INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA):IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Review Article

A Comprehensive Review On: Role Of Artificial Intelligence In Pharmaceutical Technology And Drug Delivery Design

Yuthika Ovhal*, Ashwini Gavit, Kiran Makhija, N. S. Vyawhare

Dr. D. Y. Patil College of Pharmacy Akurdi, Pune.

ARTICLE INFO

Received: 28 April 2024
Accepted: 02 May 2024
Published: 10 May 2024
Keywords:
Artificial intelligence, Drug Delivery Design, Pharmacokinetics , Pharmacodynamics, Machine learning.
DOI:
10.5281/zenodo.11179405

ABSTRACT

Artificial intelligence (AI) is becoming a powerful tool that leverages human-like knowledge to solve complex problems more efficiently. AI and machine learning advancements are poised to revolutionize drug discovery, pharmaceutical formulation, and dosage form testing. Researchers can identify disease-related targets and predict their interactions with potential treatments using AI algorithms that analyze vast biological data sets, such as proteomics and genomics.This enhances the likelihood of successful drug approvals by enabling a more focused approach to drug research. AI also reduces development costs by streamlining the research and development process. Machine learning algorithms assist in experimental design and predict the pharmacokinetics and toxicity of potential drugs, allowing for the prioritization and optimization of lead compounds without the need for costly and time-consuming animal testing. AI systems analyzing actual patient data can support personalized medical strategies, improving patient adherence and treatment outcomes. The broad applications of AI in drug discovery, drug delivery, dosage form design, process optimization, testing, and pharmacokinetics/pharmacodynamics (PK/PD) research are examined in this comprehensive overview. The paper provides an overview of various AI-based techniques in pharmaceutical technology, discussing their advantages and disadvantages.The pharmaceutical industry's continuous investment in and exploration of AI offer significant opportunities for enhancing patient care and drug development processes.

INTRODUCTION

With a variety of approaches, several sectors are working to advance in order to satisfy the needs and expectations of their clientele. One important sector that is essential to preserving lives is the pharmaceutical business. To handle global healthcare concerns and respond to medical emergencies, like the recent epidemic, it relies on ongoing innovation and the acceptance of new technologies.[1]Within the pharmaceutical sector,

***Corresponding Author:** Yuthika Ovhal
Address: *Dr. D. Y. Patil College of Pharmacy Akurdi, Pune.*
Email : yuthikaovhal@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

innovation is usually based on intensive research and development in a number of areas, such as packaging, customer focused marketing techniques, and production technologies[2]Small drug molecules to biologics are examples of novel pharmaceutical inventions, with a preference for greater potency and stability to address unmet demands in disease treatment. A great deal of anxiety surrounds the evaluation of the substantial levels of toxicity linked to novel medications, which will require in the near future, a great deal of investigation and study. One of the main goals is to supply medication molecules with the best possible properties and suitability for use in the medical field. Despite this, there are a number of challenges facing the pharmacy sector that call for additional development utilising technology driven approaches to meet the expectations of the global medical and healthcare industries[3,4,5]. The healthcare sector has a continuing need for skilled workers, which makes it necessary to provide healthcare staff with ongoing training to increase their participation in normal tasks. Within the pharmaceutical sector, determining skill shortages in the workplace is an essential task. Although it can be difficult to provide proper training, it is crucial to address the deficiencies that have been found with suitable corrective methods. Fourteen percent of supply chain disruptions were recorded in June 2022, according to a study released by some authorities. Supply chain disruption has been identified as the second most difficult obstacle to overcome, according to the survey. A number of pharmaceutical companies are looking forward to new developments in their supply chain and creative approaches to deal with these issues, which could improve business resilience[6]. Numerous activities around the world, including ongoing clinical studies, have been severely disrupted by the global coronavirus disease outbreak of 2019 (COVID-19)[7]. Disruptions to the supply chain can be caused by natural disasters, cyberattacks, price changes, pandemics, delays in logistics, and problems with products. Global industries and the supply chain network have been severely damaged by the epidemic's transportation issues. pricing fluctuation delays are caused by supplier induced delays in updating prices due to miscommunication on whether to use the new or the current pricing for materials or commodities. Cross border trade cooperation methods, rising crime rates, and unstable supply of essential resources for manufacturing and operation give birth to new challenges. To meet patient needs and ensure compliance, modified footprints must be manufactured. Due to issues with maintaining the cold chain during the pandemic, a sizable number of COVID-19 vaccinations from the pharmaceutical sector were rendered useless. Insufficient innovation and imprecise forecasting in industrial and commercial operations are the main causes of supply chain disruption that resulted from the delayed response. Customer happiness, a company's reputation, and possible revenues are all significantly impacted by supply chain interruptions in the pharmaceutical business [8, 9]. The implementation of AI is poised to bring about a significant transformation in the way the pharmaceutical industry handles supply chain operations (Figure 1). It also consolidates numerous AI research endeavors from recent decades to create effective solutions for diverse supply chain issues. Additionally, the study suggests potential research areas that could enhance decision-making tools for supply chain management in the future [10,11]. The pharmaceutical industry's supply chain operations are likely to undergo a major upheaval because to the introduction of artificial intelligence (Figure 1). Additionally, it synthesises a multitude of AI research projects from the past few decades to produce efficient solutions for various supply chain problems. Furthermore, new research

directions that could improve supply chain management decision-making tools are suggested by the study [10,11]. Although the pandemic's main effects are starting to fade, clinical trials are still somewhat impacted by it. Many pharmaceutical companies are interested in using more modern technology, including virtual and artificial intelligence platforms. As shown in Figure 1, these new technologies may be useful in restarting or recreating these clinical studies, with little engagement for face-to-face kinds [12,13,14,15,16,17, and 18]. Currently, the biggest challenges are highly skilled staff and expensive maintenance costs. The fourth primary obstacle when looking for a tech-based solution is cybersecurity and data breaches. The 21st century has seen a surge in cyberattacks on patient data that is readily available, and pharmaceutical companies are increasingly concerned about patient data and sensitive medical records since they are particularly susceptible to cybersecurity threats. Data fragmentation and disconnected system involvement, which typically arise from scattered data generated during the trials and thus require extensive manual data transcription efforts for documents along with those of the systems, are some of the major challenges associated with traditional clinical trials. Because of this lack of creativity in the trial models, the ongoing work needs to be repeated and reworked. The important areas in the healthcare industry that need extra care because of clinical trials are patient recruiting, enrollment, monitoring, retention, and medical adherence. Patient re enrollment in the same setting is facilitated by frequent site visits, which also effect patient enrollment because travelling to trial sites takes time away from participants. Applying AI to research design facilitates both optimisation and accumulation for the tasks associated with developing a patient-centric design. By using methods for gathering the massive volumes of data produced by those clinical trials, AI lowers the quantity of data labour needed for the same. By using body sensors and wearable technology, these technologies can remotely record a patient's vital signs and other important data, helping to satisfy the patient's need for regular in person connection. Real-time insights are provided during the study process by wearable AI algorithms [19]. To implement effective cybersecurity for remote workers and inside the office, new technology platforms and solutions are needed. Data security and breach techniques also require special consideration. Political fraud must also be addressed by technology, and several cases particularly during the global pandemic of the past few years have been documented. Therefore, it is necessary to take the necessary precautions to prevent healthcare fraud in addition to continuously encouraging internal conversations regarding fraudulent behaviours, which may aid in their inhibition.

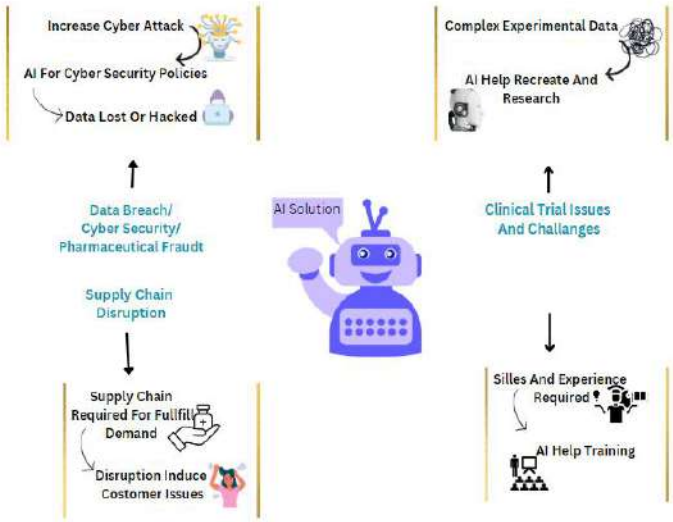

Figure.1: illustrates a potential application of artificial intelligence (AI) to address the issues facing the pharmaceutical industry: all industries need to have skilled workers in order to take advantage of their knowledge, skills, and ability to innovate new products. Problems with clinical trial experimentation and supply chain disruption are covered in the second. The data breaches and security are becoming major problems for the sector as the frequency of cyberattacks rises.

AI in Drug Discovery

Drug discovery and research have greatly benefited from AI. The following are some of the major advances made by AI in this field:

Structure Activity Relationship:

Artificial intelligence models are able to create connections between a compound's molecular makeup and biological function. By creating compounds with desired properties like high potency, selectivity, and advantageous pharmacokinetic characteristics, researchers can use this to optimise medication prospects.

Identification of the Target

AI algorithms are able to find possible therapeutic targets by analysing a variety of data sources, including clinical, proteomic, and genomic data. Artificial Intelligence aids in the development of drugs that can alter biological processes by identifying targets and molecular pathways linked to disease.

Computerised Screening

By using artificial intelligence (AI), large chemical libraries can be efficiently screened to find promising new drugs that are highly likely to bind to a particular target. AI helps scientists save time and money by prioritising and choosing compounds for experimental testing by modelling chemical interactions and predicting binding affinities.

Enhancement of Medicinal Prospects

Factors such as pharmacokinetics, safety, and efficacy can all be taken into account by AI algorithms when analysing and optimising drug candidates. This aids in the fine tuning of medicinal compounds by researchers to maximise their efficacy and minimise any drawbacks.

De Novo Drug Design

AI systems are able to suggest new chemical compounds that resemble drugs by utilising generative models and reinforcement learning. Artificial Intelligence (AI) broadens the chemical space and helps create novel therapeutic candidates by leveraging knowledge from chemical libraries and experimental data.

Using Drugs for New Purposes

AI methods are able to examine vast amounts of biomedical data in order to find medications that are currently on the market and may be useful in

treating various illnesses. AI streamlines and lowers the cost of the drug research process by repurposing current medications for novel applications.

Prediction of Toxicity

AI systems that examine the properties and chemical structures of molecules can forecast the toxicity of drugs. Trained on toxicology databases, machine learning algorithms are able to recognise potentially dangerous structural features or predict deleterious consequences. In clinical studies, this helps researchers minimise potential negative reactions and prioritise safer drugs. All things considered, the identification, optimisation, and creation of innovative therapeutic candidates may be sped up and streamlined with the use of AI in drug research and development, ultimately producing more effective and efficient drugs[20].

Target fishing (TF) in silico technique, for instance, is used in medicines to predict biological targets based on chemical structure. The information shown here is based on the biologically annotated data that is accessible in the chemical database. To further explore the mechanism of action and provide the target class information needed for efficient planning, a number of additional techniques were employed, including data mining and chemical structure docking. Combining cheminformatics tools with machine learning enabled the application of the target fishing technique in drug discovery. These two are utilised to gather in depth information about how to properly analyse complex structures and create unique therapeutic ingredients that will effectively cure complex disorders. The standard drug discovery procedures used by various companies are highly expensive since they entail a number of intricate steps that must be correctly completed, such as the identification and selection of the target proteins and a thorough understanding of the small molecules' mechanisms of action. The TF was used to expedite this procedure, which helped lower the overall cost of experiments during the drug development processes. With the aid of 3D descriptors, the reference molecules are utilised to predict the ligand target. This method was employed to determine diethylstilbestrol's strong binding ability, whereas the TF technique is frequently utilised to analyse monthly similarity scores and investigate the drug's phytopharmacology. This method is computational and proteomics based, with data points ranked according to how similar their data fusion is to therapeutic targets. It is also applied in the forecasting of possible toxicities for the ligand based drug development methodology. With the help of the TF, some crucial elements of the drug development and drug discovery phases are investigated. These elements include the identification and selection of novel targets, the prediction of phytopharmacological profiles, and the prediction of side effects related to novel therapeutic indications. In order to identify the target for these occurrences, the bioactive compound similarity to the unidentified molecule is applied. A number of medications, including methadone and loperamide, have been effectively characterised by the use of this technique; muscarinic, adrenergic, and neurokinin receptors have been identified as the drugs' respective targets [2,21,22,23,24,25,26,27,28,29]. With the application of AI models and tools, the field of drug development has made considerable strides. Table 2 provides a description of some of the most often used AI model tools for drug discovery. These are but a handful of the drug discovery tools that can be used with AI models. The discipline is developing quickly, and in an effort to speed up the identification of novel medications, new models and tools are always being created.

Table no 1 : Popular AI model tools used for drug discovery.

