degree of ionization, and intrinsic permeability of the drug must be considered because they have an indirect impact on its pharmacokinetics and target receptor family [23]. It is possible to predict physicochemical properties using a variety of AI-based methods. For example, ML uses large data sets created during earlier compound optimization to train the software [24]. Molecule descriptors, such as SMILES strings, potential energy readings, electron density around the molecule, and coordinates of atoms in 3D, are used in drug design algorithms to produce feasible molecules via DNN and thus forecast its properties [25].

The Estimation Program Interface (EPI) Suite is a quantitative structure-property relationship (QSPR) process developed by Zang et al. to ascertain the six physicochemical properties of environmental chemicals received from the Environmental Protection Agency (EPA) [24]. The lipophilicity and solubility of different substances have been predicted using neural networks based on the ADMET predictor and ALGOPS software [26]. The solubility of molecules has been predicted using DL techniques like undirected graph recursive neural networks and graph-based convolutional neural networks (CVNN) [27].

The acid dissociation constant of substances has been predicted using ANN-based models, graph kernels, and kernel ridge-based models in a number of cases [24][28]. Similar to this, data on cellular permeability of a wide range of molecules has been generated using cell lines, such as Madin-Darby canine kidney cells and human colon adenocarcinoma (Caco-2) cells, and is then fed to AI-assisted predictors [23].

In order to predict the intestinal absorptivity of 497 compounds, Kumar et al. developed six predictive models, including SVMs, ANNs, k-nearest neighbor algorithms, LDAs, probabilistic neural network algorithms, and partial least square (PLS), using 745 compounds for training. These models took into account parameters such as molecular surface area, molecular mass, total hydrogen count, molecular refractivity, molecular volume, logP, total polar surface area, the sum of E- states indices, solubility index (log S), and rotatable bonds [29]. In a similar vein, in silico models based on RF and DNN were created to estimate human intestinal absorption of various chemical substances [30]. As a result, AI plays a crucial role in the creation of a medicine by predicting both the needed bioactivity and the intended physicochemical qualities.

4.2 Prediction Of Bioactivity

The affinity of drug molecules for the target protein or receptor determines their efficacy. Drug molecules that do not bind with or have affinity for the targeted protein will not be able to provide the therapeutic response. In rare cases, therapeutic compounds may interact with unwanted proteins or receptors, resulting in toxicity. As a result, drug target binding affinity (DTBA) is essential for predicting drug-target interactions. AI-based approaches can calculate a drug's binding affinity by taking into account the traits or similarities between the drug and its target. To determine the feature vectors, feature-based interactions recognize the chemical moieties of the medication and the target. In contrast, similarity-based interaction takes into account the similarity between medication and target, and it is assumed that similar compounds will interact with the same targets [31].

For predicting drug-target interactions, web application such as ChemMapper and the similarity ensemble technique (SEA) are available [32]. Many ML and DL-based techniques, including as KronRLS, SimBoost, DeepDTA, and PADME, have been utilized to determine DTBA. To determine DTBA, ML-based techniques such as Kronecker-regularized least squares (KronRLS) analyze the similarity between medicines and protein molecules. SimBoost, on the other hand, uses regression trees to predict DTBA and takes into account both feature-based and similarity-based interactions. SMILES drug characteristics, ligand maximum common substructure (LMCS), extended connectivity fingerprint, or a mix of these can all be evaluated [31].DL approaches have shown improved performance compared with ML because they apply network-based methods that do not depend on the availability of the

3D protein structure [32]. DeepDTA, PADME, WideDTA, and DeepAffinity are some DL methods used to measure DTBA. DeepDTA accepts drug data in the form of SMILES, whereby, the amino acid sequence is entered for protein input data and for the 1D representation of the drug structure [33]. WideDTA is CVNN DL method that incorporates ligand SMILES (LS), amino acid sequences, LMCS, and protein domains and motifs as input data for assessing the binding affinity [34].

