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Advances in artificial intelligence for drug delivery and development

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Abstract
Artificial intelligence (AI) is a strong tool that uses anthropomorphic knowledge to solve complicated problems faster. The amazing breakthroughs in artificial intelligence and machine learning mean that the fields of dosage form testing, pharmaceutical formulation, and drug discovery will undergo a major transformation. Researchers can identify disease-associated targets and predict their potential interactions with therapeutic choices using AI algorithms that analyze vast biological data, such as proteomics and genomics. This increases the possibility of successful drug approvals by enabling a more effective and focused approach to drug research. Artificial Intelligence has the potential to save development costs by streamlining processes in research and development. In addition to helping with experimental design, machine learning algorithms can forecast the pharmacokinetics and toxicity of potential drugs. Costly and time-consuming procedures are not as necessary thanks to the capacity to select and optimize lead compounds. Artificial Intelligence systems that evaluate actual patient data can assist in personalized drug recommendations, improving treatment outcomes and patient adherence. This thorough analysis examines the various uses of AI in drug discovery, pharmacokinetics/pharmacodynamics (PK/PD) research, process optimization, drug delivery dosage form designs, testing, and testing.

Keywords: *Artificial intelligence, Pharmaceutical technology, Machine learning, drug delivery, drug development.*

Introduction

The study of problem-solving with programming symbols is known as artificial intelligence (AI) in

computer science. AI is quickly entering the healthcare sector and affecting automation, illness diagnosis, and clinical decision-making [1, 2]. AI has the potential to study vast amounts of data from multiple modalities, which presents chances for additional research in the pharmaceutical and healthcare fields. Several recent research go into further detail about the application of AI in healthcare and other fields. Robotic process automation, natural language processing (NLP), machine learning (ML), physical robots, and other AI technologies find use in the healthcare sector.

Among the new endeavors using AI technology in pharmacy are drug delivery formulation, development, and discovery, as well as other healthcare applications [3]. This movement has already transcended from hype to optimism. AI models are also useful in predicting in vivo reactions, the pharmacokinetic properties of the drugs, the right dosage, etc. Using in silico models contributes to the drug's affordability and effectiveness, according to the importance of pharmacokinetic prediction in drug research [4]. There are two major categories for AI technological developments. First, there are conventional computing methods like expert systems that can draw conclusions and replicate human experiences. commencing with the basic concepts, such as expert systems. In the second, artificial neural networks (ANNs) are used to create systems that mimic the workings of the brain [5].

Because AI is used in a larger range of stages and sectors, it is essential to consider its function in the pharmaceutical industry. From drug research to product management, artificial intelligence has a clear impact on the pharmaceutical industry at every level. A few approaches used in drug discovery are AI-based quantitative structure-activity relationship (QSRL) technologies, QSLRML, deep learning, machine learning (ML), support vector machines (SVMs), deep virtual screening, deep neural networks (DNNs), recurrent neural networks (RNNs), and virtual screening (VS). AI is modeled after biological neural networks, which process input data and offer an output thereafter. Multiple interconnected units make up artificial neural networks (ANNs), which are used to process data [6]. DNNs and ANNs are comparable in that they both have multiple layers of data processing units. The output data from one analysis is processed as the input data for the subsequent analysis phase in a sequential manner using RNNs. SVMs are utilized in the regression and categorization of input data. Drug development uses artificial neural networks (ANNs), model expert systems (MES), and other tools. AI in manufacturing matches production faults to establish boundaries through automated and personalized manufacturing [7]. The final result is produced with the appropriate quality by utilizing AI technologies like tablet classifiers and meta-classifiers. By closely monitoring the experiment and helping with subject selection, AI in clinical trials helps to lower the number of study dropouts. Clinical experiment ML is being employed. The aforementioned industries have been heavily impacted by AI, which has improved results [8].