AI Model Tools	Summary
DeepChem	Deep learning models for molecular property prediction, virtual screening, and generative chemistry are among the many tools and models available in this open-source toolkit for drug discovery.
GENTRL (Generative Tensorial Reinforcement Learning)	generative chemistry and reinforcement learning combined in a deep learning model to create new compounds with desired features. De novo medication design and optimization have been accomplished with its help.
RDKit	popular free and open-source cheminformatics library with several features for manipulating molecules, finding substructures, and calculating descriptors. For applications involving drug discovery, it can be used with machine learning frameworks.
ChemBERTa	An artificial language model created especially for activities related to drug research. Its capabilities include generating molecular structures, predicting characteristics, and aiding with lead optimization. It is built on the Transformer architecture and pretrained on a sizable corpus of chemical and biological literature.
GraphConv	a molecular graph-based deep learning model architecture. Utilizing the structural data included in the graph representation of molecules, it has proved successful in forecasting chemical attributes including bioactivity and toxicity.
IBM RXN for Chemistry	chemical reaction prediction using an artificial intelligence model. It helps in the development of new synthetic pathways and compound synthesis by generating possible reaction outcomes using deep learning algorithms and massive reaction databases.

Current State of Pharmaceuticals and AI's Role

Because tiny molecules have so many benefits, the pharmaceutical industry is always researching them to create better medicines and increase customer happiness. Simple chemical synthesis and inexpensive preparation of synthetic derivatives are the two aspects of this technique. Consequently, the pharmacy industry has a wide range of stable and effective small-molecule-loaded formulations. With the exception of treating uncommon diseases, generic molecules compete with numerous novel small molecules, and sophisticated data and clinical trials are necessary before they can be introduced to the market. The economic pressure to innovate increases as a result of these processes for businesses. Nonetheless, in order to make up for the crises brought on by tiny molecules and inadequate research and innovation dissemination, the biomolecular pharma sector is nonetheless expanding quickly. Their conformation and reactivity determine the effects of small molecules [30,31,32,33,34,35,36]. Nucleotides or ribonucleotides for the nucleic acid are typically found in biomolecules, which are big units, coupled with amino acids from the protein source. Both the spatial conformation and the supramolecular sequence impact their stability and function [37]. Adalimumab and insulin are two examples of highly effective biomolecules. Given that infusion is the most practical and preferred method of delivery for these biomolecules, the pharmacokinetic characteristics of these compounds are complicated. Two key facets of research using nucleic acids are pharmacokinetic modulation and molecular stabilisation. These molecular forms' pharmacokinetic exposure and improvement are essential objectives. In order to address these problems and find solutions, new technology advancements may be useful

[38,39,40,41,42, 43]. Despite the enormous potential that artificial intelligence (AI) offers for improving medicine delivery and discovery, AI currently has significant drawbacks that necessitate human intervention or the need for experts to understand the intricate outcomes. The datasets provide the basis of AI predictions, which contribute significantly. However, because of the grey area in the results, human interpretation is necessary to arrive at the correct conclusion. Algorithm bias can cause problems for AI when it comes to analysing data for predictions and evaluating theories. Furthermore, it frequently happens that molecules that are inactive are found by docking simulations [44]. To eliminate system bias concerns, human intervention is still necessary for a critical review of these characteristics in order to facilitate efficient decision making and cross-verifications. Nonetheless, there is a great deal of promise for applications of AI, therefore more work may be able to lessen the obstacles in the way of making AI dependable and productive [45]. When it comes to artificial intelligence, the approach that is used makes use of machine learning or some of its subsets, such deep learning and natural language processing. 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 (features) and outputs (labels or targets) 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 groupings [46].

Supervised AI Learning

A sort of machine learning known as "supervised learning" involves training an algorithm on a labelled dataset with an already known desired outcome. By examining the patterns and connections found in the labelled data, the algorithm gains the ability to translate input data into the appropriate output. This method is frequently applied in many different fields, including predictive modelling, natural language processing, and picture recognition. Task driven strategies entail establishing precise objectives to attain desired results from a specified set of inputs. This method trains algorithms for tasks like outcome predictions and data categorization using labelled data. Classification (i.e., label prediction) and regression (i.e., quantity prediction) are the two most common supervised learning problems. Depending on the type of data in a particular problem domain, supervised learning problems can be solved using a variety of approaches. Naïve Bayes, K-nearest neighbours, support vector machines, random forest, ensemble learning, linear regression, support vector regression, and other methods are some of these approaches [47]. As outlined below, it has a number of uses in the pharmaceutical sector:

1. **Drug Design and Discovery:**

The features or activities of novel drug candidates can be predicted through the application of supervised learning algorithms. The model may identify patterns and connections between desired outcomes and molecular properties by training on a dataset of known substances and the actions that go along with them. This helps in drug discovery and design by making it possible to anticipate the activity, potency, or toxicity of novel molecules [48].

2. **Drug Design and Discovery:**

The features or activities of novel drug candidates can be predicted through the application of supervised learning algorithms. The model may identify patterns and connections between desired outcomes and molecular properties by training on a dataset of known substances and the actions that go along with them. This helps in drug discovery

and design by making it possible to anticipate the activity, potency, or toxicity of novel molecules [48].

3. **Quality Control and Predictive Maintenance:**

Supervised learning can be applied to pharmaceutical manufacturing to support both quality control and predictive maintenance. The model can be trained on manufacturing process data, equipment sensor data, or quality testing results to forecast equipment failure, process anomalies, or deviations in product quality. This enables proactive maintenance and quality assurance [49].

4. **Finding Potential Drug Targets:**

By examining biological data, supervised learning algorithms can assist in finding possible drug targets. Training the model on data pertaining to genomic, proteomic, or transcriptomic markers and their correlation with treatment response or illness development enables it to recognise trends and pinpoint possible targets for more research [50].

5. **Diagnose and Prognosis of Diseases:**

Based on medical data, supervised learning models can be used to diagnose diseases or forecast patient outcomes. The model can be trained to predict therapy response or illness progression, or to classify patients into distinct disease groups using labelled datasets containing patient characteristics, clinical data, and disease outcomes [51].

6. **Detection of Adverse Events:**

Pharmacovigilance data can be used to identify and categorise adverse events linked to medications through the use of supervised learning algorithms. The model can be trained using labelled adverse event data to find patterns and identify potential safety signals, which will aid in adverse event characterisation and detection [52].

7. Clinical Trial Predictive Modelling: Clinical trial results can be predicted through the application of supervised learning. The model can learn to predict patient response, treatment efficacy, or safety outcomes by training on historical clinical trial data, which includes patient characteristics, treatment interventions, and trial outcomes. Optimising patient selection and trial design can be achieved with the help of this information [51].

Unsupervised AI Learning

Unsupervised learning is a kind of machine learning in which labelled data is not given to the algorithm. Rather, it has to work on its own to find patterns and connections in the data. This method can be helpful in identifying hidden structures or clusters within a dataset and is frequently applied in exploratory data analysis. The methodology being discussed is referred to as a "data-driven methodology," and its goal is to identify patterns, structures, or insights in unannotated data. Finding association rules, visualising data, dimensionality reduction, grouping, and anomaly detection are a few common unsupervised tasks. Well-liked methods for handling a variety of unsupervised learning tasks include clustering algorithms (e.g., K-means, K-medoids, single linkage, complete linkage, BOTS), association learning algorithms, and feature selection and extraction methods (e.g., Pearson correlation, principal component analysis) depending on the properties of the data [53,54]. Pharmaceutical applications can benefit greatly from unsupervised learning approaches in AI, especially in the areas of exploratory analysis, pattern recognition, and data visualisation, as will be discussed below

1. **Clustering:**

Algorithms for clustering data points together according to their shared characteristics enable the discovery of organic groups or clusters within the data. To identify groupings with comparable

traits, clustering can be used in pharmaceutical applications on a variety of datasets, including gene expression profiles, chemical structures, and patient data. This can help discover different types of substances or disorders, as well as targets and patients to stratify [55]

2. Dimensionality reduction:

High-dimensional datasets can be made less complex while retaining significant information by using techniques like principal component analysis (PCA) and t-distributed stochastic neighbour embedding (t-SNE). These techniques can assist in the identification of important variables or features, the visualisation and exploration of complicated datasets, and the support of decision-making processes. Pharmaceutical data of all kinds, such as gene expression data, drug activity profiles, or imaging data, can benefit from dimensionality reduction [56].

3. Algorithms for anomaly detection are used to find uncommon or rare data points that drastically diverge from the predicted trends. Anomaly detection is a valuable tool in the pharmaceutical sector that can be used to find problems with data quality, identify potential safety concerns, and discover adverse events. The local outlier factor (LOF) and isolation forest are two unsupervised anomaly detection methods that can be used to identify anomalous patterns or data points that need more examination [57].

4. Association Rule Mining:

Approaches to association rule mining, like the Apriori algorithm, seek to identify intriguing connections or links among the objects in a collection. Drug-drug interactions, adverse event data, and co-occurrence patterns between medical problems and drugs are among the pharmaceutical contexts where association rule mining finds application. Through the identification of medication patterns, pharmacovigilance activities, and insights into possible drug interactions, these strategies can be helpful [58].

5. Topic Modelling:

From big text datasets, latent topics or themes are extracted using topic modelling methods like latent Dirichlet allocation (LDA). Topic modelling is a useful tool in the pharmaceutical industry for identifying important research themes, new trends, or patient sentiments from analysis of clinical trial reports, scientific literature, and social media data. Understanding patient views, competitive intelligence, and literature mining can all benefit from this [59,60]. In pharmaceutical applications, unsupervised learning approaches provide insightful information and exploratory analysis. To extract actionable knowledge and guarantee the validity of the results, it is crucial to keep in mind that the interpretation of results from unsupervised learning techniques frequently calls for domain expertise and further validation.

Table no 2 : list of commonly used AI models in the pharmaceutical industry.

AI/Machine Learning Models	Description/Usage	References
Generative Adversarial Networks (GANs)	In order to produce unique chemical compounds and optimise their attributes, GANs are commonly used in the creation of medicinal products. GANs produce novel compounds by combining a generator network that generates them with a discriminator network that assesses their quality. This process produces a large pool of structurally and functionally varied therapeutic candidates.	[61]

Recurrent Neural Networks (RNNs)	In drug development, RNNs are frequently used for sequence-based tasks such peptide sequence design, genomic data analysis, and protein structure prediction. They are able to produce new sequences based on patterns they have learned and grasp sequential interdependence.	[62]
Convolutional Neural Networks (CNNs)	CNNs work well for image-based applications like finding possible drug targets and analysing chemical structures. They can help with target discovery and drug design by extracting pertinent information from molecular pictures.	[63]
Long Short-Term Memory Networks (LSTMs)	A kind of RNN that is particularly good at modelling and forecasting temporal relationships is called an LSTM. They have been utilised to forecast drug concentration-time profiles and assess medication efficacy in pharmacokinetics and pharmacodynamics research.	[64]
Transformer Models	Pharmaceutical natural language processing problems have made use of transformer models, including the well-known BERT (Bidirectional Encoder Representations from Transformers). They let researchers to make well-informed judgements about medication development by extracting valuable information from databases of patents, clinical trial data, and scientific literature.	[65]

Dosage Form Designs Using AI Tools

A number of compartments within the human body are used to analyse the effects of drug administration. The biological membranes serve as a basis for additional compartment simplification. Physical-chemical barriers are essential for biological compartments and can be applied in accordance with the body's internal drug delivery system. The rate of penetration based on the route of administration is one of the most important requirements for effective drug delivery system Based on the drug's molecular characteristics, passive diffusion occurs. Drug distribution is predicted using in silico models and computational monitoring. The medication taken orally needs to penetrate the intestinal or gastric epithelium in order to enter the stomach environment. The drug's continued bloodstream dispersion depends on this phase. The medicine is delivered to the target site which may be tissue or any of the particular cellular components during the distribution step [66,67,68,69,70,71]. Drugs can also enter the body through intracellular molecules as targets. Biological barriers, whether they are active or passive, aid in the majority of drug penetration.

analysis; however, the outcomes deviate slightly from the real drug distribution study. The way a

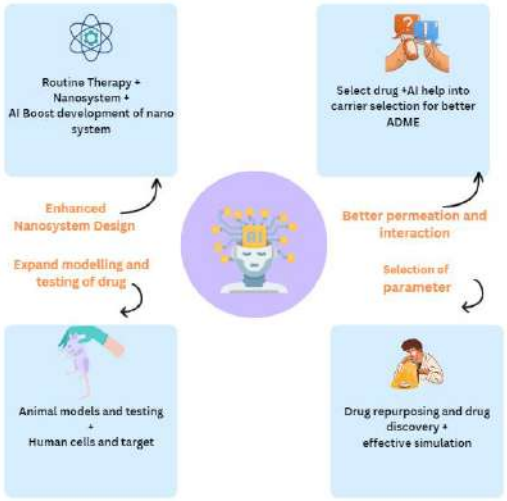

Figure.3: AI's contribution to pharmaceutical research and development. AI has the potential to improve the design of nanosystems, extend the current modeling system for drug testing, and improve the precision of parameter and factor selection in drug design, drug discovery, and drug repurposing techniques. Studying drug permeation, simulation, human cell targets, and other related topics aids in improving our understanding of the mechanics of membrane interaction with the simulated human environment.