Deep-Affinity and Protein And Drug Molecule Interaction Prediction (PADME) are techniques comparable to those published previously [35]. Deep-Affinity is an interpretable deep learning model that employs both RNN and CNN, as well as unlabeled and labelled data. In the structural and physicochemical aspects, it considers the compound in SMILES format and protein sequences[36]. PADME is a DL-based platform that predicts drug target interactions using feed-forward neural networks (DTIs). It takes as input data the combination of medication and target protein properties and anticipates the intensity of the interaction between the two. The SMILES representation and the protein sequence composition (PSC) are used to illustrate the drug and the target, respectively [35]. Unsupervised machine learning techniques, such as MANTRA and PREDICT, can be used to forecast the therapeutic efficacy of drugs and target proteins of known and unknown pharmaceuticals, which can then be extrapolated to the application of drug repurposing and interpreting the therapeutics' molecular mechanism. Using a CMap data set, MANTRA classifies substances based on comparable gene expression profiles and clusters those anticipated to have a shared mode of action and biological pathway [32]. A drug's bioactivity also contains ADME data. AI-based techniques such as XenoSite, FAME, and SMARTCyp are used to determine the drug's sites of metabolism. Additionally, tools like CypRules, MetaSite, MetaPred, SMARTCyp, and WhichCyp were utilized to pinpoint individual CYP450 isoforms that control a given drug's metabolism. SVM-based predictors performed the clearance pathway analysis of 141 authorized medicines with high accuracy [37].

4.3 Prediction Of Toxicity

It is crucial to predict the toxicity of any drug molecule in order to avoid negative effects. The frequent use of cell-based in vitro tests as preliminary studies, followed by animal trials to ascertain a compound's toxicity, raises the price of creating new medications. A number of web-based applications, such as LimTox, pkCSM, admetSAR, and Toxtree [24], can assist reduce the cost. Advanced AI-based techniques examine similarities between compounds or estimate a compound's toxicity based on input features. The Tox21 Data Challenge was organized by the National Institutes of Health, the Environmental Protection Agency (EPA), and the US Food and Drug Administration (FDA) to test various computational techniques for predicting the toxicity of 12 707 environmental chemicals and medicines. [24]. By identifying static and dynamic features within the chemical descriptors of the molecules, such as molecular weight (MW) and Van der Waals volume, a machine learning algorithm called DeepTox outperformed all other methods and was able to accurately predict the toxicity of a molecule based on predefined 2500 toxicophoric features [38].

5. Artificial Intelligence In Designing Drug Molecules

5.1 Prediction of the target protein structure

In order to treat patients effectively, choosing the appropriate target during therapeutic molecule development is essential. Several overexpressed proteins are involved in the development of the disease. Therefore, in order to specifically target disease, it is essential to predict the structure of the target protein while creating the drug molecule. AI can assist in structure-based drug development by predict the 3D protein structure since the design is in accordance with the chemical environment of the target protein location. This makes it easier to predict a compound's impact on the target and safety concerns prior to its synthesis or manufacture. [39]. By comparing the distances between nearby amino acids and the corresponding angles of the peptide bonds, the AI tool AlphaFold, which is based on DNNs, was used to predict the 3D target protein structure. With 25 out of 43 structures correctly predicted, this method produced excellent results.

RNN was used to predict the protein structure in a study by AlQurashi. The author considered a recurrent geometric network (RGN), which consists of three stages: computation, geometry, and assessment. The basic protein sequence was encoded in this case, and the torsional angles for a certain residue and a partially finished backbone derived from the geometric unit upstream of this were then taken into account as input and gave a new backbone as output. The result from the final unit was a 3D structure. The distance-based root mean square deviation (dRMSD) metric was used to evaluate the variance between anticipated and experimental structures. The RGN settings were tuned to minimize the dRMSD between the predicted and experimental structures [40]. AlQurashi projected that his AI approach would predict the protein structure more quickly than AlphaFold. While predicting protein structures with sequences comparable to those of the reference structures, AlphaFold is probably more accurate [41].