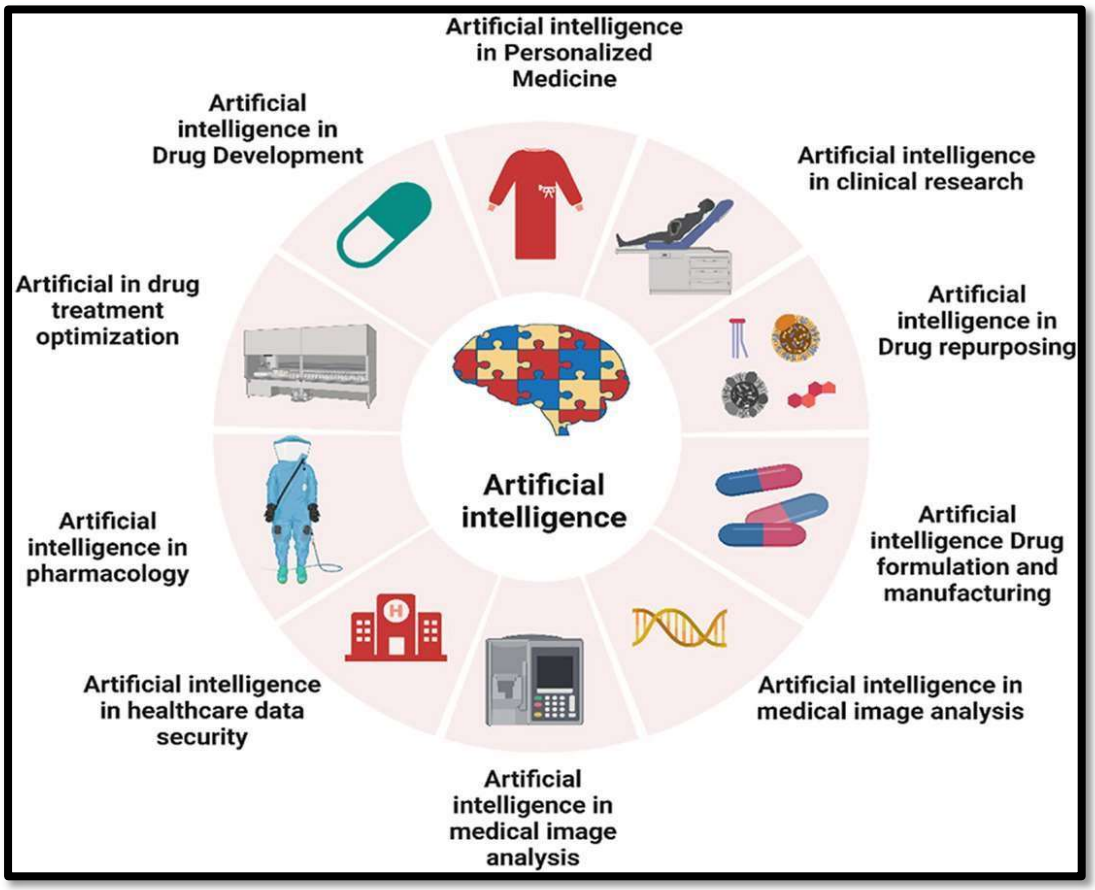

Figure 1: Benefits of using Artificial Intelligence in drug development

The Role of AI in Present-Day Pharmaceutical Challenges

Small molecules have numerous benefits, thus the pharmaceutical business is always researching them to improve goods and customer satisfaction [9]. One can make synthetic derivatives cheaply and with ease using the straightforward chemical synthesis procedure. As a result, the pharmaceutical industry has access to numerous stable and effective small-molecule-loaded formulations [10]. Clinical studies and sophisticated data are necessary for the introduction of many novel small compounds, except treatments for uncommon disorders, as they compete with generic molecules. Companies are under additional financial pressure to innovate as a result of these procedures [11]. Still, in an attempt to offset the crises brought on by small molecules and inadequate distribution of discoveries and research, the biomolecular drug sector is expanding quickly. Their shape and reactivity determine how small molecules behave [12-13].

As infusion is the most convenient and favored method of delivery for these biomolecules, the pharmacokinetic features of these compounds are intricate. An essential component of research involving nucleic acids is the manipulation of pharmacokinetics and molecular stability. Objectives such as pharmacokinetic exposure and molecular form enhancement are critical. To address these problems and provide solutions, new technical advancements could be beneficial [14]. While AI has enormous potential to advance drug delivery and research, it also has serious limitations that require human participation or the knowledge of intellectuals to fully comprehend the complex consequences.