medication behaves in the body is greatly influenced by its interactions with biological elements and its accessibility in biological settings. The molecular characteristics of the medication control this process. Passive permeation is ineffective for many tiny molecules and physiologically active substances, necessitating the use of a particular drug delivery mechanism. Membrane transport drives the process of active permeation, which is dependent on intricate biological interactions. Through computation and methodical modelling techniques, this intricate process needs to be investigated utilising a wide range of precise characteristics. The pharmacokinetic characteristics of the drug delivery system are investigated using this more recent computational model. The predictability of preclinical models is one of the main gaps in the research and development of the pharmacy sector. Predictability is predicated on the parameters used, and complicated in silico models are no exception. As shown in Figure 3, all of these situations are related to drug interactions with membranes and are best understood in the context of the modelled environment. AI allows for more efficient research and analysis of this simulated world[72,73,74,75]. AI offers cutting-edge technology for this kind of multilayer data processing. A deeper comprehension of the research units will result from the analysis's thoroughness. In order to get the best results, the methodically applied model and parameter evaluation are based on a variety of variables, including simulation, scoring, and refinement, at every stage of the research process. AI may be able to offer an automated system that can be used for all of these tasks, allowing for improved estimation and anticipated data refinement for continuous improvement. The system biology type of the databases indicates that a thorough understanding of the drug biological interaction is necessary for improved AI training in the biological environment. Artificial neural networks, among other cutting edge AI technologies, can be used to conduct pharmacokinetic investigations.In addition, AI

offers a plethora of resources, including phenotypic, chemical, and genomic databases, to facilitate the efficient investigation of the intricate unit roles of molecules inside drugs and to improve comprehension of drug interactions. In order to effectively comprehend the medication's disposition and toxicity, some of the methodologies are also used to investigate how the drug delivery system affects the drug's pharmacokinetics. Prior to conducting actual trials, many novel approaches to drug delivery systems entail designing quality features in addition to key attributes and analysing how they will affect the trials. AI has the advantage of gathering data from many sources and indicating whether the chosen drug delivery method is performing as expected. In order to pick the optimum active pharmaceutical to treat a patient's condition or meet their needs, it is necessary to analyse a comprehensive set of data, which includes patient, pharmacokinetic, and molecular information. The identification of molecular entity traits against those of known molecules for comparison is accomplished through the use of passive AI. The accuracy with which drug delivery methods are chosen which AI provides determines the efficacy of treatment. AI is beneficial for both the drug repurposing technique and the drug discovery process. This discusses how to adapt the current treatments to the new illness. Formulation, pharmacokinetics, and medication development are heavily influenced by the needs of the patient and the state of the disease. The availability of detailed information databases is a significant barrier when using AI to construct delivery systems. This is necessary for an impartial assessment of the models and their parameters. By utilising existing knowledge, AI supports applications in the future. Artificial Intelligence (AI) tools can handle and process massive amounts of data, improving the approach to the product's logical design.

AI in Drug Delivery

The pharmaceutics industry's adoption of AI and big data has given rise to computational pharmaceutics, a field that uses multiscale modelling techniques to improve medication delivery systems. In order to evaluate massive datasets and forecast medication behaviour, computational pharmaceutics uses AI algorithms and machine learning approaches (Table 3). Without the need for lengthy trial and error studies, researchers may assess multiple scenarios and optimise drug delivery systems by simulating the drug formulation and delivery processes. This shortens the time it takes to develop new drugs, lowers expenses, and boosts output. Drug delivery systems at many scales, from molecular interactions to macroscopic behaviour, are modelled in computational pharmaceutics.

In order to forecast drug behaviour at every scale, artificial intelligence systems are able to examine intricate correlations between formulation elements, physiological parameters, and drug qualities. This facilitates the design of effective drug delivery systems and enables a more thorough understanding of drug delivery mechanisms. It aids in forecasting the stability, in vitro drug release profile, and physicochemical characteristics of the medication. In vivo-in vitro correlation studies and improved evaluation of in vivo pharmacokinetic parameters and medication distribution are also conducted using the same method. Early in the development phase, researchers can detect possible dangers and difficulties related to drug delivery systems by employing the appropriate set of artificial intelligence techniques. This makes it possible to proactively make changes and adjustments to reduce risks and enhance the effectiveness of medications. The likelihood of unanticipated results is decreased when AI and computer modelling are used instead of costly and time-consuming trial and error trials [76,77].

AI in the Development of Oral Solid Dosage Forms

To develop human-like abilities, artificial intelligence (AI) uses sophisticated hardware and software. Many industries, including the pharmaceutical one, have benefited from this breakthrough in recent years, particularly during the product development stage. The time, money, and resources needed for production and efficient delivery to final consumers via the supply chain can be reduced by using these technical advancements. Furthermore, it offers an enhanced framework for comprehending how process characteristics affect product formulation and manufacture.The application of machine learning techniques to the prediction of solid dispersion stability over a six-month period was investigated by Run Han et al. Hanlu Gao et al. looked at using machine leaching in solid dispersion dissolving research. They created a classification model using a random forest algorithm, which aids in further differentiating between the parachute and spring forms of dissolution profiles. With 85.5 percent accuracy and 85.6 percent sensitivity, it also helped to sustain supersaturation. The regression model produced by the random forest technique served as the basis for the prediction of the time-dependent drug release [78]. Tablets are among the most widely used dosage forms in the pharmaceutical industry, which is dominated by solid dosage forms. Several elements, depending on the kind of tablet, go into tablet preparation. Searching for an optimal formulation and researching the desired features involved in it can be aided by AI. AI is also anticipated to handle duties using automated technologies and algorithms. Redefining current good manufacturing practice (cGMP) policies is a difficulty presented by the adoption of AI for regulatory bodies. A variety of artificial intelligence (AI) technologies, including neural networks, fuzzy logic, and artificial neural networks (ANNs), in addition to genetic algorithms, are used to design stable dosage forms and improve comprehension of the inputs and outputs for operations and processing. While evolutionary algorithms are used to forecast the outcomes of the utilisation of input parameters, artificial neural networks (ANNs) are utilised to improve prediction abilities for solid dosage forms [79]. Within the drug delivery segment, tablets are a widely utilised solid dose that hold a significant share of the market. This product is made by using excipients and active medicinal components, which are then compressed or moulded to take on the desired shape and size. To control the intended product outcome, such as medication release, dissolving, and tablet disintegration, a variety of excipients are added to tablets. The formulator has established these elements in order to cater to the particular requirements of the intended patient population.Certain excipients, such as lubricants and glideants, are necessary to make the production process easier. Predicting medication release in the context of systemic drug delivery is another application for AI. Furthermore, it is utilised to explore the impacts of critical processing factors that are essential to the production of tablets, with the aim of guaranteeing uniform quality control protocols. Some artificial intelligence applications have been employed to detect tablet malfunctions [80,81].

Table.3:List Of Commonly Used AI Models In Pharmaceutical Product Development.

AI/Machine Learning Models	Description/Usage	References
Artificial Neural	ANNs have been used to simulate and improve the kinetics of medication release from various dose forms. The best	[82]

Networks (ANNs)	formulations may be found with their help, and they can forecast how active pharmaceutical ingredients (APIs) will release under different circumstances.	
Genetic Algorithms	Natural selection and genetics serve as the foundation for genetic algorithms, which are optimization approaches. To obtain desired dosage form properties, they can be used to optimise drug release patterns, formulation compositions, and process parameters.	[83]
Support Vector Machines (SVMs)	In dosage form optimization, support vector machines (SVMs) have been employed to forecast and simulate the interactions between formulation factors, including drug release profiles, processing parameters, and excipient composition. They help make formulation design space more optimal.	[84]
Particle Swarm Optimization (PSO)	For dosage form optimization, PSO is a population-based optimization technique that can be applied. It has been used to optimise dissolution profiles, particle size distribution, and other formulation factors.	[85]
Artificial Intelligence-based Expert Systems	The decision-making process of human experts is simulated by expert systems through the use of AI techniques such as fuzzy logic and rule-based systems. By taking several formulation and process variables into account, they can be used for dosage form optimization.	[86]
Monte Carlo Simulation	Drug product performance has been optimized by taking uncertainty and variability in formulation and process parameters into account through the use of Monte Carlo simulation methods. They support the design of robust processes and their formulation.	[87]

Estimating Drug Release Using Formulations

There is no doubt that stable quality control may be achieved by drug release prediction. In vivo and in vitro techniques are used in drug release studies, and they are regarded as basic technologies that are routinely assessed or tested during the product development process. The contribution of important material qualities and processing parameters determine when the medicine is released from oral solid dosage forms. Compaction parameters, such as the pressure used to set tablet hardness, tablet geometry, and drug loading characteristics are some of the common factors affecting drug release. Drug release studies are typically necessary for comprehensive analysis, and a variety of analysis techniques, such as spectrophotometric analysis approaches, have been used. Setting the drug release results in accordance with the formulator's specifications necessitates repeated testing and batch preparation in order to produce an optimised batch, which is a laborious and time consuming process [88]. As a result, there are fewer runs needed to optimise the batch, which further reduces labour and expenses during pilot batch scale and production processes. AI is included into the drug formulation and will help forecast drug release. In order to effectively choose the best batch for additional large scale processing, AI can assist in predicting the drug release profiles, dissolution profiles, and exploration of the disintegration time. Artificial neural networks (ANNs) have been used by certain researchers to construct AI algorithms for the prediction of dissolution profiles into the hydrophilic matrix type of sustained-release tablets. When analysing the data and predicting the

dissolution profile, regression analysis and the support machine vector (SVM) are also used. Process analytical technology (PAT) was utilised in conjunction with important material properties to obtain data for the drug release modelling investigation. It was discovered that while predicting a model, the particle size distribution was the most important variable. Lastly, as part of the evaluation metrics, the ANN was used to identify the most correct models.

AI Implementation for Tablet Defect Identification

Pharmaceutical manufacturing quality control procedures have been transformed by the use of AI in tablet defect identification. Images of tablets are analysed using computer vision and artificial intelligence (AI) algorithms, making it possible to automatically and effectively identify flaws like chips, cracks, discolouration, or changes in size and shape. The system gains the ability to precisely classify and identify many sorts of faults, attaining high levels of recall and precision, by training AI models on massive datasets of labelled photos. Although the interior structure of tablets has been studied using conventional techniques like X-ray computed tomography, these techniques still take a lot of time and interfere with the need for quick tablet production. To find tablet flaws, X-ray tomography and deep learning are combined. Using image analysis performed using X-ray tomography, Ma et al. investigated the use of neural networks for tablet defect identification. These scientists combined mannitol with excipients like microcrystalline cellulose to produce many batches of tablets. Utilising an approach known as image augmentation, the created batches were examined. During the course of the same study, three distinct models were employed, one of which being UNetA, which may be utilised to differentiate tablet features from bottle characteristics. Supplementary analysis was utilised in Module 2 to identify specific pills. UNetB was utilised to analyse the internal cracks present in the internal structure of the tablet. Improved accuracy in tablet defect checking has been achieved by using UNet networks, which have led to significant time, cost, and workload savings in defect identification [89,90]. In addition to increasing fault identification speed and accuracy, this AI-powered detection lessens the need for manual inspection, which minimises human error and subjective assessment. Artificial intelligence (AI) systems possess real-time monitoring capabilities that guarantee the rapid identification of flaws, hence enabling timely intervention and averting the introduction of defective tablets into circulation. All things considered, the use of AI in tablet defect detection improves product quality, boosts output, and guarantees the security and effectiveness of pharmaceuticals.

AI for Physicochemical Stability Prediction

In pharmaceutical research, AI has shown to be a potent technique for forecasting the physicochemical stability of oral dosage forms. AI is able to evaluate and interpret vast datasets containing pharmacological qualities, formulation parameters, and environmental factors in order to forecast the stability of oral formulations. This is achieved by utilising machine learning methods and computer models. Artificial Intelligence models are capable of evaluating variables such medication deterioration, excipient interactions, and environmental impacts on formulation stability. By using these prediction tools, researchers can improve the efficacy and shelf life of oral dosage forms by identifying possible stability problems early in the development process, optimising formulation designs, and making well informed judgements. By using AI to forecast stability, stability research procedures become more productive and economical, which eventually results in the production of safe and effective medication.Using various techniques,

some researchers have investigated the application of machine learning for solid dispersion determination. In order to investigate the use of machine learning for solid dispersion prediction, Han et al. implemented ANN in conjunction with KNN algorithms and a light gradient boosting machine (LightGBM). The SVM was also used in this manner. A nonparametric kind of supervised learning classifier is called a KNN. It was used to the individual data point as well as the grouping in order to categorise or finish the predictions [91]. LightGBM is an open-source and free distributed gradient boosting framework that uses machine learning. It is typically applied to machine learning activities as well as classification and assessment rating. About fifty medicinal compounds with 646 data points for physical stability were taken from the public database for this investigation and used to build the training model. Molecular representations, molecular descriptors (e.g., molecular weight), and the count of hydrogen bond acceptors were used in the database development process. Moreover, the melting point and heavy atom count served as molecular descriptors. An accelerated stability study was carried out over a period of three months in order to further assess the model's performance in relation to the physical stability forecast. For the same experiments, they found an overall accuracy of 82% [92,93].