In a study, a nonlinear three-layered NN toolbox based on a feed-forward supervised learning and backpropagation error algorithm was used with MATLAB to predict the 2D structure of a protein. The input and output data sets were trained in MATLAB, and the NNs served as learning algorithms and performance judges. The prediction of the 2D structure was accurate to 62.72% [42].

5.2 Predicting Drug Protein Interaction

Drug-protein interactions are crucial to a therapy's effectiveness. To understand a medicine's efficacy and effectiveness, predict how it will interact with a receptor or protein is crucial [39]. This also enables drug repurposing and avoids polypharmacology. The accurate prediction of ligand-protein interactions made possible by a variety of AI techniques has improved therapeutic efficacy [39][43]. In order to find nine new compounds and their interactions with four important targets, Wang et al. described a model utilizing the SVM approach that was constructed based on primary protein sequences and structural properties of small molecules and trained on 15 000 protein-ligand interactions [44].

Yu et al. used two RF models to predict potential drug-protein interactions by combining pharmacological and chemical data and validating them with excellent sensitivity and specificity against well-known platforms, such as SVM. Additionally, these modes could forecast drug-target relationships, which could then be expanded to anticipate associations between target-disease and target-target, accelerating the drug discovery process [45]. The Neighborhood Cleaning Rule and the Synthetic Minority Over-Sampling Technique were used by Xiao et al. to collect optimum data for the creation of iDrugTarget. This is a mixture of four sub-predictors (iDrug-GPCR, iDrug-Chl, iDrug-Enz, and iDrug-NR) for figuring out how a drug interacts with G-protein-coupled receptors (GPCRs), ion channels, enzymes, and nuclear receptors, in that order. Target-jackknife tests were used to compare this predictor to other predictors, and the former outperformed the latter in terms of consistency and prediction accuracy [46].

AI has also been used to help reuse already-approved drugs and avoid polypharmacology because of its potential to predict drug-target interactions. A drug that has been repurposed is immediately qualified for Phase II clinical trials [10]. Releasing an outdated medication results in financial savings because doing so only costs $8.4 million as opposed to $41.3 million to release a completely new pharmacological entity [47]. A fresh connection between a drug and a disease can be predicted using the "guilt by association" strategy, which can be knowledge-based or computationally driven [48]. In networks that are computationally driven, the ML methodology—which uses techniques like SVM, NN, logistic regression, and DL—is widely used. Logistic regression platforms like PREDICT, SPACE, and other ML techniques consider drug-drug, disease-disease, target-molecule, chemical structure, and gene expression profiles when repurposing a medicine [49].

Drug-protein interactions can also foretell the likelihood of polypharmacology, or a drug's propensity to interact with many receptors and cause unintended side effects [51]. In order to create safer medicinal compounds, AI can build a novel molecule using the principles of polypharmacology [52]. Multiple substances can be linked to a variety of targets and off-targets using AI systems like SOM and the enormous databases that are already available. The pharmacological characteristics of medications and potential targets can be connected using Bayesian classifiers and SEA algorithms [50].

De novo medication design with AI De novo drug design has been popular in recent years as a method for creating therapeutic compounds. De novo drug design is being replaced by emerging DL approaches since the former has drawbacks including difficult synthesis routes and problematic bioactivity prediction of the novel molecule [25]. Thousands of distinct synthesis paths can be predicted for each of the millions of structures that can be produced using computer-aided synthesis planning [93].

Because of its many benefits, including online learning, optimization of previously learned data, and suggestions for potential synthesis routes for compounds, the use of AI in the de novo design of molecules can be advantageous to the pharmaceutical industry and result in quick lead design and development [53][54].

6. Artificial intelligence In Advancing Pharmaceutical Product Development

The subsequent inclusion of a novel therapeutic molecule into an appropriate dosage form with the requisite delivery properties is necessary. The traditional method of trial and error can be replaced in this area by AI [55]. With the use of QSPR, a variety of computational methods can be used to overcome concerns with stability, dissolution, porosity, and other aspects of formulation design [56]. Decision-support tools operate through a feedback mechanism to monitor the entire process and sporadically adjust it [57]. They employ rule-based systems to choose the type, nature, and quantity of the excipients based on the physicochemical parameters of the medicine.

