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

Review Article

Machine Learning in Pharmacokinetics and Pharmacodynamics

Sakshi Jagtap, Srushti Gaikwad, Rasika Kadam, Prajakta Patil*

Annasaheb Dange College of B Pharmacy, Ashta 416301

ARTICLE INFO

Published: 15 Apr 2026
Keywords:
Machine Learning; Pharmacokinetics (PK); Pharmacodynamics (PD); ADME Prediction; Dose–Response Modeling; Personalized Medicine; Drug Development
DOI:
10.5281/zenodo.19595366

ABSTRACT

The integration of machine learning (ML) into pharmacology and drug discovery has transformed the way therapeutic candidates are identified, optimized, and evaluated. Traditional drug development is time-consuming, expensive, and associated with high failure rates; ML offers data-driven strategies to accelerate decision-making across the drug development pipeline. A critical component determining the success of ML models is feature engineering, particularly the selection of meaningful molecular descriptors that capture the physicochemical and structural properties of compounds. Descriptors such as molecular weight, lipophilicity (LogP), hydrogen bond donors and acceptors, topological indices, and SMILES-based representations enable accurate prediction of pharmacokinetic, pharmacodynamic, and toxicity profiles. This review discusses the role of supervised, unsupervised, semi-supervised, and reinforcement learning approaches in pharmacological research, highlighting their applications in virtual screening, QSAR modelling, drug repurposing, ADMET prediction, and personalized medicine. The article further emphasizes recent advancements in deep learning and molecular representation techniques that enhance predictive accuracy and reduce experimental burden. Overall, ML-driven pharmacology represents a paradigm shift toward faster, cost-effective, and more precise drug development.

INTRODUCTION

The scientific foundation of clinical therapeutics and drug development is pharmacokinetics (PK) and pharmacodynamics (PD). While PD describes how a drug affects the body, including its mechanism of action, efficacy, and toxicity, PK describes how a drug travels through the body, including absorption, distribution, metabolism, and excretion (ADME). PK/PD modeling has historically depended on statistical and mechanistic methods based on compartmental models and differential equations [1,2].

However, the availability of extensive biomedical data and the growing complexity of biological systems have revealed shortcomings in traditional modeling techniques. In this regard, machine

***Corresponding Author:** Prajakta Patil
Address: *Annasaheb Dange College of B Pharmacy, Ashta 416301*
Email : prajaktapatil4601@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.

learning (ML), a branch of artificial intelligence (AI), has become a game-changing instrument that can improve PK/PD modeling by handling high-dimensional datasets, improving predictive accuracy, and providing data-driven insights [3,4]. A paradigm shift from strictly mechanistic modeling to hybrid and data-centric frameworks is represented by the incorporation of machine learning into PK/PD modeling. Traditional PK/PD models, like one-compartment or multi-compartment models, frequently rely on predetermined functional forms and necessitate biological process assumptions [5].

Nonlinear relationships, inter-individual variability, and complex drug interactions may be difficult for these models to capture, despite their interpretability and physiological relevance. Supervised learning, unsupervised learning, and reinforcement learning are examples of machine learning algorithms that provide adaptable options that can reveal hidden patterns without requiring rigid prior assumptions [6]. When modeling PK/PD relationships, methods like random forests, support vector machines, neural networks, and deep learning architectures have demonstrated great promise, especially when working with large and diverse datasets [7]. The ability of machine learning to process and integrate a variety of data sources is one of its main benefits in PK/PD modeling. Large volumes of data are produced by modern drug development, including metabolomic, proteomic, genomic, and clinical trial data [8]. Conventional modeling techniques frequently find it difficult to successfully integrate such multi-modal datasets. In contrast, machine learning techniques can easily incorporate these kinds of data to produce more complete models.

Deep learning techniques can identify complex relationships between drug exposure and therapeutic response by learning patterns from raw data [9]. This is particularly valuable in personalized medicine, where factors such as age, genetics, and comorbidities significantly influence treatment outcomes.

In PK/PD modeling, machine learning (ML) is widely used to predict drug behavior and optimize dosing regimens [10,11]. By utilizing historical data, ML models can accurately estimate pharmacodynamic responses and drug concentration–time profiles, improving efficacy while reducing toxicity. Techniques such as gradient boosting and artificial neural networks are commonly applied to model nonlinear dose–response relationships and predict key parameters like drug clearance and bioavailability, ultimately supporting better clinical trial decisions[12-14].