Application of AI to Mucosal, Parenteral, and Transdermal Route Products

AI can be used in the development and production of biologics, injectables, and other complex formulations. composition development may be aided by the use of AI systems to predict complex physicochemical aspects of medication composition. AI models evaluate manufacturing procedures, excipients, formulation ingredients, and stability to optimise pH, solubility, stability, and viscosity. As a result, parenteral formulations become more stable. Parenteral product production can be optimised using AI in terms of quality, efficiency, and variability. Through the analysis of real-time process data, AI algorithms can identify aspects related to the process that impact the quality of the product and propose suitable improvements. Productivity in production increases as a result, as do batch failures and product uniformity. Huge datasets from analytical testing, such as particle size analysis, spectroscopy, and chromatography, may contain trends and variances in product quality that can be discovered by AI algorithms. This promotes the early detection and correction of quality issues, guaranteeing high quality products. Using past data and process variables, AI models may predict contamination, stability, and regulatory deviations. During the production of parenteral products, AI based monitoring systems may evaluate crucial process parameters in real time. Utilising information from sensors, instruments, and process controls, AI algorithms may detect anomalies, predict deviations, and respond quickly. In addition to minimising noncompliance, this preserves product quality. Artificial Intelligence optimises parenteral product production equipment maintenance operations. To anticipate equipment failure or deterioration and plan proactive maintenance, artificial intelligence (AI) models examine sensor data, equipment performance history, and maintenance records. This increases productivity, reduces maintenance, and eliminates needless downtime.AI can support regulatory compliance for parenteral and complicated biological products. Process data and product attributes can be analysed by AI algorithms to assess compliance, identify potential noncompliance issues, and generate recommendations for process improvement. This supports regulatory and GMP compliance [94]. To determine if the particles were swimming, sinking, or sticking into the inner side of the container, for instance, AI was utilised in the particle inspection

process. The optical setup, strategy, algorithm, and inspection were advised in order to properly inspect each individual particle. To analyse the floating particles, the particle tracking technique was applied in conjunction with image removal. Liquid inside the container is allowed to flow, allowing high-resolution photos to capture the behaviour of the moving particles and tracing the direction of the particles' movement using AI. Appropriate partical separation is another application of the deep learning method. The production of bubbles, which are typically not dangerous to patients but require careful distinction between particles and bubbles, is one of the more serious problems related to parenteral batch defects. The algorithms utilised for these kinds of visual inspections and the problems they raised were AI-based image processing algorithms. Using surface qualifies 7500, which analyses hundreds of millions of data points per second with the aid of graphics processing modules, surface crack detection is one of the other camera-based applications of artificial intelligence [94,95,96,97,98]. By utilising AI data analysis, pattern recognition, and predictive modelling, manufacturers can enhance product performance, reduce production hazards, and produce parenteral pharmaceutical solutions that are safe and effective as well as technologically advanced. In the fields of pharmaceuticals and materials science, Bannigan et al. emphasise the availability and promise of state of the art machine learning (ML) technology. They show that by precisely forecasting in vitro drug release from long acting injectables (LAIs), machine learning (ML) can hasten the development of novel drug delivery systems. The study highlights how interpretable machine learning models are and how they might shed light on the decision making process. Tree based models, like LGBM, showed promise in cutting down on the time and expense involved in developing LAI formulations, even though neural network models underperformed because of the limited dataset. As a proof of concept for machine learning in medication formulation, the study aims to stimulate future research on more sophisticated and customised ML techniques [99,100]. For complicated formulations, the traditional trial and error method of developing pulmonary, transdermal, ocular, and other mucosal drug delivery systems is ineffective due to a lack of thorough understanding. Nonetheless, new opportunities have emerged due to recent developments in computational pharmaceutics, particularly in the areas of machine learning and multiscale simulations. Product development has become more effective as a result of recent advancements in the use of PK/PD modelling, mathematical modelling, and molecular simulations for various drug delivery methods. Because they provide thorough insights and facilitate logical formulation design, in silico modelling and simulations have special benefits. In the Pharma 4.0 age, integrating in silico approaches, resolving data hurdles, and interdisciplinary collaborations can result in more effective and goal oriented drug formulation design [101,102,103,104].

AI in Medical Devices

A medical device is any type of apparatus, implement, instrument, machine, appliance, or reagent used for certain medical purposes. It can be used in vitro to treat patients' medical problems on its own or in conjunction with software or other relevant systems. AI has significantly advanced the field of medical devices, revolutionising healthcare in a number of ways. The epidemic has increased the need for and popularity of remote health monitoring and personalised medicine in many nations, which has led to an increase in the use of AI and machine learning in the healthcare industry. The following is a description of several instances of AI being used in medical devices:

1. **Diagnostic Support:**

AI systems are able to examine data from medical imaging tests, like MRIs, CT scans, and X-rays, to help doctor diagnose and identify illnesses. For instance, malignant tumours in medical photos or anomalies in electrocardiograms (ECGs) can be identified with the use of AI powered algorithms [105].

2. **Remote Monitoring:**

Artificial intelligence enabled medical equipment can keep an eye on patients' health from a distance, tracking vital signs and other pertinent data continuously. Patients with chronic diseases can benefit most from this as they can receive individualised care in the comfort of their own homes. AI systems are able to examine the gathered data and give healthcare professionals notifications or insights [106].

3. Wearables:

Biosensors, fitness trackers, and smartwatches are examples of wearable technology that incorporates AI. Heart rate, sleep patterns, physical activity, and blood glucose levels are just a few of the health factors that these devices can track. In order to give users useful insights for enhancing their health and well being, AI algorithms assist in analysing the data [107].

4. **Rehabilitation and prosthetics:**

AI is applied in cutting-edge prosthetic devices to provide more natural movement and functionality. Through the application of machine learning algorithms, prosthetics can be adjusted to better match the user's intents by learning from their movements. By evaluating motion and giving patients feedback to help them move better and monitor their progress, AI can also help with rehabilitation [108]. In order to improve patient care, monitoring, diagnosis, and treatment, these examples show how AI is incorporated into medical devices. Precision in diagnosis, better treatment outcomes, and enhanced overall healthcare delivery are all facilitated by AI's capacity to analyse vast volumes of data, spot trends, and offer tailored insights. Furthermore, it helps in the creation of novel goods that benefit patients and in successfully attracting new clientele to attract major corporations and expand the healthcare industry's commercial potential. Personalised medicine for patients and other important industries are among the current uses of AI by medical technology businesses. These include diagnosis, prevention, and care.

AI in Pharmacodynamics and Pharmacokinetics

Drug discovery, preclinical research, clinical trials, and regulatory approval are just a few of the many steps in the intricate process of developing new drugs. Since they establish the ideal dosage, mode of administration, and safety of a medicine in the body, pharmacokinetics and pharmacodynamics are essential components of drug development [85]. For pharmacokinetics and pharmacodynamics research, traditional experimental techniques can be costly and time-consuming, and they might not always yield reliable estimates of the safety and efficacy of drugs[109, 110]. Studies on pharmacokinetics and pharmacodynamics have often been carried out through experimental techniques including animal research and human clinical trials. Important issues with these methodologies include sample size, interindividual variability, and ethical considerations. Furthermore, it's possible that these studies don't always yield precise estimates of the pharmacokinetics and pharmacodynamics of drugs in humans. Computational models and artificial intelligence (AI) techniques have been created to overcome these constraints and forecast drug pharmacokinetics and pharmacodynamics more accurately, quickly, and affordably[111,112].In the domains of pharmacokinetics, pharmacodynamics, and drug discovery, artificial intelligence has demonstrated enormous promise [113]. AI has become a useful tool for forecasting and improving drug

pharmacokinetics and pharmacodynamics with the development of robust computing and machine learning techniques. AI can open new avenues for PKPD studies and their implications for treatment, even though the difficulties associated with massive data and trustworthy datasets are difficult to
ignore[113,114,115,116,117].

Pharmacokinetic Parameter Prediction Using AI-Based Techniques

Pharmacokinetic parameter prediction is one area where machine learning (ML) and deep learning (DL) algorithms are widely used. To predict drug absorption, distribution, metabolism, and excretion (ADME) characteristics, a number of machine learning (ML) techniques have been used, including the Bayesian model, random forest, support vector machine, artificial neural network, and decision tree. Convolutional neural networks (CNNs), long short-term memory (LSTM), and recurrent neural networks (RNNs) are three examples of DL algorithms that are frequently used in the prediction of drug absorption, bioavailability, clearance, volume of distribution, and half-life, among other pharmacokinetic parameters. A computational method called the quantitative structure-activity relationship (QSAR) uses a molecule's chemical structure to predict its biobiological activity. This technique has been used to pharmacokinetics, where it can be used to predict the ADME characteristics of drugs[92,118,119,120,121].

AI Based Computing Technique for PBPK

Drug distribution and clearance in the body are frequently simulated using PBPK models. These models are sophisticated, and creating them calls for a large amount of data as well as computer power. AI based techniques can streamline the creation of PBPK models by identifying the most pertinent model elements through the use of machine learning algorithms (Table 4). In order to minimise the necessity for animal research and human clinical trials, AI based computational techniques can also optimise the PBPK model's parameters [122,123,124]. Pharmacokinetic characteristics of pharmacological molecules play a major role in determining their safety and efficacy. The duration of the drug's active ingredient in the body determines its safety, but the drug's dosage is determined by how quickly the ingredient leaves the body. As a result, in vivo exposure is a crucial tool for evaluating the safety and effectiveness of drugs. Prior to conducting clinical trials, the medication discovery and development process entails assessment and evaluation. The main contributors to compound attrition in the development of therapeutic compounds are absorption, distribution, metabolism, and elimination (ADME). In vivo pharmacokinetic studies are conducted in animals as part of drug discovery research, and human subjects are studied in vitro in addition to animal subjects. To maximise the drug's exposure to people, the first method of dosage is applied. Hepatocytes and liver microsomes undergo both in vitro and in vivo extrapolations. Studies involving human and animal subjects' liver microsomes are conducted in vitro, whereas hepatic clearance is carried out through in vivo protocols. Using in vivo preclinical data and allometric scaling techniques, the human pharmacokinetic parameters are computed. The same technique is also used to assess drug clearance, bioavailability, and volume of distribution. With the help of PBPK modelling and the mathematical framework, the time course and ADME properties are simulated. Typically, these are utilised in the final phases of drug research to comprehend in vivo behaviour and extrapolate it to humans. Because in vivo data are more complex than in vitro pharmacokinetic parameters, artificial intelligence (AI) and machine learning (ML) are used in their analysis and evaluation [125].

Estimating the Parameters of Drug Release and Absorption

Drug release and absorption parameters have been effectively predicted by using AI-based models. Artificial intelligence algorithms are capable of predicting the release kinetics of pharmaceuticals by analysing data from different drug delivery methods. AI models can estimate the rate and extent of drug release over time by taking into account variables such the drug's physicochemical properties, formulation features, and delivery system release mechanism. Additionally, the release kinetics of medications from various drug delivery methods, including oral tablets, transdermal patches, and inhalers, can be predicted using AI based models [126]. The absorption rate and bioavailability of drugs can be predicted by AI-based models that take into account the features of the drug's formulation, permeability, and solubility. To predict the effectiveness of medication absorption into the bloodstream, these models can evaluate the physicochemical characteristics of the drug, such as lipophilicity and molecular weight, and connect them with absorption data. All things considered, drug release and absorption parameters can be effectively predicted using AI based models. These models can help create more efficient drug delivery systems, lead drug development decisions, and optimise drug formulations by utilising machine learning algorithms and analysing a variety of aspects[119,120,121,122,123,124,127].

Estimating the Parameters of Drug Metabolism and Excretion

Drug pharmacokinetics can be better understood by using AI based models, which have shown to be useful in forecasting drug metabolism and excretion parameters. Drug metabolism can be predicted by AI algorithms by examining the physicochemical and molecular structures of the medications. AI models can recognise structural elements linked to particular metabolic transformations by training on extensive datasets of known drug metabolism data. These models give information about the main enzymes involved in drug metabolism and allow for the prediction of possible metabolites[128]. Drug metabolism can be estimated by using AI based models that compute enzyme kinetics, including reaction rates and interactions between the enzyme and the substrate. Artificial intelligence models can evaluate the possible influence of metabolism on drug clearance and efficacy by taking into account variables including genetic differences, enzyme expression levels, and drug-drug interactions. Predicting possible drug interactions and optimising drug dosage regimes can both benefit from this information [129]. Drug physicochemical characteristics, such as molecular weight, lipophilicity, and ionisation, can be analysed by AI systems to forecast drug clearance rates. AI models can calculate the pace at which medications are removed from the body by training on datasets that contain data on drug clearance pathways. This data is essential for choosing the right dosage schedules and guaranteeing the safety and effectiveness of medications [130]. AI algorithms have the ability to forecast how drugs will interact with transporters that are involved in metabolism, excretion, distribution, and absorption. AI models evaluate the possibility of drug–drug interactions or changed pharmacokinetics as a result of transporter intermediated effects by taking into account the physicochemical parameters of the drug and the features of the transporter. This information is helpful in figuring out how drugs behave and how best to formulate them [131,132,133,134]. These models aid in the prediction of a drug's fate in the body by employing artificial intelligence algorithms to analyse enormous volumes of data on drug excretion and metabolism. They support the

development of safer and more efficient pharmaceuticals as well as the optimisation of drug dosage and identification of possible drug interactions. Furthermore, by prioritising drug candidates according to their anticipated metabolic and excretion profiles, researchers and pharmaceutical corporations can make drug development procedures more efficient. This is made possible by AI models.

Table.4: PKPD study-specific algorithms and their benefits and drawbacks that were utilised in the creation of AI models.

Algorithm/Software	Aim/Target	Advantage	Limitation	PK/PD/Both	Reference
Bayesian/WinBUGS	To manage information below the quantifiable limit	For model-fitting, previous data from the literature can be used directly, Simple to use.	extended computation time, negative data that cannot exist in some PK/PD model.	Both	[135]
Bayesian/PKBUGS (v 1.1)/WinBUGS (v 1.3)	Pharmacokinetic evaluation of data on sirolimus concentrations for therapeutic medication surveillance	Integrating historical data with current data is simple. Finding potential relationships between covariates	Few datasets and inadequately informative data	PK	[136]
Support Vector Machine/Least Square-SVM	Analyzing a sample drug's concentration according to each patient's unique characteristics	With a unique model for each new patient, In order to forecast drug concentration, SVM-based methods outperform PK modelling.	Sample outliers have a significant impact on the model, reducing its accuracy	PK	[137]
XGBoost	Calculating the medication area under the curve (AUC) for mycophenolate mofetil (MMF) or tacrolimus	Accurate predictions were made using pharmacokinetic (PK) records from individuals undergoing liver, heart, and kidney transplants.	The chance of target attainment and appropriate dosing cannot be calculated.	Pk	[138,139]
Drug Target Interaction Convolutional	determining the interactions between drugs and their targets	Time-saving Cost-effective	Large datasets are required	PD	[140]

Neural Network (DTICNN)	and forecasting possible pharmacological compounds.				