The datasets play a major role in forming the foundation for AI forecasts. Nonetheless, human interpretation is required to reach the correct conclusion due to the results' grey areas. Algorithmic bias

can be a task for AI when processing data for predictions and assessing hypotheses. Additionally, a common result of docking simulations is the detection of inactive molecules [15]. Therefore, a thorough examination of these elements still necessitates human involvement to make conclusions and do cross-verifications to eliminate system bias concerns. However, given its enormous potential for use, a great deal of effort may be able to lessen AI's drawbacks and improve its effectiveness and dependability [16]. The type of algorithm used is also a critical aspect, and the learning process can be either supervised or unsupervised. While unsupervised learning works with uncertain outcomes, supervised learning uses known inputs and outputs to facilitate machine learning. Using a variety of inputs or attributes, the supervised technique predicts output (such as labels or targets). Unsupervised classification, on the other hand, seeks to form feature-homogeneous groups [17]. Various AI models have been investigated in pharmaceutical product development to improve various parts of the process (Figure 2).

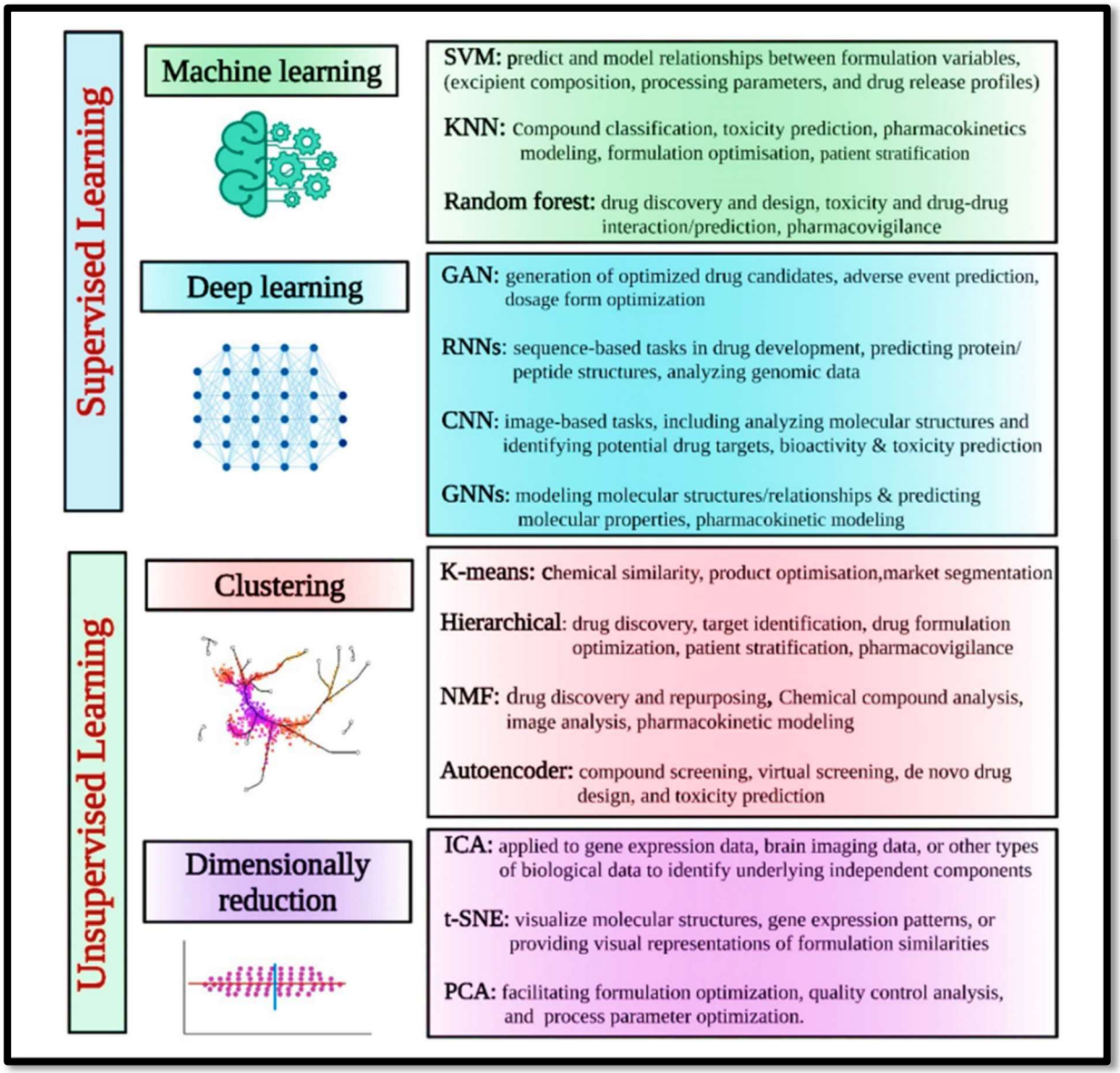

Figure 2. A collection of AI tools that are investigated in pharmaceuticals

Role of artificial intelligence in drug development

With the increasing amount of chemical space available, the search for new medicinal compounds is getting harder and taking longer, which is causing a daily gap to open up between drug discovery and development [18]. Recently, there has been a lot of interest in AI as a possible transformational tool for the pharmaceutical sector. High-throughput screening and trial-and-error research have historically been labor-intensive methods used in the difficult and drawn-out process of finding and developing novel drugs, known as drug discovery. Thus, for many phases of drug discovery—including finding and verifying drug targets, modeling drugs, and improving their druggable qualities—methods based on the principles of artificial intelligence are highly beneficial. To enhance the decision-making process, it is also imperative to establish patient-centered clinical trials [19]. Insufficient technology makes it difficult to synthesize a large number of medicinal molecules from a chemical space. Still, this can be achieved by using AI to improve the process of developing new drugs.