Moreover, ML helps address inter-individual variability, a major challenge in traditional PK/PD models. Variability due to genetic, environmental, and clinical factors is often difficult to capture with conventional methods. ML approaches, especially nonlinear and nonparametric ones, can better model these complex interactions. Additionally, clustering and dimensionality reduction techniques enable the identification of patient subgroups, facilitating more targeted and personalized therapies.

1.1 Overview of machine learning algorithms used in pharmacology

1.1.1. Introduction

Machine learning (ML), a subfield of artificial intelligence, is transforming pharmaceutical research by enabling data-driven insights and decision-making. [15,16] The pharmaceutical sector generates vast amounts of data from sources such as chemical libraries, clinical trials, and genomic studies. [17] ML techniques can efficiently process and analyze these complex

datasets, thereby accelerating drug discovery, reducing development costs, and improving overall success rates.

1.1.2. Key Applications of Machine Learning in Pharmaceuticals

1.1.2.1 Drug Discovery and Design

ML algorithms are widely used to predict molecular properties, biological activity, and drug–target interactions. [18,19] Techniques such as deep learning and Quantitative Structure–Activity Relationship (QSAR) modeling are commonly applied.[20-22] These methods help researchers screen millions of chemical compounds to identify promising drug candidates efficiently.

1.1.2.2Target Identification and Validation

Machine learning plays a crucial role in identifying potential biological targets by analyzing genomic and proteomic data. [23,24] It enhances the understanding of disease mechanisms and significantly reduces the time required for experimental validation.

1.1.2 .3 Drug Repurposing

Machine learning enables the identification of new therapeutic uses for existing drugs. This approach is particularly valuable during urgent situations, such as the COVID-19 pandemic, as it significantly shortens the time compared to developing new drugs from scratch. [25-27]

1.1.2.4 Personalized Medicine

ML supports the development of personalized treatment strategies by analysing patient-specific data, including genomic, clinical, and lifestyle information. [28] This leads to improved therapeutic outcomes and a reduction in adverse drug reaction.

1.1.2.5 Manufacturing and Quality Control

In pharmaceutical manufacturing, ML is applied for predictive maintenance of equipment, real-time monitoring of drug quality, and optimization of production processes, ensuring higher efficiency and consistency. [28,29]

2. Types of machine learning algorithms used in pharmacology

Machine learning (ML) techniques in pharmacology are broadly categorized into supervised, unsupervised, semi-supervised, and reinforcement learning, each contributing uniquely to drug research and development. Supervised learning, which relies on labeled datasets, is the most widely used approach and is applied in drug discovery, QSAR modeling, ADME/toxicity prediction, pharmacokinetic pharmacodynamic (PK/PD) modeling, and personalized medicine. [30] By learning from known experimental outcomes, supervised algorithms such as random forests, support vector machines, and neural networks can predict drug activity, safety, dose–response relationships, and patient-specific therapeutic responses, thereby reducing experimental costs and improving the success rate of clinical trials.

2.1 Supervised learning is the most commonly utilized approach, where models are trained using labelled datasets to predict outcomes such as drug efficacy, toxicity, and pharmacokinetic/ pharmacodynamic (PK/PD) properties. [31] Frequently used algorithms include regression models, support vector machines, decision trees, random forests, gradient boosting, and artificial neural networks. These methods are widely

applied in areas such as QSAR modelling, biomarker discovery, and dose–response analysis.

2.2 Unsupervised learning is applied when labelled data are not available, enabling the identification of hidden patterns within complex datasets. [32-34] Techniques such as k-means clustering and hierarchical clustering are used to group similar compounds or patient populations, while dimensionality reduction methods like principal component analysis (PCA) help simplify high-dimensional biological data.

Semi-supervised learning integrates both labelled and unlabelled data, making it particularly valuable in pharmacological studies where labelled data are limited. [35,36] This approach enhances model accuracy by utilizing large amounts of available unlabelled information.