Limitations of AI Applications

Though AI based models are beneficial, they have several drawbacks as well, like the requirement for huge datasets, potential biases, and interpretability issues. As such, to guarantee the efficacy and safety of medications, AI based models ought to be employed in conjunction with conventional experimental techniques. The following highlights a few of the drawbacks:

Insufficient Transparency

Because it is challenging to comprehend how an artificial intelligence (AI) model makes predictions, it is commonly referred to as a "black box" and uses intricate algorithms. Gaining regulatory approval for AI based drug development tools may be difficult due to this lack of transparency, as it may be difficult to prove that the model is producing trustworthy and accurate predictions. Moreover, when a model's predictions don't align with researchers' or doctors' expectations, a lack of openness may also contribute to a loss of confidence in the model's predictions [141,142].

Restricted Data Availability

For AI models to make accurate predictions, a substantial amount of data is needed. But occasionally, there might not be enough information available for a specific medication or group, which could produce biased or less accurate conclusions. For example, establishing AI models for rare diseases may face considerable challenges due to limited data availability. Furthermore, outcomes from AI models may be skewed if the data utilised to train them is not representative of the target population. Furthermore, not all data types are easily accessible, such as real world evidence or longitudinal data, which can restrict the use of AI models. These restrictions show how important it is to carefully assess the representativeness and quality of the data utilised to develop AI model.

Limited Capacity to Explain Variability

Large datasets are often used to train AI models, yet these datasets may have biases towards the average responses seen in the data. Therefore, for those who differ greatly from the average reaction, the models might not be able to predict medication responses with any degree of accuracy. This is especially troubling for medications that cause a wide range of responses in various patients (like cancer), where the variability might be substantial [143].

Result Interpretation

Even for professionals in the area, AI models can produce outputs that are challenging to understand due to their complexity. Clinicians and researchers may find it difficult to comprehend and interpret the results if the models are unable to clearly explain how they came to their conclusions. It could occasionally be challenging to interpret the data into useful information for medication development or clinical practice. Further limiting their use is the possibility that using AI models may demand a technical proficiency that not all researchers and practitioners possess. Improved interpretability and explainability of AI models are therefore required [144,145].

Ethical Considerations

The application of AI in medication development raises ethical questions, as it does with any other use of the technology. Since AI models frequently employ sensitive health data for training, one important worry is patient privacy. Data security and safety are important factors that need to be taken seriously and are not to be disregarded. Ensuring the collection and utilisation of patient

data in a manner that upholds their rights and preserves their privacy is crucial. When employing AI for medication development, data ownership raises additional ethical issues. It may not always be evident who owns the data or has the right to use it when information is obtained from patients without their express consent. Conflicts between researchers, patients, and pharmaceutical firms may result from this [146,147]. To successfully incorporate AI into medication research, regulatory bodies are entrusted with creating strict standards, methods, and uniform review procedures. The ethical concerns of patient safety and animal welfare should be included in these measures, among other factors. Because animal testing is essential to the drug development process, it is imperative that efforts be made to minimise, improve, and replace animal models whenever possible in order to uphold ethical standards. AI models need to be thoroughly validated and tested in order to assure their accuracy and dependability, with patient safety being the top priority. The publishing of the FDA discussion paper, "Using Artificial Intelligence & Machine Learning in the Development of Drug and Biological Products," is a significant step towards addressing the ethical and regulatory implications of AI in drug research. An overview of AI's application in clinical, nonclinical, and drug discovery research is given in this document. It also provides guidelines for the best ways to use AI and machine learning. This FDA move opens up new avenues for the healthcare industry and represents a significant turning point in the regulation of AI use in that field. It establishes the foundation for upcoming regulatory developments in drug development by indicating the acknowledgement of the possible advantages and difficulties related to AI in the domain [148].

FUTURISTIC OVERVIEW

In the future, AI may completely transform the pharmaceutical sector by accelerating the search for new drugs and their development. Lead compound identification will be accelerated by the use of virtual screening tools, which will quickly evaluate massive chemical libraries and identify therapeutic candidates with the necessary properties. With the use of AI, precise medicine might analyse patient histories, proteomes, and genomes to classify patients, forecast treatment outcomes, and personalise medication regimens. By applying deep learning and generative models, researchers can produce novel molecules with target-binding properties that increase drug efficacy and decrease side effects. AI will also make patient specific dosage formulations possible. In order to improve treatment outcomes, AI algorithms will optimise medication compositions and distribution strategies by taking into account patient specific factors including age, weight, genetics, and sickness state. By forecasting the toxicity and side effects of potential drugs, AI systems will transform the process of evaluating safety. Monitoring devices with AI capabilities will enable remote patient care and medication adherence. In order to provide more individualised treatment and improved compliance, wearable technology and sensors will continuously collect data. AI enhances patient recruitment, selection, and trial design. Biomarkers, genetic profiles, and electronic health data will all be used by AI algorithms to identify suitable individuals, reduce trial costs, and expedite approval. AI models will optimise continuous production operations by monitoring and controlling key parameters in real time. AI algorithms will use data analysis and feedback to make pharmaceutical manufacturing more consistent and effective. In order to support regulatory choices, AI will analyse vast volumes of data. It will help regulatory agencies approve medications more quickly and increase safety. From diagnosis to clinical risk prediction and triage, artificial intelligence is being used in more

and more areas of healthcare on a regular basis [149,150]. Artificial Intelligence (AI) in clinical settings may improve healthcare efficiency and diagnosis accuracy. Research & development for pharmaceuticals consumes enormous amounts of time and resources, thus new approaches and strategies must be used [151]. Large scale opportunities in the medical field are being made possible by artificial intelligence. These include the ability to analyse large amounts of multivariate data, solve complex problems related to the development of workable medication delivery systems, make decisions with greater accuracy, categorise diseases, optimise dosage ratios, develop drugs quickly, predict drug bioactivities and interactions, cellular response, the efficacy of combination medications, treatment outcomes, and ma As every section has shown, artificial intelligence (AI) and machine learning hold great promise for transforming medicine delivery and enhancing the efficacy of treatments for infectious diseases. As fascinating as the possibilities this futuristic picture offers, it's crucial to understand that before AI's full potential in pharmaceutical product development can be realised, issues with data quality, regulatory frameworks, and ethical standards must be resolved. In the future, though, AI driven technologies have the potential to transform the pharmaceutical sector and enhance patient outcomes through ongoing improvements and partnerships between industry, academia, and regulatory agencies.

CONCLUSION

Drug delivery technologies are changing as a result of artificial intelligence, making personalised, adaptive, and targeted medicines possible. Pharmaceutical researchers and healthcare professionals can maximise medicine efficaciousness, reduce side effects, and improve patient outcomes by utilising AI's strengths in data analysis, pattern identification, and optimisation. Pharmacokinetics and pharmacodynamics have seen a transformation thanks to AI-based techniques. Compared to conventional experimental approaches, they have a number of benefits. Artificial intelligence-based models are capable of forecasting pharmacokinetic parameters, simulating drug distribution and clearance throughout the body, and optimising therapeutic dosage and delivery methods. Animal research and human clinical trials may not be as necessary with the use of AI-based computational techniques for PBPK models, which can streamline the creation of such models and optimise their parameters.With the help of artificial intelligence (AI) and big data, computational pharmaceutics transforms the drug distribution process by offering a more effective, economical, and data-driven method. It makes it possible to optimise medication formulations, customise treatments, comply with regulations, and minimise risk, all of which eventually result in better drug manufacturing procedures and better patient outcomes. All things considered, the use of AI technologies has enormous potential to expedite medication development, enhance patient outcomes, and completely transform the pharmaceutical sector.

REFERENCES:

1. Krikorian G., Torreele E. We Cannot Win the Access to Medicines Struggle Using the Same Thinking That Causes the Chronic Access Crisis. Health Hum. Rights. 2021;23:119–127. [PMC free article] [PubMed] [Google Scholar]
2. Chavda V.P., Vihol D., Patel A., Redwan E.M., Uversky V.N. Bioinformatics Tools for Pharmaceutical Drug Product Development. John Wiley & Sons, Ltd.; Hoboken, NJ, USA: 2023. Introduction to Bioinformatics, AI, and ML for Pharmaceuticals; pp. 1–18. [Google Scholar]
3. Scannell J.W., Blanckley A., Boldon H., Warrington B. Diagnosing the Decline in

Pharmaceutical R&D Efficiency. Nat. Rev. Drug Discov. 2012;11:191–200. doi: 10.1038/nrd3681. [PubMed] [CrossRef] [Google Scholar]
4. Munos B. Lessons from 60 Years of Pharmaceutical Innovation. Nat. Rev. Drug Discov. 2009;8:959–968. doi: 10.1038/nrd2961. [PubMed] [CrossRef] [Google Scholar]
5. Mak K.-K., Pichika M.R. Artificial Intelligence in Drug Development: Present Status and Future Prospects. Drug Discov. Today. 2019;24:773–780. doi: 10.1016/j.drudis.2018.11.014. [PubMed] [CrossRef] [Google Scholar]
6. Biggest Challenges Facing the Pharmaceutical Industry in 2023. [(accessed on 5 May 2023)]. Available online: https://www.pssindia.com/2023/01/23/biggest-challenges-facing-the-pharmaceutical-industry-in-2023/
7. Chavda V., Valu D., Parikh P., Tiwari N., Chhipa A., Shukla S., Patel S., Balar P., Paiva-Santos A., Patravale V. Conventional and Novel Diagnostic Tools for the Diagnosis of Emerging SARS-CoV-2 Variants. Vaccines. 2023;11:374. doi: 10.3390/vaccines11020374. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
8. Zignify. [(accessed on 2 May 2023)]. Available online: https://zignify.net/what-is-supply-chain-disruption-and-what-are-its-causes/#:~:text=LogisticsDelaysandFailures,resultingincongestionanddelays
9. Kgmg. [(accessed on 2 May 2023)]. Available online: https://kpmg.com/xx/en/home/insights/2022/12/the-supply-chain-trends-shaking-up-2023.html
10. Times of India Pharmaceutical Supply Chain Management: Crises and Innovations. [(accessed on 15 May 2023)]. Available online: https://timesofindia.indiatimes.com/blogs/voices/pharmaceutical-supply-chain-management-crises-and-innovations/
11. Sharma R., Shishodia A., Gunasekaran A., Min H., Munim Z.H. The Role of Artificial Intelligence in Supply Chain Management: Mapping the Territory. Int. J. Prod. Res. 2022;60:7527–7550. doi: 10.1080/00207543.2022.2029611. [CrossRef] [Google Scholar]
12. Grilo A.L., Mantalaris A. The Increasingly Human and Profitable Monoclonal Antibody Market. Trends Biotechnol. 2019;37:9–16. doi: 10.1016/j.tibtech.2018.05.014. [PubMed] [CrossRef] [Google Scholar]
13. Sarpatwari A., Barenie R., Curfman G., Darrow J.J., Kesselheim A.S. The US Biosimilar Market: Stunted Growth and Possible Reforms. Clin. Pharmacol. Ther. 2019;105:92–100. doi: 10.1002/cpt.1285. [PubMed] [CrossRef] [Google Scholar]
14. Daka A., Peer D. RNAi-Based Nanomedicines for Targeted Personalized Therapy. Adv. Drug Deliv. Rev. 2012;64:1508–1521. doi: 10.1016/j.addr.2012.08.014. [PubMed] [CrossRef] [Google Scholar]
15. Colombo S., Zeng X., Ragelle H., Foged C. Complexity in the Therapeutic Delivery of RNAi Medicines: An Analytical Challenge. Expert Opin. Drug Deliv. 2014;11:1481–1495. doi: 10.1517/17425247.2014.927439. [PubMed] [CrossRef] [Google Scholar]
16. Müller R. Junghanns Nanocrystal Technology, Drug Delivery and Clinical Applications. Int. J. Nanomed. 2008;3:295–310. doi: 10.2147/IJN.S595. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