Different in silico techniques are applied for virtual screening, which typically yields a better analysis, faster removal, and more variety [20]. The physical, chemical, and toxicological properties are taken into consideration by drug design algorithms when choosing a lead compound to bind with and produce activities. Bioactivity and efficacy can be enhanced by many physicochemical characteristics. Using AI-based QSAR techniques, QSAR is designed with the possibility of using the drug candidate in mind. The discovery and development of biological activity can take ten years to control if the conventional methods for generating statistical differences are adhered to [21]. As a novel drug is being designed, factors such as the drug's inherent permeability, degree of ionization, partition coefficient, and solubility influence target receptor binding. A simplified Molecular Input Line Entry System (SMILES) is one example of a molecular descriptor used by algorithms to predict binding qualities. Generally, a quantitative structure-property relationship (QSPR) is used to determine the six physicochemical parameters, which are collectively referred to as the Assessment Program Interface Suite. Predictions of the lipophilicity and solubility of different substances have been made using deep learning and neural networks based on the ADMET predictor and ALGOPS software. Predicting solubility involves a lot of undirected graphs [22]. Utilizing artificial intelligence, SPIDER is a method for assessing how natural substances behave and how best to exploit them in drug discovery. Because it was primarily intended to predict the targets for pharmacological agents like "Lapa Chone," it was able to show that 5-Lipoxygenase is reversibly and allosterically inhibited by "Lapa Chone." The toxicity of unknown substances is being evaluated using a more advanced technique called Read Across Structure Activities Relationship (RASAR) [23]. Establishing and identifying the relationship between a molecule's structure and properties that could be harmful is being done with great care. This is made possible with the assistance of the chemical database. A Deep Neural Network, or DNN, is a system that interacts with an artificially connected network of neurons to conduct several types of data transformations [24]. It establishes the guidelines for classifying drugs into their corresponding therapeutic classes based on data from toxicological and pharmacological studies. For instance, the development of next-generation AI methods is based on Generative Adversarial Networks (GANs). Machine learning is an important aspect of artificial intelligence (ML). The cornerstone of this field is the application of statistical attributes [25].