3. Application of machine learning in pharmacokinetics

The study of a drug's passage through the body, including absorption, distribution, metabolism, and excretion (ADME), is known as pharmacokinetic. Conventional PK modelling depends on: one compartment and multi-compartment models. [37]

3.1 Role of Machine Learning

Machine learning methods are capable of processing extensive datasets and detecting intricate patterns. [38-40] Unlike traditional techniques, ML can model nonlinear relationships, making it highly effective in pharmacokinetic research, particularly in predicting drug behaviour and variability.

Key Applications

- **ADME Prediction:**

Algorithms such as neural networks, support vector machines, and random forests are used to estimate pharmacokinetic properties, aiding in early drug screening.

- **Population PK Modeling:**

ML improves the identification of patient-specific factors influencing drug kinetics, enabling better understanding of variability among individuals.

- **Dose Personalization:**

By predicting drug concentration profiles, ML supports individualized dosing strategies, improving therapeutic outcomes.

- **Drug Interaction Analysis:**

Machine learning models can identify possible drug-drug interactions, contributing to safer medication use.

- **Temporal Data Modelling:**

Advanced deep learning models like LSTM networks are used to analyze time-dependent pharmacokinetic data.

3.2 Prediction of ADME properties using machine learning

Drug discovery is time-consuming, expensive, and has high failure rates. Poor pharmacokinetic properties are a major cause of drug failure. ADME profiling is essential to understand drug behavior in the body [41].

Traditional experimental methods:

- Time-intensive
- Expensive
- Limited scalability

- ML offers a faster, cost-effective, and scalable alternative for early ADME prediction.

3.3 Overview of ADME Properties

3.3.1 Absorption

Describes drug entry into systemic circulation.

Influencing factors:

- Solubility
- Intestinal permeability
- Transport mechanisms
- Example: Caco-2 permeability models.

3.3.2 Distribution

Refers to drug dispersion throughout body tissues.

Key parameters:

- Plasma protein binding
- Volume of distribution

3.3.3 Metabolism

Involves chemical transformation of drugs (mainly in liver).

Important enzymes: Cytochrome P450 family.

3.3.4 Excretion

- Removal of drugs via kidney or bile.
- Affects drug half-life and toxicity.

3.4 Role of Machine Learning in ADME Prediction

Machine learning (ML) has become a powerful computational tool for predicting Absorption, Distribution, Metabolism and Excretion (ADME) properties during early drug discovery. [42,43] Traditional experimental ADME testing is expensive, time-consuming, and resource-intensive. ML models overcome these limitations by learning patterns from molecular descriptors, chemical structures, and biological assay data to predict pharmacokinetic behavior before laboratory testing.

ML enables rapid prediction of drug-like properties, making it possible to screen thousands of molecules in a short time. This leads to significant cost reduction, supports high-throughput screening, and helps identify poor drug candidates early, thereby reducing late-stage clinical failures.

Key advantages:

- Rapid prediction
- Cost efficiency
- High-throughput screening
- Reduction in late-stage failures

3.4.1 Machine Learning Techniques Used

Several ML algorithms are widely used for ADME modeling:

Linear Regression

Linear regression models predict continuous ADME parameters such as solubility, clearance, and permeability. Although simple, they serve as baseline models for comparison. [44]

Support Vector Machines (SVM)

SVM models are useful for classification problems, such as predicting whether a compound

is toxic or non-toxic, permeable or non-permeable. [45]

Random Forest (RF)

Random Forest models combine multiple decision trees and can effectively handle nonlinear relationships between molecular features and ADME properties.[46]

Gradient Boosting Machines (GBM)

GBM models sequentially improve prediction accuracy and are widely used due to their high predictive performance.[47]

3.4.2 Deep Learning

Deep learning models provide enhanced capability for handling complex chemical data.

Artificial Neural Networks (ANNs)

ANNs can model complex nonlinear patterns and are used to predict multiple ADME properties simultaneously.[48]

Convolutional Neural Networks (CNNs)

CNNs analyze molecular graphs and chemical images, allowing automatic feature extraction from structures.[49]

Recurrent Neural Networks (RNNs)

RNNs process sequential data such as SMILES strings, enabling prediction of molecular behavior from sequence-based representations.[50]

3.**4.3 Data Sources for ADME Prediction**

Commonly used datasets:

- PubChem Bioassay
- ChEMBL
- DrugBank
- ADMET databases

Data includes:

- Molecular structures
- Experimental ADME values
- Bioactivity data

3.4.4 Feature Engineering

Feature engineering represents a critical step in the successful application of machine learning (ML) in cheminformatics and pharmacology.[51] Since ML algorithms cannot directly interpret chemical structures, molecular information must be translated into numerical representations known as molecular descriptors. These descriptors encode physicochemical, structural, and topological properties of molecules, enabling predictive modeling of biological activity, pharmacokinetics, toxicity, and drug-likeness. Carefully selected descriptors significantly enhance model accuracy, robustness, and generalizability.