Guo et al. combined expert systems (ES) and artificial neural networks (ANN) to produce a hybrid method for the production of piroxicam direct-filling hard gelatin capsules that adhere to the parameters of its dissolution profile. Based on the input parameters, the MODEL EXPERT SYSTEM (MES) generates decisions and suggestions for formulation development. Contrarily, ANN makes formulation development simple by using backpropagation learning to connect formulation parameters to the intended response, which is jointly regulated by the control module [55].

The influence of the powder's flow property on the die-filling and tablet compression process has been studied using a variety of mathematical tools, including computational fluid dynamics (CFD), discrete element modelling (DEM), and the Finite Element Method [58][59]. The effect of tablet geometry on its dissolution profile can also be studied using CFD [60]. The quick manufacture of pharmaceutical items may benefit greatly from the integration of these mathematical models with AI.

7. Artificial Intelligence In Pharmaceutical Manufacturing

Modern manufacturing systems are attempting to impart human knowledge to machines as a result of the growing complexity of production processes, as well as the growing desire for efficiency and greater product quality [61]. The pharmaceutical industry may profit from the use of AI in manufacturing. Utilizing the automation of many pharmaceutical activities, tools like computational fluid dynamics (CFD) use Reynolds-Averaged Navier-Stokes solvers technology to examine the effects of agitation and stress levels in various pieces of equipment (such stirred tanks). Similar systems, such big eddy simulations and direct numerical simulations, use sophisticated techniques to address challenging flow problems in manufacturing [58].

The innovative Chemputer platform aids digital automation for molecule synthesis and manufacture by including numerous chemical codes and working through the use of a scripting language known as Chemical Assembly [15]. With yield and purity very similar to manual synthesis, it has been used to successfully synthesize and produce sildenafil, diphenhydramine hydrochloride, and rufinamide [62]. AI technology can effectively complete the estimated granulation in granulators with capacities ranging from 25 to 600 l [63]. Neuro-fuzzy logic and technology were used to correlate key factors with their answers. In order to anticipate the proportion of granulation fluid to be supplied, the necessary speed, and the diameter of the impeller in both geometrically identical and dissimilar granulators, they developed a polynomial equation [64].

The pharmaceutical industry has used DEM extensively, for example, to investigate the segregation of powders in a binary mixture, the effects of varying blade speed and shape, predict the potential path of the tablets during coating, and analyze the amount of time that tablets spend in the spray zone [58]. In order to decrease tablet capping on the production line, ANNs and fuzzy models investigated the relationship between machine settings and the capping problem [65].

AI tools like the meta-classifier and tablet-classifier are used to control the final product's quality standard by flagging potential production errors in tablets [66]. A patent application demonstrates a system that employs a processor that receives patient information to determine the ideal drug and dose regimen for each patient, then constructs the appropriate transdermal patch in accordance with that information [67].

8. Artificial Intelligence In Quality Control and Quality Assurance

A balance of different criteria must be achieved throughout the production of the desired product from raw materials [66]. It takes human intervention to maintain batch-to-batch consistency and conduct quality control testing on the products. This illustrates the need for AI implementation at this time and may not be the optimal strategy in every situation [58]. By implementing a "Quality by Design" approach, the FDA modified Current Good Manufacturing Practices (cGMP) in order to better understand the crucial process and precise standards that determine the ultimate quality of the pharmaceutical product [68].

Gams et al. created decision trees using a combination of human effort and artificial intelligence (AI) by analyzed preliminary data from production batches. The operators further turned them into rules and examined them in order to direct the manufacturing cycle going forward [66]. Goh et al. used ANN to analyze the dissolution profile of theophylline pellets, a sign of batch-to-batch consistency, and they found that it accurately predicted the dissolution of the tested formulation with an error of only 8% [69].