Pharmaceutical companies employ in silico target fishing technology (TF) to forecast biological targets based on chemical structure. This data is supplied based on the biologically annotated information found in the chemical database. In addition, several other techniques, including data mining and chemical structure docking, were employed to explore the mechanism of action in conjunction with the target class information needed for efficient planning [26]. Using cheminformatics tools and machine learning, the TF was applied in drug development. These two are utilized to attain an in-depth understanding of the appropriate examination of intricate structures and the formation of innovative drug components for the

successful management of complicated illnesses [27]. Many companies use standard drug discovery techniques, which can be quite expensive due to the number of intricate steps involved in concluding. These steps include the identification and selection of target proteins as well as a thorough understanding of the small molecules' mechanisms of action. The application of the TF aided in accelerating this procedure and lowering the overall cost of experiments during the drug development processes [28].

AI in Pharmaceutical Sciences

Pharmaceutical sciences encompass a broad spectrum of scientific methods related to the discovery and development of new drugs. It takes a lot of work to increase healthcare services. The most cutting-edge approach to improving the healthcare system is offered by AI. Enormous amounts of data are frequently needed for AI and ML to produce improved results, and the majority of pharmaceutical and healthcare companies have enormous data sets. In 2019, for example, data about the US healthcare system was produced by the McKinsey Global Institute (MGI) that may have been worth $100 billion [29]. Numerous sources, including academic institutions, research and development teams, commercial facilities, and community and clinical pharmacies, produce data. When applying AI in this industry, it is crucial to take ethics into account. The primary concern pertains to the possibility of AI being utilized in decision-making processes that impact individuals' health and welfare, including drug development, clinical trial design, and distribution and marketing strategies [30]. An additional worry regarding employment losses from automation is the application of AI in the pharmaceutical sector. It is crucial to take into account any possible effects on employees and offer assistance to those who may be affected. Data security and privacy are further issues that are brought up by AI in the pharmaceutical sector. AI systems run the danger of sensitive personal data being accessed or exploited because they depend on massive volumes of data to operate [31]. Both the reputation of the participating companies and the individuals engaged may suffer greatly as a result of this. Complying with applicable legislation and upholding persons' privacy are essential while collecting and using sensitive medical data [32]. In general, cautious thought and the implementation of deliberate strategies to solve these issues are necessary for the ethical application of AI in the pharmaceutical sector. This may entail taking steps like making certain AI systems are trained on representative and diverse data, routinely assessing and auditing to check for bias, and putting in place stringent data protection and security procedures. The pharmaceutical sector may employ AI sensibly and morally by resolving these problems [33].

AI for Drug Delivery

The utilization of big data and artificial intelligence (AI) in the pharmaceutical sector led to the development of computational pharmaceutics, which uses multiscale modeling methods to progress drug delivery systems. AI algorithms and machine learning techniques are utilised in computational pharmaceutics to assess big datasets and forecast drug activity. This eliminates the necessity for time-consuming trial-and-error research and allows researchers to refine drug delivery systems and assess several scenarios [34]. This lowers expenses, shortens the time needed to develop new drugs, and boosts output.

Drug delivery systems are modeled at several scales in computational pharmaceutics. To forecast drug behavior at every scale, AI algorithms are capable of analyzing complex relationships between drug properties, physiological factors, and formulation components. This facilitates a deeper understanding of drug delivery mechanisms and aids in the development of efficient drug delivery systems. It facilitates the forecasting of the drug's physicochemical properties, stability, and in vitro drug release profile [35]. In vivo-in vitro correlation studies and improved evaluation of in vivo pharmacokinetic parameters and drug distribution are also conducted using the same method. Researchers can spot possible dangers and difficulties with drug delivery systems early in the development process by using the appropriate combination of AI technologies. This enables proactive alterations and adjustments to minimize dangers

and enhance the efficacy of drugs. The likelihood of unanticipated results is decreased when AI and computer modeling are used instead of costly and time-consuming trial-and-error experiments.
Among the solid dosage forms, tablets are one of the most commonly utilized in the pharmaceutical sector. Depending on the kind of tablet, there are numerous elements involved in its preparation. Finding the best formulation and researching the desired characteristics that go into it are two tasks that AI may assist with. Additionally, AI is anticipated to handle duties using automated technologies and algorithms [36]. Redefining policies addressing current good manufacturing practice (cGMP) is made more difficult for regulatory authorities by the use of AI.
AI comprises multiple technologies, such as neural networks, fuzzy logic, and genetic algorithms. Stable dosage forms can be created with these technologies, and the interaction between inputs and outputs for operations and processing can be improved [37]. The drug release modeling analysis data was obtained via the use of process analytical technology (PAT) in conjunction with significant material attributes. Finding the particle size distribution to be the most significant variable in a model's prediction was the result. Finally, the most accurate models were determined using the ANN as one of the evaluation measures.