Molecular Weight

Molecular weight (MW) is one of the most fundamental physicochemical descriptors used in drug discovery. It reflects the overall size of a molecule and strongly influences pharmacokinetic behavior. Compounds with very high molecular weight often exhibit reduced membrane permeability and limited oral bioavailability, whereas extremely small molecules may lack sufficient target specificity. Consequently, MW is frequently incorporated into ML models predicting absorption, distribution, and bioavailability. In many predictive frameworks, molecular weight serves as a baseline descriptor

contributing to drug-likeness evaluation and ADME profiling. [52-54]

LogP (Lipophilicity)

LogP, the logarithm of the partition coefficient between octanol and water, is a key indicator of lipophilicity. It determines the balance between aqueous solubility and membrane permeability, two essential parameters governing drug absorption and distribution. Optimal lipophilicity is required to achieve efficient membrane transport while maintaining adequate solubility. Excessive lipophilicity may lead to poor aqueous solubility and increased toxicity, whereas overly hydrophilic molecules may fail to permeate biological membranes. In ML-based drug design, LogP is widely used for predicting bioavailability, skin permeation, blood–brain barrier penetration, and toxicity risk. [55]

Hydrogen Bond Donors and Acceptors

Hydrogen bonding capacity is another critical determinant of drug–target interactions and pharmacokinetic behavior. [56] Hydrogen bond donors (HBD) and hydrogen bond acceptors (HBA) quantify the ability of molecules to participate in intermolecular interactions with biological macromolecules and aqueous environments. These descriptors play a major role in predicting solubility, permeability, receptor binding affinity, and oral bioavailability. They are also integral components of widely accepted drug-likeness guidelines and are routinely incorporated into ML models for activity and ADME prediction.

Topological and Structural Descriptors

Topological and structural descriptors provide detailed information about the molecular framework, including atom connectivity, branching patterns, ring systems, rotatable bonds, molecular surface area, and molecular volume. These descriptors capture the geometric and spatial characteristics that govern molecular recognition and binding. Since biological activity is highly dependent on molecular shape and flexibility, such descriptors are particularly valuable in predicting binding affinity, selectivity, metabolic stability, and toxicity. Machine learning models trained with topological descriptors often demonstrate improved capability in identifying structure–activity relationships (SAR). [57-60]

SMILES-Based Molecular Representation

The Simplified Molecular Input Line Entry System (SMILES) offers a text-based representation of chemical structures that enables integration with modern deep learning techniques. SMILES strings allow molecules to be treated as sequential data, facilitating the application of natural language processing methods, recurrent neural networks, and transformer architectures. In recent years, SMILES-based encoding has become central to generative models, molecular property prediction, and reaction modeling. These representations can also be transformed into molecular fingerprints or graph-based embeddings, further enriching ML model performance. [61,62]

Table No.1 Common Applications of Machine Learning in Pharmacology and Drug Discovery with Examples

Application Area	ML Task	Description	Example / Case Study	Impact on Drug Development
Drug Discovery	Virtual screening	Predicts active compounds from large chemical libraries	Deep learning models screening millions of molecules to identify	Reduces time and cost of hit identification