17. Jain K.K., Jain K.K. The Handbook of Nanomedicine. Springer; Berlin/Heidelberg, Germany: 2017. Nanomolecular Diagnostics; pp. 133–200. [CrossRef] [Google Scholar]
18. Kalepu S., Nekkanti V. Insoluble Drug Delivery Strategies: Review of Recent Advances and Business Prospects. Acta Pharm. Sin. B. 2015;5:442–453. doi: 10.1016/j.apsb.2015.07.003. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
19. Deloitte Using-Ai-to-Accelerate-Clinical-Trials. [(accessed on 1 May 2023)]. Available online: https://www2.deloitte.com/us/en/blog/health-care-blog/2022/using-ai-to-accelerate-clinical-trials.html
20. Shah H., Chavda V., Soniwala M.M. Bioinformatics Tools for Pharmaceutical Drug Product Development. Wiley; Hoboken, NJ, USA: 2023. Applications of Bioinformatics Tools in Medicinal Biology and Biotechnology; pp. 95–116. [Google Scholar]
21. Jenkins J.L., Bender A., Davies J.W. In Silico Target Fishing: Predicting Biological Targets from Chemical Structure. Drug Discov. Today Technol. 2006;3:413–421. doi: 10.1016/j.ddtec.2006.12.008. [CrossRef] [Google Scholar]
22. Afzal A.M., Mussa H.Y., Turner R.E., Bender A., Glen R.C. A Multi-Label Approach to Target Prediction Taking Ligand Promiscuity into Account. J. Cheminform. 2015;7:24. doi: 10.1186/s13321-015-0071-9. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
23. Wang L., Xie X.-Q. Computational Target Fishing: What Should Chemogenomics Researchers Expect for the Future of in Silico Drug Design and Discovery? Future Med. Chem. 2014;6:247–249. doi: 10.4155/fmc.14.5. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
24. Iorio F., Bosotti R., Scacheri E., Belcastro V., Mithbaokar P., Ferriero R., Murino L., Tagliaferri R., Brunetti-Pierri N., Isacchi A., et al. Discovery of Drug Mode of Action and Drug Repositioning from Transcriptional Responses. Proc. Natl. Acad. Sci. USA. 2010;107:14621–14626. doi: 10.1073/pnas.1000138107. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
25. Begam B.F., Kumar J.S. A Study on Cheminformatics and Its Applications on Modern Drug Discovery. Procedia Eng. 2012;38:1264–1275. doi: 10.1016/j.proeng.2012.06.156. [CrossRef] [Google Scholar]
26. Lomenick B., Olsen R.W., Huang J. Identification of Direct Protein Targets of Small Molecules. ACS Chem. Biol. 2011;6:34–46. doi: 10.1021/cb100294v. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
27. Pushpakom S., Iorio F., Eyers P.A., Escott K.J., Hopper S., Wells A., Doig A., Guilliams T., Latimer J., McNamee C., et al. Drug Repurposing: Progress, Challenges and Recommendations. Nat. Rev. Drug Discov. 2019;18:41–58. doi: 10.1038/nrd.2018.168. [PubMed] [CrossRef] [Google Scholar]
28. Nettles J.H., Jenkins J.L., Bender A., Deng Z., Davies J.W., Glick M. Bridging Chemical and Biological Space: “Target Fishing” Using 2D and 3D Molecular Descriptors. J. Med. Chem. 2006;49:6802–6810. doi: 10.1021/jm060902w. [PubMed] [CrossRef] [Google Scholar]
29. Galati S., Di Stefano M., Martinelli E., Poli G., Tuccinardi T. Recent Advances in In Silico Target Fishing. Molecules. 2021;26:5124. doi: 10.3390/molecules26175124. [PMC free

article] [PubMed] [CrossRef] [Google Scholar]
30. Dickherber A., Morris S.A., Grodzinski P. NCI Investment in Nanotechnology: Achievements and Challenges for the Future. Wiley Interdiscip. Rev. Nanomed. Nanobio Technol. 2015;7:251–265. doi: 10.1002/wnan.1318. [PubMed] [CrossRef] [Google Scholar]
31. National Nanotechnology Initiative NNI Budget Supplements and Strategic Plans. [(accessed on 1 May 2023)]; Available online: https://www.nano.gov/NNIBudgetSupplements andStrategicPlans
32. Colombo S., Beck-Broichsitter M., Bøtker J.P., Malmsten M., Rantanen J., Bohr A. Transforming Nanomedicine Manufacturing toward Quality by Design and Microfluidics. Adv. Drug Deliv. Rev. 2018;128:115–131. doi: 10.1016/j.addr.2018.04.004. [PubMed] [CrossRef] [Google Scholar]
33. Troiano G., Nolan J., Parsons D., Van Geen Hoven C., Zale S. A Quality by Design Approach to Developing and Manufacturing Polymeric Nanoparticle Drug Products. AAPS J. 2016;18:1354–1365. doi: 10.1208/s12248-016-9969-z. [PubMed] [CrossRef] [Google Scholar]
34. Puri M., Pathak Y., Sutariya V.K., Tipparaju S., Moreno W. Artificial Neural Network for Drug Design, Delivery and Disposition. Academic Press; Cambridge, MA, USA: 2015. [Google Scholar]
35. Vyas M., Thakur S., Riyaz B., Bansal K., Tomar B., Mishra V. Artificial Intelligence: The Beginning of a New Era in Pharmacy Profession. Asian J. Pharm. 2018;12:72–76. [Google Scholar]
36. Hassanzadeh P., Atyabi F., Dinarvand R. The Significance of Artificial Intelligence in Drug Delivery System Design. Adv. Drug Deliv. Rev. 2019;151–152:169–190. doi: 10.1016/j.addr.2019.05.001. [PubMed] [CrossRef] [Google Scholar]
37. Chavda V., Bezbaruah R., Valu D., Desai S., Chauhan N., Marwadi S., Deka G., Ding Z. Bioinformatics Tools for Pharmaceutical Drug Product Development. John Wiley & Sons, Ltd.; Hoboken, NJ, USA: 2023. Clinical Applications of “Omics” Technology as a Bioinformatic Tool; pp. 117–145. [Google Scholar]
38. Sacha G.M., Varona P. Artificial Intelligence in Nanotechnology. Nanotechnology. 2013;24:452002. doi: 10.1088/0957-4484/24/45/452002. [PubMed] [CrossRef] [Google Scholar]
39. Wong W., Chee E., Li J., Wang X. Recurrent Neural Network-Based Model Predictive Control for Continuous Pharmaceutical Manufacturing. Mathematics. 2018;6:242. doi: 10.3390/math6110242. [CrossRef] [Google Scholar]
40. Wise J., Möller A., Christie D., Kalra D., Brodsky E., Georgieva E., Jones G., Smith I., Greiffenberg L., McCarthy M., et al. The Positive Impacts of Real-World Data on the Challenges Facing the Evolution of Biopharma. Drug Discov. Today. 2018;23:788–801. doi: 10.1016/j.drudis.2018.01.034. [PubMed] [CrossRef] [Google Scholar]
41. Taylor D., Bowden S.G., Knorr R., Wilson D.R., Proudfoot J., Dunlop A.E. The Pistoia Alliance Controlled Substance Compliance Service Project: From Start to Finish. Drug Discov. Today. 2015;20:175–180. doi: 10.1016/j.drudis.2014.09.021. [PubMed] [CrossRef] [Google Scholar]
42. Lee C.K.H., Choy K.L., Chan Y.N. A Knowledge-Based Ingredient Formulation System for Chemical Product Development in the Personal Care Industry. Comput. Chem. Eng. 2014;65:40–53. doi:

10.1016/j.compchemeng.2014.03.004. [CrossRef] [Google Scholar]
43. Schmidhuber J. Deep Learning in Neural Networks: An Overview. Neural Netw. 2015;61:85–117. doi: 10.1016/j.neunet.2014.09.003. [PubMed] [CrossRef] [Google Scholar]
44. When Virtual Screening Yields Inactive Drugs: Dealing with False Theoretical Friends—Cerón-Carrasco—2022—ChemMedChem—Wiley Online Library. [(accessed on 27 June 2023)]. Available online: https://chemistry-europe.onlinelibrary.wiley.com/doi/full/10.1002/cmdc.202200278 [PMC free article] [PubMed]
45. Roboticsbiz Ai-in-Drug-Discovery-Benefits-Drawback-and-Challenges. [(accessed on 5 May 2023)]. Available online: https://roboticsbiz.com/ai-in-drug-discovery-benefits-drawback-and-challenges/
46. Sarker I.H. Machine Learning: Algorithms, Real-World Applications and Research Directions. SN Comput. Sci. 2021;2:160. doi: 10.1007/s42979-021-00592-x. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
47. Dara S., Dhamercherla S., Jadav S.S., Babu C.M., Ahsan M.J. Machine Learning in Drug Discovery: A Review. Artif. Intell. Rev. 2022;55:1947–1999. doi: 10.1007/s10462-021-10058-4. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
48. Kavasidis I., Lallas E., Gerogiannis V.C., Charitou T., Karageorgos A. Predictive Maintenance in Pharmaceutical Manufacturing Lines Using Deep Transformers. Procedia Comput. Sci. 2023;220:576–583. doi: 10.1016/j.procs.2023.03.073. [CrossRef] [Google Scholar]
49. Bagherian M., Sabeti E., Wang K., Sartor M.A., Nikolovska-Coleska Z., Najarian K. Machine Learning Approaches and Databases for Prediction of Drug–Target Interaction: A Survey Paper. Brief. Bioinform. 2021;22:247–269. doi: 10.1093/bib/bbz157. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
50. Kumar Y., Koul A., Singla R., Ijaz M.F. Artificial Intelligence in Disease Diagnosis: A Systematic Literature Review, Synthesizing Framework and Future Research Agenda. J. Ambient. Intell. Humaniz. Comput. 2023;14:8459–8486. doi: 10.1007/s12652-021-03612-z. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
51. Chapman A.B., Peterson K.S., Alba P.R., DuVall S.L., Patterson O.V. Detecting Adverse Drug Events with Rapidly Trained Classification Models. Drug Saf. 2019;42:147–156. doi: 10.1007/s40264-018-0763-y. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
52. Elkin M.E., Zhu X. Predictive Modeling of Clinical Trial Terminations Using Feature Engineering and Embedding Learning. Sci. Rep. 2021;11:3446. doi: 10.1038/s41598-021-82840-x. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
53. Chavda V.P., Sorathiya A., Valu D., Marwadi S. Computation in BioInformatics: Multidisciplinary Applications. John Wiley & Sons; Hoboken, NJ, USA: 2021. Role of Data Mining in Bioinformatics; pp. 69–84. [CrossRef] [Google Scholar]
54. Parikh S., Patel R., Khunt D., Chavda V.P., Vora L. Bioinformatics Tools for Pharmaceutical Drug Product Development. John Wiley & Sons, Ltd.; Hoboken, NJ, USA: 2023. Data Analytics and Data Visualization for the Pharmaceutical Industry; pp. 55–76. [Google Scholar]

55. Karim M.R., Beyan O., Zappa A., Costa I.G., Rebholz-Schuhmann D., Cochez M., Decker S. Deep Learning-Based Clustering Approaches for Bioinformatics. Brief. Bioinform. 2021;22:393–415. doi: 10.1093/bib/bbz170. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
56. Vamathevan J., Clark D., Czodrowski P., Dunham I., Ferran E., Lee G., Li B., Madabhushi A., Shah P., Spitzer M., et al. Applications of Machine Learning in Drug Discovery and Development. Nat. Rev. Drug Discov. 2019;18:463–477. doi: 10.1038/s41573-019-0024-5. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
57. Goldstein M., Uchida S. A Comparative Evaluation of Unsupervised Anomaly Detection Algorithms for Multivariate Data. PLoS ONE. 2016;11:e0152173. doi: 10.1371/journal.pone.0152173. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
58. Noguchi Y., Ueno A., Otsubo M., Katsuno H., Sugita I., Kanematsu Y., Yoshida A., Esaki H., Tachi T., Teramachi H. A New Search Method Using Association Rule Mining for Drug-Drug Interaction Based on Spontaneous Report System. Front. Pharmacol. 2018;9:197. doi: 10.3389/fphar.2018.00197. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
59. Liu L., Tang L., Dong W., Yao S., Zhou W. An Overview of Topic Modeling and Its Current Applications in Bioinformatics. SpringerPlus. 2016;5:1608. doi: 10.1186/s40064-016-3252-8. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
60. Zhao W., Chen J.J., Perkins R., Liu Z., Ge W., Ding Y., Zou W. A Heuristic Approach to Determine an Appropriate Number of Topics in Topic Modeling. BMC Bioinform. 2015;16:S8. doi: 10.1186/1471-2105-16-S13-S8. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
61. Sousa T., Correia J., Pereira V., Rocha M. Generative Deep Learning for Targeted Compound Design. J. Chem. Inf. Model. 2021;61:5343–5361. doi: 10.1021/acs.jcim.0c01496. [PubMed] [CrossRef] [Google Scholar]
62. Rajalingham R., Piccato A., Jazayeri M. Recurrent Neural Networks with Explicit Representation of Dynamic Latent Variables Can Mimic Behavioral Patterns in a Physical Inference Task. Nat. Commun. 2022;13:5865. doi: 10.1038/s41467-022-33581-6. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
63. Nag S., Baidya A.T.K., Mandal A., Mathew A.T., Das B., Devi B., Kumar R. Deep Learning Tools for Advancing Drug Discovery and Development. 3 Biotech. 2022;12:110. doi: 10.1007/s13205-022-03165-8. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
64. Liu X., Liu C., Huang R., Zhu H., Liu Q., Mitra S., Wang Y. Long Short-Term Memory Recurrent Neural Network for Pharmacokinetic-Pharmacodynamic Modeling. Int. J. Clin. Pharmacol. Ther. 2021;59:138–146. doi: 10.5414/CP203800. [PubMed] [CrossRef] [Google Scholar]
65. Turchin A., Masharsky S., Zitnik M. Comparison of BERT Implementations for Natural Language Processing of Narrative Medical Documents. Inform. Med. Unlocked. 2023;36:101139. doi: 10.1016/j.imu.2022.101139. [CrossRef] [Google Scholar]
66. Chavda V.P. Applications of Targeted Nano Drugs and Delivery Systems. Elsevier; Amsterdam, The Netherlands: 2019.