AI can also be used to regulate in-line manufacturing processes in order to attain the target product standard [68]. The freeze-drying process is monitored using an ANN-based method that employs a combination of self-adaptive evolution, local search, and backpropagation algorithms. This can be utilized to anticipate the temperature and desiccated-cake thickness at a future time point (t + t) for a specific set of operating circumstances, thereby assisting in the quality control of the final product [70].

An automated data input platform, such as an Electronic Lab Notebook, combined with advanced, intelligent algorithms can ensure product quality [71]. Furthermore, data mining and various knowledge discovery techniques in the Total Quality Management expert system can be employed as valuable approaches in making difficult judgments, resulting in the development of new technologies for intelligent quality control [72].

9. Artificial Intelligence In Clinical Trial Design

Clinical trials take 6-7 years and a significant financial investment to establish the safety and efficacy of a medicinal product in people for a specific illness condition. However, just one out of every ten molecules that enter these trials is approved, resulting in a substantial loss for the industry [73]. These failures might occur as a result of poor patient selection, a lack of technological needs, or a lack of infrastructure. However, with the large amount of digital medical data available, these failures can be decreased by the use of AI [74].

Enrolling participants consumes one-third of the clinical study timeline. The enrollment of suitable patients ensures the success of a clinical study, which otherwise results in 86% of failure cases [75]. AI can help in the selection of a specific diseased population for enrollment in Phase II and III clinical trials by applying patient-specific genome-exposome profile analysis, which can aid in the early prediction of possible therapeutic targets in the patients chosen [10][74]. Preclinical molecule discovery and prediction of lead compounds prior to the start of clinical trials using other aspects of AI, such as predictive ML and other reasoning techniques, aid in the early prediction of lead molecules that would pass clinical trials with consideration of the selected patient population [74].

Drop out of patients from clinical trials accounts for 30% of clinical trial failure, resulting in additional recruiting requirements for the trial's completion, resulting in a waste of time and money. This can be avoided by closely monitoring the patients and assisting them in adhering to the clinical trial procedure [75]. AiCure developed mobile software to track regular medication intake by patients with schizophrenia in a Phase II trial, which boosted patient adherence by 25%, assuring the clinical trial's successful completion [10].

10. intelligence in Pharmaceutical Product Management

10.1 Artificial Intelligence In Market Positioning

Market positioning is the process of establishing a product's identity in the market in order to persuade customers to acquire it, making it a key component in almost all business strategies for enterprises to build their own distinct identity [76][77]. This strategy was employed in the promotion of the pioneer brand Viagra, which was marketed not only for the treatment of erectile dysfunction in males, but also for other disorders impacting quality of life [78].

Companies can now achieve natural brand recognition in the public realm with the use of technology and e-commerce as a platform. Companies use search engines as one of the technology platforms to get a prominent place in online marketing and aid in product positioning, as affirmed by the Internet Advertising Bureau. Companies are constantly attempting to rank their websites higher than those of other companies in order to gain attention for their brand in a short amount of time [79].

Other techniques, such as statistical analysis methods and particle swarm optimization algorithms (introduced by Eberhart and Kennedy in 1995) used in conjunction with NNs, produced a more accurate picture of markets. They can assist in determining the product's marketing strategy based on accurate consumer demand prediction [80].

10.2 Artificial Intelligence Market Prediction and Analysis

A company's success is determined by the constant expansion and growth of its business. Despite having access to large funding, R&D production in the pharmaceutical business is declining due to companies' failure to adopt new marketing technologies [81]. The 'Fourth Industrial Revolution' in digital technologies is assisting innovative digitalized marketing through a multicriteria decision-making approach, which collects and analyses statistical and mathematical data and implements human inferences to make AI-based decision-making models explore new marketing methodology [82].

AI also aided in a full examination of a product's core requirements from the customer's perspective, as well as analyzing market demand, which aids in decision-making using prediction tools. It can also forecast sales and conduct market research. AI-based software engages customers and raises physician awareness by providing adverts that connect them to the product site with a single click [83]. Furthermore, these strategies employ natural language processing tools to examine keywords entered by clients and associate them with the likelihood of purchasing the goods [84][85].