			COVID-19 antiviral candidates	
Drug–Target Interaction	Binding affinity prediction	Estimates how strongly a drug binds to its target protein	ML prediction of kinase inhibitor binding affinities using molecular descriptors	Accelerates lead optimization
QSAR Modeling	Activity prediction	Correlates molecular structure with biological activity	Predicting antibacterial activity of novel compounds using QSAR models	Supports rational drug design
ADMET Prediction	Absorption, distribution, metabolism, excretion, toxicity	Early evaluation of PK and safety properties	Predicting oral bioavailability and blood–brain barrier penetration	Reduces late-stage clinical failure
Toxicity Prediction	Safety assessment	Predicts hepatotoxicity, cardiotoxicity, mutagenicity	ML models predicting drug-induced liver injury (DILI)	Improves drug safety screening
Drug Repurposing	New uses for existing drugs	Identifies new therapeutic indications	Identification of existing antivirals repurposed for COVID-19 treatment	Saves development time and cost
Personalized Medicine	Patient response prediction	Predicts individual response based on genomics and clinical data	Predicting cancer patient response to chemotherapy using genomic profiles	Enables precision therapy
Biomarker Discovery	Pattern recognition in omics data	Identifies disease biomarkers from genomic/proteomic datasets	Identifying biomarkers for early cancer diagnosis	Supports targeted therapy development
Clinical Trial Optimization	Patient stratification	Selects suitable patient populations for trials	ML selecting patients likely to respond to immunotherapy	Improves clinical trial success rate
Dose Optimization	Dose–response modeling	Predicts optimal dosing regimens	ML predicting insulin dose requirements in diabetic patients	Improves efficacy and reduces toxicity
Drug Formulation	Formulation prediction	Assists in designing drug delivery systems	Predicting nanoparticle size and drug release using ML models	Enhances bioavailability and stability
Pharmacovigilance	Adverse drug reaction detection	Detects safety signals from real-world data	Mining electronic health records to identify rare adverse drug reactions	Improves post-marketing safety monitoring

4. Machine learning approaches in pharmacodynamic modeling

The relationship between a drug's concentration and its biological effects is the main focus of pharmacodynamics (PD). Conventional PD modeling uses empirical or mechanistic models (such as Emax models), but these methods frequently have trouble with biological systems that are complex and nonlinear.[63]

Researchers are now incorporating machine learning techniques to enhance prediction accuracy, reveal hidden patterns, and customize medication therapy thanks to advancements in the field.

4.1 Machine Learning's Function in Pharmacodynamics

PD modeling is improved by machine learning through:

Recognizing nonlinear dose-response correlations

- Managing high-dimensional biological data (proteomics, genomics)
- Making patient-specific forecasts possible
- Enhancing medication effectiveness and toxicity forecasting

4.2. Typical Machine Learning Methods

4..2.1 Guided Education

- utilized in situations where labeled data (dose → response) is accessible
- Baseline PD models using linear regression
- The Random Forest
- SVMs, or support vector machines

Uses:

- Anticipating medication response
- Calculating EC50 and Emax

4.2.2 Unsupervised Education

- utilized for pattern recognition in the absence of labeled outputs.
- K-means and hierarchical clustering
- PCA, or principal component analysis

Uses:

- Stratification of patients
- Finding biomarkers

4.2.3 In-depth Education

- Neural network-based advanced machine learning method.
- ANNs, or artificial neural networks
- CNNs, or convolutional neural networks
- RNNs, or recurrent neural networks

Uses:

- PK/PD relationships that are complex
- Modeling time-series drug responses

4.2.4 Learning by Reinforcement

learns the best dosage techniques by making mistakes.

Uses:

- Customized dosage schedules
- Optimization of adaptive therapy

4.3 PK/PD Modeling Integration

- Conventional pharmacokinetic/ pharmacodynamic (PK/PD) models are frequently integrated with machine learning:
- Models that combine machine learning and mechanics

- PD models based on data
- Precision dosing based on models

4.4. Healthcare Applications

4.4.1 Medical Precision

- ML aids in customizing medication treatment based on:
- Profile of genetics
- illness state
- Variability among patients

4.4.2 The Development of Drugs

- Estimate medication effectiveness early
- Cut down on clinical trial failures
- Optimize the choice of dosage

4.4.3 Prediction of Toxicity

- Early identification of negative medication reactions
- Safety evaluation of novel medications

5. Machine learning in dose response & drug target interaction studies.

In modern pharmacology, it is crucial to understand both the effect a drug produces and the mechanism through which it interacts with biological systems. The dose–response relationship illustrates how variations in drug concentration influence physiological outcomes, while drug–target interactions (DTIs) explain the binding of drugs to specific biological molecules such as enzymes, receptors, or proteins.