Nanotherapeutics and Nanobiotechnology; pp. 1–13. [Google Scholar]

67. Colombo S. Artificial Intelligence in Healthcare. Elsevier; Amsterdam, The Netherlands: 2020. Applications of Artificial Intelligence in Drug Delivery and Pharmaceutical Development; pp. 85–116. [Google Scholar]
68. Das P.J., Preuss C., Mazumder B. Artificial Neural Network for Drug Design, Delivery and Disposition. Elsevier; Amsterdam, The Netherlands: 2016. Artificial Neural Network as Helping Tool for Drug Formulation and Drug Administration Strategies; pp. 263–276. [Google Scholar]
69. Bhhatarai B., Walters W.P., Hop C.E.C.A., Lanza G., Ekins S. Opportunities and Challenges Using Artificial Intelligence in ADME/Tox. Nat. Mater. 2019;18:418–422. doi: 10.1038/s41563-019-0332-5. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
70. Siepmann J., Siepmann F. Modeling of Diffusion Controlled Drug Delivery. J. Control. Release. 2012;161:351–362. doi: 10.1016/j.jconrel.2011.10.006. [PubMed] [CrossRef] [Google Scholar]
71. Yang S.-Y., Huang Q., Li L.-L., Ma C.-Y., Zhang H., Bai R., Teng Q.-Z., Xiang M.-L., Wei Y.-Q. An Integrated Scheme for Feature Selection and Parameter Setting in the Support Vector Machine Modeling and Its Application to the Prediction of Pharmacokinetic Properties of Drugs. Artif. Intell. Med. 2009;46:155–163. doi: 10.1016/j.artmed.2008.07.001. [PubMed] [CrossRef] [Google Scholar]
72. Yu L.X., Ellison C.D., Hussain A.S. Applications of Pharmacokinetic Principles in Drug Development. Springer; Boston, MA, USA: 2004. Predicting Human Oral Bioavailability Using in Silico Models; pp. 53–74. [Google Scholar]
73. Yang S.-Y., Huang Q., Li L.-L., Ma C.-Y., Zhang H., Bai R., Teng Q.-Z., Xiang M.-L., Wei Y.-Q. An Integrated Scheme for Feature Selection and Parameter Setting in the Support Vector Machine Modeling and Its Application to the Prediction of Pharmacokinetic Properties of Drugs. Artif. Intell. Med. 2009;46:155–163. doi: 10.1016/j.artmed.2008.07.001. [PubMed] [CrossRef] [Google Scholar]
74. Yu L.X., Ellison C.D., Hussain A.S. Applications of Pharmacokinetic Principles in Drug Development. Springer; Boston, MA, USA: 2004. Predicting Human Oral Bioavailability Using in Silico Models; pp. 53–74. [Google Scholar]
75. Menden M.P., Iorio F., Garnett M., McDermott U., Benes C.H., Ballester P.J., Saez-Rodriguez J. Machine Learning Prediction of Cancer Cell Sensitivity to Drugs Based on Genomic and Chemical Properties. PLoS ONE. 2013;8:e61318. doi: 10.1371/journal.pone.0061318. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
76. Lou H., Lian B., Hageman M.J. Applications of Machine Learning in Solid Oral Dosage Form Development. J. Pharm. Sci. 2021;110:3150–3165. doi: 10.1016/j.xphs.2021.04.013. [PubMed] [CrossRef] [Google Scholar]
77. Jiang J., Ma X., Ouyang D., Williams R.O. Emerging Artificial Intelligence (AI) Technologies Used in the Development of Solid Dosage Forms. Pharmaceutics. 2022;14:2257. doi: 10.3390/pharmaceutics14112257. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

78. Han R., Xiong H., Ye Z., Yang Y., Huang T., Jing Q., Lu J., Pan H., Ren F., Ouyang D. Predicting Physical Stability of Solid Dispersions by Machine Learning Techniques. J. Control. Release. 2019;311:16–25. doi: 10.1016/j.jconrel.2019.08.030. [PubMed] [CrossRef] [Google Scholar]
79. Navya K., Kamaraj R., Bharathi M. The Trending Role of Artificial Intelligence and Its Applications in Formulation of Solid Dosage Forms: A Review. ECS Trans. 2022;107:20049–20055. doi: 10.1149/10701.20049ecst. [CrossRef] [Google Scholar]
80. Ghourichay M.P., Kiaie S.H., Nokhodchi A., Javadzadeh Y. Formulation and Quality Control of Orally Disintegrating Tablets (ODTs): Recent Advances and Perspectives. BioMed Res. Int. 2021;2021:6618934. doi: 10.1155/2021/6618934. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
81. Jivraj M., Martini L.G., Thomson C.M. An Overview of the Different Excipients Useful for the Direct Compression of Tablets. Pharm. Sci. Technol. Today. 2000;3:58–63. doi: 10.1016/S1461-5347(99)00237-0. [PubMed] [CrossRef] [Google Scholar]
82. Sun Y., Peng Y., Chen Y., Shukla A.J. Application of Artificial Neural Networks in the Design of Controlled Release Drug Delivery Systems. Adv. Drug Deliv. Rev. 2003;55:1201–1215. doi: 10.1016/S0169-409X(03)00119-4. [PubMed] [CrossRef] [Google Scholar]
83. Bannigan P., Aldeghi M., Bao Z., Häse F., Aspuru-Guzik A., Allen C. Machine Learning Directed Drug Formulation Development. Adv. Drug Deliv. Rev. 2021;175:113806. doi: 10.1016/j.addr.2021.05.016. [PubMed] [CrossRef] [Google Scholar]
84. Mukhamediev R.I., Popova Y., Kuchin Y., Zaitseva E., Kalimoldayev A., Symagulov A., Levashenko V., Abdoldina F., Gopejenko V., Yakunin K., et al. Review of Artificial Intelligence and Machine Learning Technologies: Classification, Restrictions, Opportunities and Challenges. Mathematics. 2022;10:2552. doi: 10.3390/math10152552. [CrossRef] [Google Scholar]
85. 98. Sengupta S., Basak S., Peters R. Particle Swarm Optimization: A Survey of Historical and Recent Developments with Hybridization Perspectives. Mach. Learn. Knowl. Extr. 2018;1:157–191. doi: 10.3390/make1010010. [CrossRef] [Google Scholar]
86. 99. Paul D., Sanap G., Shenoy S., Kalyane D., Kalia K., Tekade R.K. Artificial Intelligence in Drug Discovery and Development. Drug Discov. Today. 2021;26:80–93. doi: 10.1016/j.drudis.2020.10.010. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
87. Eberle L.G., Sugiyama H., Schmidt R. Improving Lead Time of Pharmaceutical Production Processes Using Monte Carlo Simulation. Comput. Chem. Eng. 2014;68:255–263. doi: 10.1016/j.compchemeng.2014.05.017. [CrossRef] [Google Scholar]
88. Galata D.L., Könyves Z., Nagy B., Novák M., Mészáros L.A., Szabó E., Farkas A., Marosi G., Nagy Z.K. Real-Time Release Testing of Dissolution Based on Surrogate Models Developed by Machine Learning Algorithms Using NIR Spectra, Compression Force and Particle Size Distribution as Input Data. Int. J. Pharm. 2021;597:120338. doi: 10.1016/j.ijpharm.2021.120338. [PubMed] [CrossRef] [Google Scholar]
89. Ma X., Kittikunakorn N., Sorman B., Xi H., Chen A., Marsh M., Mongeau A., Piché N., Williams R.O., Skomski D. Application of

Deep Learning Convolutional Neural Networks for Internal Tablet Defect Detection: High Accuracy, Throughput, and Adaptability. J. Pharm. Sci. 2020;109:1547–1557. doi: 10.1016/j.xphs.2020.01.014. [PubMed] [CrossRef] [Google Scholar]

90. Yost E., Chalus P., Zhang S., Peter S., Narang A.S. Quantitative X-Ray Microcomputed Tomography Assessment of Internal Tablet Defects. J. Pharm. Sci. 2019;108:1818–1830. doi: 10.1016/j.xphs.2018.12.024. [PubMed] [CrossRef] [Google Scholar]
91. Khanam J.J., Foo S.Y. A Comparison of Machine Learning Algorithms for Diabetes Prediction. ICT Express. 2021;7:432–439. doi: 10.1016/j.icte.2021.02.004. [CrossRef] [Google Scholar]
92. Bhattamisra S.K., Banerjee P., Gupta P., Mayuren J., Patra S., Candasamy M. Artificial Intelligence in Pharmaceutical and Healthcare Research. Big Data Cogn. Comput. 2023;7:10. doi: 10.3390/bdcc7010010. [CrossRef] [Google Scholar]
93. Wang N., Sun H., Dong J., Ouyang D. PharmDE: A New Expert System for Drug-Excipient Compatibility Evaluation. Int. J. Pharm. 2021;607:120962. doi: 10.1016/j.ijpharm.2021.120962. [PubMed] [CrossRef] [Google Scholar]
94. Mohan B., Kamaraj R., Navyaja K. Role of Artificial Intelligence in Parenteral Formulation: A Review. ECS Trans. 2022;107:20013–20020. doi: 10.1149/10701.20013ecst. [CrossRef] [Google Scholar]
95. Pokhriyal P., Chavda V.P., Pathak M. Bioinformatics Tools for Pharmaceutical Drug Product Development. Wiley; Hoboken, NJ, USA: 2023. Future Prospects and Challenges in the Implementation of AI and ML in Pharma Sector; pp. 401–416. [Google Scholar]
96. Wilco Image Processing Wilco Image Processing. [(accessed on 5 May 2023)]. Available online: https://www.wilco.com/technologies/image-processing/
97. Zarrinpar A., Lee D.-K., Silva A., Datta N., Kee T., Eriksen C., Weigle K., Agopian V., Kaldas F., Farmer D., et al. Individualizing Liver Transplant Immunosuppression Using a Phenotypic Personalized Medicine Platform. Sci. Transl. Med. 2016;8:333. doi: 10.1126/scitranslmed.aac5954. [PubMed] [CrossRef] [Google Scholar]
98. Ho D., Wang P., Kee T. Artificial Intelligence in Nanomedicine. Nanoscale Horiz. 2019;4:365–377. doi: 10.1039/C8NH00233A. [PubMed] [CrossRef] [Google Scholar]
99. Bannigan P., Bao Z., Hickman R.J., Aldeghi M., Häse F., Aspuru-Guzik A., Allen C. Machine Learning Models to Accelerate the Design of Polymeric Long-Acting Injectables. Nat. Commun. 2023;14:35. doi: 10.1038/s41467-022-35343-w. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
100. Magill E., Demartis S., Gavini E., Dian Permana A., Raj Singh Thakur R., Faris Adrianto M., Waite D., Glover K., Picco C.J., Korelidou A., et al. Solid Implantable Devices for Sustained Drug Delivery. Adv. Drug Deliv. Rev. 2023;199:114950. doi: 10.1016/j.addr.2023.114950. [PubMed] [CrossRef] [Google Scholar]
101. Wang N., Zhang Y., Wang W., Ye Z., Chen H., Hu G., Ouyang D. How Can Machine Learning and Multiscale Modeling Benefit Ocular Drug Development? Adv. Drug Deliv. Rev. 2023;196:114772. doi: 10.1016/j.addr.2023.114772. [PubMed] [CrossRef] [Google Scholar]

102. Vora L.K., Moffatt K., Tekko I.A., Paredes A.J., Volpe-Zanutto F., Mishra D., Peng K., Raj Singh Thakur R., Donnelly R.F. Microneedle Array Systems for Long-Acting Drug Delivery. Eur. J. Pharm. Biopharm. 2021;159:44–76. doi: 10.1016/j.ejpb.2020.12.006. [PubMed] [CrossRef] [Google Scholar]
103. Wu Y., Vora L.K., Mishra D., Adrianto M.F., Gade S., Paredes A.J., Donnelly R.F., Singh T.R.R. Nanosuspension-Loaded Dissolving Bilayer Microneedles for Hydrophobic Drug Delivery to the Posterior Segment of the Eye. Biomater. Adv. 2022;137:212767. doi: 10.1016/j.bioadv.2022.212767. [PubMed] [CrossRef] [Google Scholar]
104. Bagde A., Dev S., Madhavi K., Sriram L., Spencer S.D., Kalvala A., Nathani A., Salau O., Mosley-Kellum K., Dalvaigari H., et al. Biphasic Burst and Sustained Transdermal Delivery in Vivo Using an AI-Optimized 3D-Printed MN Patch. Int. J. Pharm. 2023;636:122647. doi: 10.1016/j.ijpharm.2023.122647. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
105. Koh D.-M., Papanikolaou N., Bick U., Illing R., Kahn C.E., Kalpathi-Cramer J., Matos C., Martí-Bonmatí L., Miles A., Mun S.K., et al. Artificial Intelligence and Machine Learning in Cancer Imaging. Commun. Med. 2022;2:133. doi: 10.1038/s43856-022-00199-0. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
106. Malche T., Tharewal S., Tiwari P.K., Jabarulla M.Y., Alnuaim A.A., Hatamleh W.A., Ullah M.A. Artificial Intelligence of Things- (AIoT-) Based Patient Activity Tracking System for Remote Patient Monitoring. J. Healthc. Eng. 2022;2022:8732213. doi: 10.1155/2022/8732213. [PMC free article] [PubMed] [CrossRef] [Google Scholar] Retracted
107. .Verma D., Singh K.R., Yadav A.K., Nayak V., Singh J., Solanki P.R., Singh R.P. Internet of Things (IoT) in Nano-Integrated Wearable Biosensor Devices for Healthcare Applications. Biosens. Bioelectron. X. 2022;11:100153. doi: 10.1016/j.biosx.2022.100153. [CrossRef] [Google Scholar]
108. Nayak S., Kumar Das R. Service Robotics. IntechOpen; London, UK: 2020. Application of Artificial Intelligence (AI) in Prosthetic and Orthotic Rehabilitation. [Google Scholar]
109. Tuntland T., Ethell B., Kosaka T., Blasco F., Zang R.X., Jain M., Gould T., Hoffmaster K. Implementation of Pharmacokinetic and Pharmacodynamic Strategies in Early Research Phases of Drug Discovery and Development at Novartis Institute of Biomedical Research. Front. Pharmacol. 2014;5:174. doi: 10.3389/fphar.2014.00174. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
110. Mager D.E., Woo S., Jusko W.J. Scaling Pharmacodynamics from In Vitro and Preclinical Animal Studies to Humans. Drug Metab. Pharmacokinet. 2009;24:16–24. doi: 10.2133/dmpk.24.16. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
111. Alsultan A., Alghamdi W.A., Alghamdi J., Alharbi A.F., Aljutayli A., Albassam A., Almazroo O., Alqahtani S. Clinical Pharmacology Applications in Clinical Drug Development and Clinical Care: A Focus on Saudi Arabia. Saudi Pharm. J. 2020;28:1217–1227. doi: 10.1016/j.jsps.2020.08.012. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
112. Keutzer L., You H., Farnoud A., Nyberg J., Wicha S.G., Maher-Edwards G., Vlasakakis