Several business-to-business (B2B) companies have introduced self-service solutions that enable free browsing of health items, which can be easily located by providing specifications, placing orders, and tracking their shipping. Pharmaceutical companies are also launching online programmers such as 1 mg, Medline, Netmeds, and Ask Apollo to meet patients' unmet requirements [82]. Market prediction is also important for various pharmaceutical distribution organizations that can apply AI in the sector, such as 'Business clever Smart Sales Prediction Analysis', which employs a combination of time series forecasting and real-time application. This enables pharmaceutical companies to forecast product sales in advance, avoiding the expenditures of excess stock or client loss due to shortages [86].

11. Artificial Intelligence Based Advance Application

11.1 Artificial Intelligence Based Nanorobots for Drug Delivery

Nanorobots are primarily composed of integrated circuits, sensors, power supplies, and secure data backup, all of which are maintained using computational technologies such as AI [87][88]. They are engineered to avoid collisions, identify targets, detect and attach, and then excrete from the body. Nano/microrobot advancements allow them to go to the desired region based on physiological parameters such as pH, boosting efficacy and lowering systemic adverse effects [88]. The development of implantable nanorobots for controlled drug and gene delivery necessitates consideration of characteristics such as dose modification, sustained release, and control release, and drug release necessitates automation controlled by AI tools such as NNs, fuzzy logic, and integrators [89]. Microchip implants are utilized for both programmed release and detecting the implant's position in the body.

11.2 Artificial Intelligence Emergence in Nanomedicine

Nanomedicines combine nanotechnology and medicine to diagnose, treat, and monitor complicated diseases such as HIV, cancer, malaria, asthma, and inflammatory diseases. Nanoparticle-modified drug delivery has become essential in the field of therapeutics and diagnostics in recent years due to improved efficacy and therapy [90][91]. Many formulation development difficulties could be solved by combining nanotechnology and AI [92].

A methotrexate nanosuspension was computationally created by evaluating the energy released by the drug molecules' interaction and monitoring the variables that could lead to formulation aggregation [56]. Coarse-grained simulation, in conjunction with chemical calculations, can help determine drug-dendrimer interactions and assess drug encapsulation within the dendrimer. Furthermore, tools such as LAMMPS and GROMACS 4 can be utilized to investigate the effect of surface chemistry on nanoparticle internalization into cells [56].

AI aided in the development of silicasomes, which are composed of iRGD, a tumor-penetrating peptide, and irinotecan-loaded multifunctional mesoporous silica nanoparticles. This boosted silicasomes uptake three to fourfold because iRGD enhances silicasomes transcytosis, resulting in improved treatment outcome and overall survival [91].

11.3 Pharmaceutical Market of Artificial Intelligence

To reduce the monetary cost and chances of failures that accompany VS, pharmaceutical businesses are shifting towards AI. The AI market grew from US$200 million in 2015 to US$700 million in 2018, and it is predicted to grow to $5 billion by 2024 [94]. AI is expected to disrupt the pharmaceutical and medical sectors, with a 40% estimated rise from 2017 to 2024. Various pharmaceutical corporations have made and continue to make investments in AI, as well as cooperated with AI companies to build critical healthcare technologies. DeepMind Technologies, a Google company, collaborated with the Royal Free London NHS Foundation Trust to help people with acute renal injury. Major pharmaceutical companies and AI players are detailed in Figure 3 [10].