AI for Pharmacokinetics and Pharmacodynamics

Drug discovery, preclinical research, clinical trials, regulatory approval, and other processes are all part of the convoluted process of creating new drugs. Pharmacokinetics and pharmacodynamics are essential components of drug development because they establish the safest dosage, mode of administration, and interaction between a drug and the body [38]. Traditional experimental procedures can be expensive and time-consuming for pharmacokinetics and pharmacodynamics research, and their results may not always produce accurate estimations of the safety and efficacy of drugs. Investigations on animals and human clinical trials have been used in the past to research pharmacokinetics and pharmacodynamics.
The sample size, interindividual variability, and ethical concerns are among the many noteworthy drawbacks of these approaches. Additionally, these studies may not always be able to accurately predict the pharmacokinetics and pharmacodynamics of drugs in humans [39]. These limitations have been overcome by the development of computer models and artificial intelligence approaches to provide faster, more economical, and more precise drug pharmacokinetic and pharmacodynamic prediction methods [40]. Although there are significant challenges in obtaining large, reliable datasets, AI has the potential to transform PKPD research and its treatment implications.
Some machine learning (ML) techniques, including the Bayesian model, random forest, support vector machine, and ANN have been used to predict the features of ADME [41]. Convolutional neural networks (CNNs), long short-term memory (LSTM), and recurrent neural networks (RNNs) are examples of DL algorithms that are commonly used to predict pharmacokinetic parameters, such as drug absorption, bioavailability, clearance, volume of distribution, and half-life. Using a computational technique known as the quantitative structure-activity relationship, or QSAR, one can anticipate a molecule's biological activity based on its chemical structure. Because it may be used to forecast a drug's solubility, permeability, and metabolism, this approach has found application in the field of pharmacokinetics [42]. Drug distribution and elimination inside the body are commonly modeled by Physiologically Based Pharmacokinetic (PBPK) models, which demand a large amount of data and computational capacity. The objective of AI-driven techniques for developing PBPK models is to lessen dependency on human clinical trials and animal research [43].

AI in Personalized Treatment

AI can find significant associations that are relevant to the diagnosis, management, and mitigation of the disease by using the raw data sheets. In this emerging subject, nearly all branches of medical science can apply a variety of more current techniques for computational understanding [44]. To answer complicated

clinical problems, it can be difficult to gather, evaluate, and use a vast amount of knowledge. With the development of medical AI, doctors can now more easily resolve difficult clinical problems. A network of interconnected computer processors called neurons can process data simultaneously. A binary threshold function was used in the development of the first artificial neuron. The most often used model was the multilayer feed-forward perceptron, which featured layers for input, middle, and output. Links with a numerical weight connect each neurone to the other neurons [45].