G., Moghaddam G.K., Svensson E.M., Menden M.P., et al. Machine Learning and Pharmacometrics for Prediction of Pharmacokinetic Data: Differences, Similarities and Challenges Illustrated with Rifampicin. Pharmaceutics. 2022;14:1530. doi: 10.3390/pharmaceutics14081530. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

113. Chavda V.P., Ertas Y.N., Walhekar V., Modh D., Doshi A., Shah N., Anand K., Chhabria M. Advanced Computational Methodologies Used in the Discovery of New Natural Anticancer Compounds. Front. Pharmacol. 2021;12:702611. doi: 10.3389/fphar.2021.702611. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
114. Chaturvedula A., Calad-Thomson S., Liu C., Sale M., Gattu N., Goyal N. Artificial Intelligence and Pharmacometrics: Time to Embrace, Capitalize, and Advance? CPT Pharmacomet. Syst. Pharmacol. 2019;8:440–443. doi: 10.1002/psp4.12418. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
115. Patel V., Shah M. Artificial Intelligence and Machine Learning in Drug Discovery and Development. Intell. Med. 2022;2:134–140. doi: 10.1016/j.imed.2021.10.001. [CrossRef] [Google Scholar]
116. Vatansever S., Schlessinger A., Wacker D., Kaniskan H.Ü., Jin J., Zhou M., Zhang B. Artificial Intelligence and Machine Learning-aided Drug Discovery in Central Nervous System Diseases: State-of-the-arts and Future Directions. Med. Res. Rev. 2021;41:1427–1473. doi: 10.1002/med.21764. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
117. Houy N., Le Grand F. Optimal Dynamic Regimens with Artificial Intelligence: The Case of Temozolomide. PLoS ONE. 2018;13:e0199076. doi: 10.1371/journal.pone.0199076. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
118. Westreich D., Lessler J., Funk M.J. Propensity Score Estimation: Neural Networks, Support Vector Machines, Decision Trees (CART), and Meta-Classifiers as Alternatives to Logistic Regression. J. Clin. Epidemiol. 2010;63:826–833. doi: 10.1016/j.jclinepi.2009.11.020. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
119. Chintawar S., Gattani V., Vyas S., Dawre S. Bioinformatics Tools for Pharmaceutical Drug Product Development. Wiley; Hoboken, NJ, USA: 2023. Role of Artificial Intelligence in Machine Learning for Diagnosis and Radiotherapy; pp. 315–344. [Google Scholar]
120. Suresh A., Udendhran R., Balamurgan M. Hybridized Neural Network and Decision Tree Based Classifier for Prognostic Decision Making in Breast Cancers. Soft Comput. 2020;24:7947–7953. doi: 10.1007/s00500-019-04066-4. [CrossRef] [Google Scholar]
121. Daoui O., Elkhattabi S., Chtita S., Elkhalabi R., Zgou H., Benjelloun A.T. QSAR, Molecular Docking and ADMET Properties in Silico Studies of Novel 4,5,6,7-Tetrahydrobenzo[D]-Thiazol-2-Yl Derivatives Derived from Dimedone as Potent Anti-Tumor Agents through Inhibition of C-Met Receptor Tyrosine Kinase. Heliyon. 2021;7:e07463. doi: 10.1016/j.heliyon.2021.e07463. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
122. Zhuang X., Lu C. PBPK Modeling and Simulation in Drug Research and Development. Acta Pharm. Sin. B. 2016;6:430–440. doi:

10.1016/j.apsb.2016.04.004. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

123. Healthcare Artificial Intelligence, Causal Machine Learning & Data Analytics—GNS Healthcare. [(accessed on 5 May 2023)]. Available online: https://www.aitiabio.com/new-technology/
124. Jones H., Rowland-Yeo K. Basic Concepts in Physiologically Based Pharmacokinetic Modeling in Drug Discovery and Development. CPT Pharmacomet. Syst. Pharmacol. 2013;2:63. doi: 10.1038/psp.2013.41. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
125. Obrezanova O. Artificial Intelligence for Compound Pharmacokinetics Prediction. Curr. Opin. Struct. Biol. 2023;79:102546. doi: 10.1016/j.sbi.2023.102546. [PubMed] [CrossRef] [Google Scholar]
126. Mhatre S., Shukla S., Chavda V.P., Gandikota L., Patravale V. Bioinformatics Tools for Pharmaceutical Drug Product Development. Wiley; Hoboken, NJ, USA: 2023. AI and ML for Development of Cell and Gene Therapy for Personalized Treatment; pp. 371–400. [Google Scholar]
127. Chou W.-C., Lin Z. Machine Learning and Artificial Intelligence in Physiologically Based Pharmacokinetic Modeling. Toxicol. Sci. 2023;191:1–14. doi: 10.1093/toxsci/kfac101. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
128. Van Tran T.T., Tayara H., Chong K.T. Artificial Intelligence in Drug Metabolism and Excretion Prediction: Recent Advances, Challenges, and Future Perspectives. Pharmaceutics. 2023;15:1260. doi: 10.3390/pharmaceutics15041260. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
129. Li Y., Meng Q., Yang M., Liu D., Hou X., Tang L., Wang X., Lyu Y., Chen X., Liu K., et al. Current Trends in Drug Metabolism and Pharmacokinetics. Acta Pharm. Sin. B. 2019;9:1113–1144. doi: 10.1016/j.apsb.2019.10.001. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
130. Parikh P.K., Savjani J.K., Gajjar A.K., Chhabria M.T. Bioinformatics Tools for Pharmaceutical Drug Product Development. Wiley; Hoboken, NJ, USA: 2023. Bioinformatics and Cheminformatics Tools in Early Drug Discovery; pp. 147–181. [Google Scholar]
131. Alsmadi M.M., Idkaidek N. The Analysis of Pethidine Pharmacokinetics in Newborn Saliva, Plasma, and Brain Extracellular Fluid After Prenatal Intrauterine Exposure from Pregnant Mothers Receiving Intramuscular Dose Using PBPK Modeling. Eur. J. Drug Metab. Pharmacokinet. 2023;48:281–300. doi: 10.1007/s13318-023-00823-x. [PubMed] [CrossRef] [Google Scholar]
132. Zhang Z., Tang W. Drug Metabolism in Drug Discovery and Development. Acta Pharm. Sin. B. 2018;8:721–732. doi: 10.1016/j.apsb.2018.04.003. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
133. Khan S.R., Al Rijjal D., Piro A., Wheeler M.B. Integration of AI and Traditional Medicine in Drug Discovery. Drug Discov. Today. 2021;26:982–992. doi: 10.1016/j.drudis.2021.01.008. [PubMed] [CrossRef] [Google Scholar]
134. Selvaraj C., Chandra I., Singh S.K. Artificial Intelligence and Machine Learning Approaches for Drug Design: Challenges and Opportunities for the Pharmaceutical Industries. Mol. Divers. 2022;26:1893–1913. doi: 10.1007/s11030-021-10326-z. [PMC free

article] [PubMed] [CrossRef] [Google Scholar]

135. Zhou H., Hartford A., Tsai K. A Bayesian Approach for PK/PD Modeling with PD Data Below Limit of Quantification. J. Biopharm. Stat. 2012;22:1220–1243. doi: 10.1080/10543406.2011.585441. [PubMed] [CrossRef] [Google Scholar]
136. Dansirikul C., Morris R.G., Tett S.E., Duffull S.B. A Bayesian Approach for Population Pharmacokinetic Modelling of Sirolimus. Br. J. Clin. Pharmacol. 2006;62:420–434. doi: 10.1111/j.1365-2125.2005.02533.x. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
137. You W., Widmer N., De Micheli G. Example-Based Support Vector Machine for Drug Concentration Analysis; Proceedings of the 2011 Annual International Conference of the IEEE Engineering in Medicine and Biology Society; Boston, MA, USA. 30 August–3 September 2011; New York, NY USA: IEEE; 2011. pp. 153–157. [PubMed] [Google Scholar]
138. Woillard J.-B., Labriffe M., Prémaud A., Marquet P. Estimation of Drug Exposure by Machine Learning Based on Simulations from Published Pharmacokinetic Models: The Example of Tacrolimus. Pharmacol. Res. 2021;167:105578. doi: 10.1016/j.phrs.2021.105578. [PubMed] [CrossRef] [Google Scholar]
139. Woillard J., Labriffe M., Debord J., Marquet P. Tacrolimus Exposure Prediction Using Machine Learning. Clin. Pharmacol. Ther. 2021;110:361–369. doi: 10.1002/cpt.2123. [PubMed] [CrossRef] [Google Scholar]
140. Peng J., Li J., Shang X. A Learning-Based Method for Drug-Target Interaction Prediction Based on Feature Representation Learning and Deep Neural Network. BMC Bioinform. 2020;21:394. doi: 10.1186/s12859-020-03677-1. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
141. Kiseleva A., Kotzinos D., De Hert P. Transparency of AI in Healthcare as a Multilayered System of Accountabilities: Between Legal Requirements and Technical Limitations. Front. Artif. Intell. 2022;5:879603. doi: 10.3389/frai.2022.879603. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
142. Kelly C.J., Karthikesalingam A., Suleyman M., Corrado G., King D. Key Challenges for Delivering Clinical Impact with Artificial Intelligence. BMC Med. 2019;17:195. doi: 10.1186/s12916-019-1426-2. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
143. Sarmadi A., Hassanzadeganroudsari M., Soltani M. Bioinformatics Tools for Pharmaceutical Drug Product Development. Wiley; Hoboken, NJ, USA: 2023. Artificial Intelligence and Machine Learning Applications in Vaccine Development; pp. 233–253. [Google Scholar]
144. Johnson K.B., Wei W., Weeraratne D., Frisse M.E., Misulis K., Rhee K., Zhao J., Snowdon J.L. Precision Medicine, AI, and the Future of Personalized Health Care. Clin. Transl. Sci. 2021;14:86–93. doi: 10.1111/cts.12884. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
145. Ahmed Z., Mohamed K., Zeeshan S., Dong X. Artificial Intelligence with Multi-Functional Machine Learning Platform Development for Better Healthcare and Precision Medicine. Database. 2020;2020:baaa010. doi: 10.1093/database/baaa010. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
146. Gerke S., Minssen T., Cohen G. Artificial Intelligence in Healthcare. Elsevier;

Amsterdam, The Netherlands: 2020. Ethical and Legal Challenges of Artificial Intelligence-Driven Healthcare; pp. 295–336. [Google Scholar]

147. Naik N., Hameed B.M.Z., Shetty D.K., Swain D., Shah M., Paul R., Aggarwal K., Ibrahim S., Patil V., Smriti K., et al. Legal and Ethical Consideration in Artificial Intelligence in Healthcare: Who Takes Responsibility? Front. Surg. 2022;9:266. doi: 10.3389/fsurg.2022.862322. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
148. FDA . Using Artificial Intelligence & Machine Learning in the Development of Drug and Biological Products. Food and Drug Administration; Silver Spring, MD, USA: 2023. [Google Scholar]
149. Pokhriyal P., Chavda V.P., Pathak M. Bioinformatics Tools for Pharmaceutical Drug Product Development. Wiley; Hoboken, NJ, USA: 2023. Future Prospects and Challenges in the Implementation of AI and ML in Pharma Sector; pp. 401–416. [Google Scholar]
150. Levin S., Toerper M., Hamrock E., Hinson J.S., Barnes S., Gardner H., Dugas A., Linton B., Kirsch T., Kelen G. Machine-Learning-Based Electronic Triage More Accurately Differentiates Patients With Respect to Clinical Outcomes Compared With the Emergency Severity Index. Ann. Emerg. Med. 2018;71:565–574.e2. doi: 10.1016/j.annemergmed.2017.08.005. [PubMed] [CrossRef] [Google Scholar]
151. Chen M., Decary M. Artificial Intelligence in Healthcare: An Essential Guide for Health Leaders. Healthc. Manag. Forum. 2020;33:10–18. doi: 10.1177/0840470419873123. [PubMed] [CrossRef] [Google Scholar]

HOW TO CITE: Yuthika Ovhal, Ashwini Gavit, Kiran Makhija, N. S. Vyawhare, A Comprehensive Review On: Role Of Artificial Intelligence In Pharmaceutical Technology And Drug Delivery Design, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 5, 425-461. https://doi.org/10.5281/zenodo.11179405