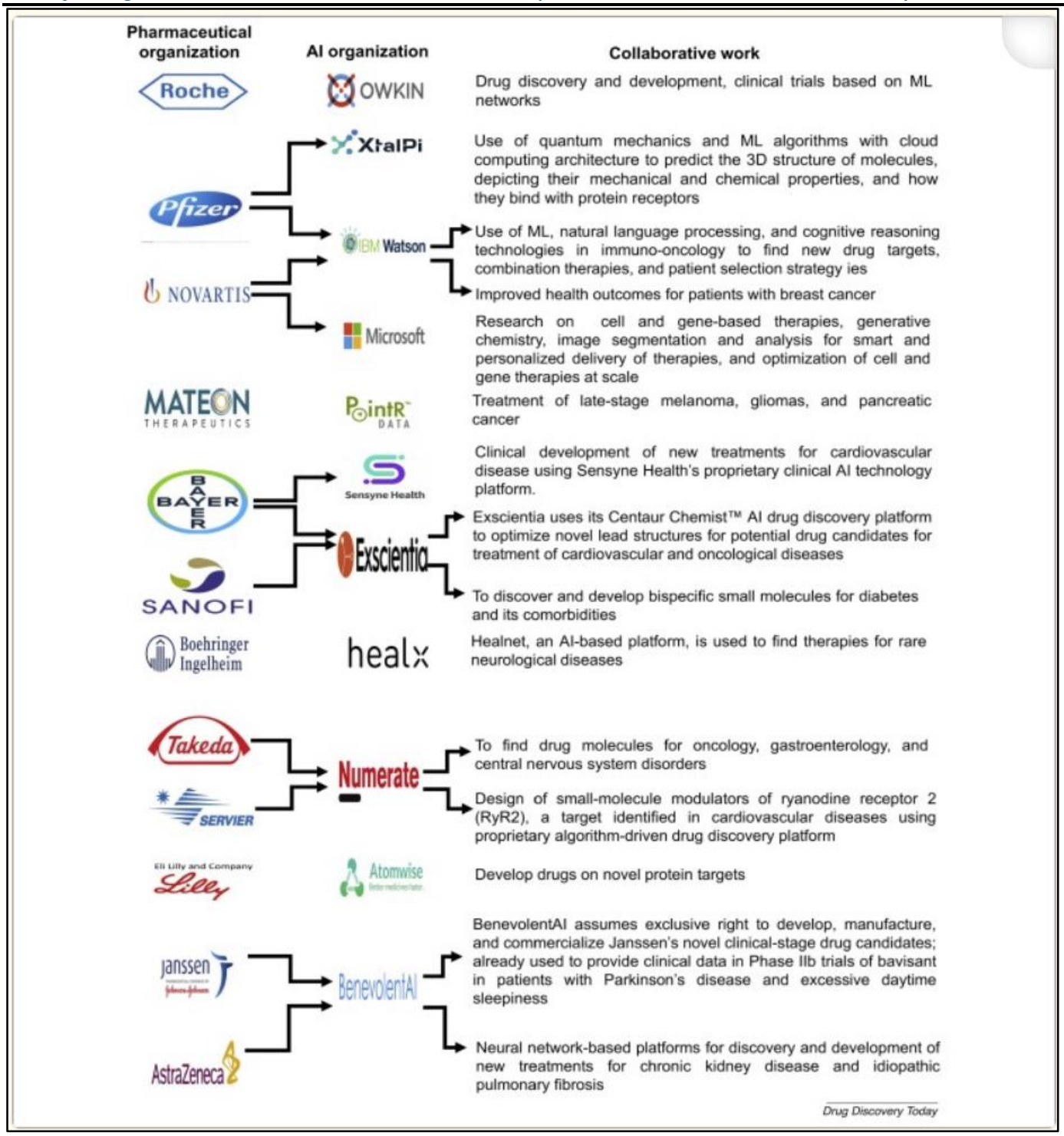

figure no 3 : leading pharmaceutical companies and their collaboration with artificial intelligence (AI) groups working in oncology, cardiovascular disease, and central nervous system problems.

Conclusion

Drug design and development will continue to be an early user of new and growing experimental and computational tools. Among the challenges is deciding whether to use these technologies to improve the existing pipeline and processes or to reengineer the processes in light of these technologies. Big data, digital healthcare, remote monitoring, and genomics will increase the need to investigate how computational and reasoning approaches might be used to improve the process in terms of clinical significance as well as cost reduction. Artificial intelligence methods hold enormous potential for achieving these aims, but their success is dependent on matching the correct question to the proper technology.

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