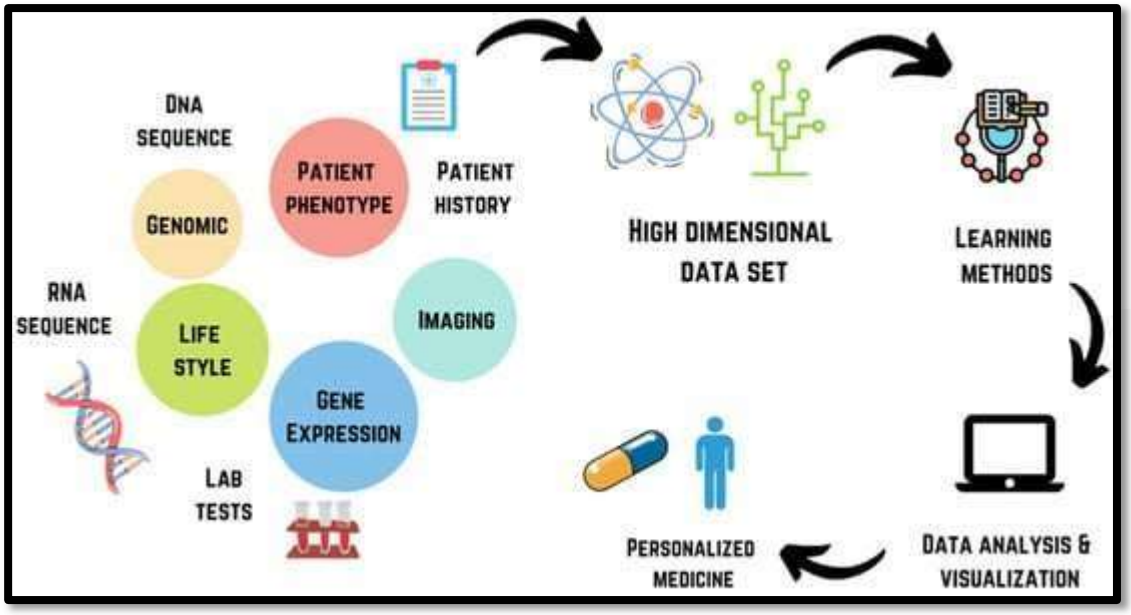

Figure 3: AI in personalizing the treatment

When scheduling radiation therapy, the use of a new technology known as computerized treatment planning is quite beneficial. Thanks to automated treatment planning, plans are becoming more precise, consistent, and error-free [46]. The treatment planning system may assess the patient's anatomy and physiology in addition to simulating the reasoning process that is generally followed in manual treatment planning [47]. Three-dimensional dose distribution and spatial dose have demonstrated promising accuracy of dosage models. Radiomics in conjunction with several imaging biomarkers can yield comprehensive tumour information. To predict the toxicity and outcomes of radiation therapy for individual patients, radiomics can be used [48].

- AI systems possess the ability to effortlessly examine enormous amounts of medical data, encompassing genetic information, biological literature, and patient records [49]. This study contributes to the creation of individualized treatment plans by identifying patterns, relationships, and links.
- Based on a patient's genetic profile, lifestyle, and medical history, AI models can forecast the course of their illness and how well they will respond to treatment. This increases the knowledge that medical professionals have to select customized treatment plans [50].
- Through the analysis of medical images, pathology slides, and extra diagnostic data, AI-driven systems have the potential to improve the precision and effectiveness of diagnostic procedures [51].
- Artificial intelligence (AI) systems can spot subtle patterns and anomalies that human observers would overlook, leading to more accurate early diagnosis of conditions [52]. This helps scientists to create customized care plans for particular patient groups.

- Artificial intelligence-driven monitoring systems and virtual assistants can continuously monitor patient health data, offer customized feedback, and notify medical practitioners of any alarming changes [53-54]. Improving patient outcomes is achieved by enabling proactive and distant care for chronic illnesses.

AI in medical image analysis (MIA)

Many clinical applications, such as therapy evaluation, diagnosis, process monitoring, and early detection medical procedures, depend on medical imaging (MIA) [55]. These are only a few examples of the clinical settings where MIA plays a critical role. To understand medical image analysis in computer vision, one needs to grasp the fundamental concepts and applications of ANN and deep learning. Medical image services such as radiology, nuclear drug imaging, PET (positron emission tomography), digital computed tomography (CT), mammography images, ultrasound scans, magnetic resonance imaging (MRI), magnetic resonance angiography, and pathological tests are highly sought after within the healthcare system. Moreover, the lack of radiologists makes medical image analysis difficult and time-consuming in many cases [56].

AI in Retina: Human health assessment has been greatly enhanced by retinal high-resolution imaging [57]. With the help of high-definition drugs and a single retinal photo, an ophthalmologist or retinal expert may generate highly personalized data, develop a customized treatment plan, and put into place an ever-improving learning healthcare system.

AI in Cancer: The fields of cancer detection and therapy have come to rely more on artificial intelligence (AI) due to its extensive applications [58]. Anticipating the lymphoma subtypes of non-Hodgkin lymphoma involved using gene expression data in a multilayer perceptron neural network. Neural network subtypes for lymphoma are present in the output layer of the network, whilst 20,863 genes make up the input layer. An artificial intelligence neural network has produced highly accurate lymphoma subtype predictions [59]. An artificial intelligence deep learning method was utilised to categorise the cell-of-origin (COO) of DLBCL using the genetic and transcriptional data obtained by RNA-Seq in the next-generation sequencing (NGS) platform.

AI generated tests that were affordable, efficient, and repeatable for classification and further clinical use. AI speeds up and increases the precision of cancer diagnosis [60]. Using AI-based PET imaging for lymphomas, the tumour load is evaluated and subsequently used for tumour characterisation, heterogeneity measurement, and treatment outcome prediction.

- Colorectal cancer (CRC) screening technology is used to determine the degree of malignancy in patients with gastrointestinal cancers, and visual nightly surveillance for Helicobacter pylori infection is a crucial component in predicting the progression of gastric cancer. Early detection of the cancer is possible, and adequate blood testing, endoscopic imaging, and artificial intelligence can all affect how the disease progresses [61]. However, AI lacks the blindfolded controlled studies and randomisation that are required, thus it can only gather retrospective data.
- AI may be used to interpret low-dose computed tomography (LDCT) images from lung cancer screening, potentially improving diagnosis accuracy and reducing the false-positive rating. To provide accurate prognostications on serial imaging, AI can also measure morphological alterations linked to tumours and non-tumors [62].
- In the past ten years, AI has demonstrated significant promise for the diagnosis of breast cancer. To predict treatment response in breast cancer patients, even prior to the start of neoadjuvant chemotherapy (NAC), AI-assisted approaches combine quantitative and qualitative MRI data. Breast density and breast cancer risk assessment, as well as lesion recognition, classification, and division are areas where artificial intelligence (AI) shows potential [63]. By being able to

distinguish benign from malignant breast lesions and reduce the likelihood of misinterpreting false-negative mammography, radiologists can benefit therapeutically from AI-based software.

AI in Other Chronic Diseases*:*

Chronic diseases require regular monitoring, which can be made easier using artificial intelligence (AI) by using virtual medical assistants. Arterial fibrillation can be predicted with the help of an integrated system that combines deep learning, a single-lead ECG sensor, and accelerometer data with smartwatch data to track physical activity [64]. Case-based reasoning, which is developed using AI approaches, is a common tool for managing diabetes. Automatic technology can recognize problems for each patient and retain the optimal course of action.

Now, it is employed to enhance insulin therapy. Additional techniques, such the vector regression method, are also widely used in the management of diabetes. Artificial intelligence (AI)-based tools that predict the short- and long-term HbA1c response after starting insulin therapy can also be helpful to patients with type 2 diabetes [65]. Molecular phenotyping, genomics, epigenetic alterations, and digital biomarker generation are instances of sophisticated artificial intelligence techniques that can be used to the molecular level of illness management. Patients can now control their diabetes more effectively by using web-based apps on their mobile phones and devices.

Conclusion

AI is revolutionizing drug delivery technology by enabling targeted, customized, and adaptable drugs. Pharmacists and other healthcare workers can improve patient outcomes, reduce side effects, and increase medicine efficacy by utilising AI's strengths in data analysis, pattern detection, and optimization. Pharmacokinetics and pharmacodynamics have radically changed thanks to AI-based techniques. In a number of aspects, they are better than conventional experimental techniques. AI-powered models can mimic medication distribution and clearance in the body, forecast pharmacokinetic parameters, and optimise drug dosage and administration techniques. Clinical trials involving humans and animal experimentation can be avoided by using AI-based computational tools for PBPK models, which can expedite the process of creating these models and optimize their parameters. Computational pharmaceutics—a data-driven, more efficient, and cost-effective approach to drug administration—is made possible by big data and AI. Ultimately, it enhances drug production processes and enhances patient outcomes by facilitating risk mitigation, tailored treatment plans, regulatory compliance, and drug formulation optimization. Taking everything into account, the pharmaceutical industry has a great deal of potential to transform, go from Era 4.0 to Era 5.0, and expedite the creation of new drugs.

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