Traditional experimental and mathematical approaches are often limited when dealing with complex biological variability. The adoption of Machine Learning techniques has significantly improved the ability to analyze, predict, and interpret these relationships more efficiently.[64-67]

5.1. Role of Machine Learning in Dose–Response Evaluation

5.1.1 Basic Concept

Dose–response analysis is essential for determining:

- The strength of a drug (potency)
- The highest effect achievable (maximum response)
- The safe therapeutic range
- Conventional models, such as the Hill equation, rely on predefined assumptions that may not accurately represent real biological systems.

5.1.2 Machine Learning Techniques Used

a. Regression-Based Methods

- Simple and advanced regression models
- Random forest algorithms
- Boosting techniques

Function: These methods estimate how changes in dose levels influence the biological response.

b. Neural Network-Based Models

- Artificial neural networks
- Deep learning architectures

Function: Capable of identifying complex and nonlinear relationships in large datasets.

c. Probabilistic Models

Gaussian process-based approaches

Function: Provide both predictions and uncertainty estimation, especially useful with smaller datasets.

5.1.3 Machine Learning in Drug–Target Interaction Studies

5.1.3.1 Importance of DTIs

Drug–target interactions play a vital role in determining:

- Therapeutic action
- Specificity of the drug
- Risk of adverse effects

Experimental identification of these interactions is resource-intensive, making computational approaches highly advantageous.

5.1.3.2 ML Strategies for Predicting DTIs

a. Similarity-Oriented Methods

- Based on chemical resemblance of drugs
- Based on biological similarity of targets

Concept: Compounds or proteins with similar features are likely to interact in similar ways.

b. Classification Models

- Support vector machines
- Random forest classifiers
- Logistic regression

Function: These models predict whether a drug–target interaction exists.

c. Deep Learning Approaches

- Convolutional neural networks for structural data
- Graph-based neural networks for molecular representation

Function: Capture intricate interaction patterns from complex datasets

d. Network-Based Approaches

- Biological network modeling
- Link prediction techniques

6. Future Perspective

The role of Machine Learning (ML) in pharmaceutical sciences, especially in pharmacokinetics (PK) and pharmacodynamics (PD), is anticipated to grow substantially in the near future. Continuous progress in computational technologies, along with the increasing availability of large and diverse datasets, is driving this evolution.

Progress in Advanced AI Models

Modern deep learning techniques, including artificial neural networks and transformer-based architectures, are expected to improve the prediction of complex biological and pharmacological relationships. These approaches are capable of modeling intricate, non-linear interactions within PK/PD systems.

Incorporation of Multi-Omics Data

Future developments will emphasize the integration of multi-omics datasets such as

genomics, proteomics, and metabolomics. This will enable more precise and individualized therapeutic strategies, thereby advancing personalized medicine.

Utilization of Real-World Evidence (RWE)

The growing use of real-world data, including electronic health records and patient monitoring systems, will enhance the predictive performance and clinical applicability of ML models. This approach will improve understanding of drug behavior across varied populations.

Development of Explainable AI (XAI)

Increasing attention is being given to the transparency of ML models. Explainable AI techniques will allow researchers and healthcare professionals to interpret model predictions, thus improving reliability and regulatory compliance.

Automation of Drug Development Processes

ML technologies are expected to automate various stages of drug discovery, including target identification, lead optimization, and toxicity prediction. This will significantly reduce both the time and cost involved in pharmaceutical development.

Regulatory Advancements and Standardization

Regulatory authorities are beginning to acknowledge the importance of ML in healthcare. Future frameworks will likely establish standardized protocols for validation, ensuring safe and effective implementation in PK/PD studies.

Expansion of Cloud and Big Data Technologies

The integration of cloud computing and big data analytics will facilitate efficient processing and storage of large-scale pharmaceutical datasets, supporting collaborative and scalable research efforts.

CONCLUSION

Machine learning has emerged as a transformative tool in pharmacology and drug discovery, enabling faster and more cost-effective identification of drug candidates, prediction of ADMET properties, and optimization of therapeutic outcomes. The success of these models largely depends on robust feature engineering, where molecular descriptors and modern chemical representations translate complex molecular information into machine-readable formats.

Despite significant progress, challenges such as limited high-quality datasets, model interpretability, and integration into regulatory workflows remain. Future advancements in explainable AI, multi-omics integration, and personalized medicine are expected to further enhance the reliability and applicability of ML in pharmaceutical research. Overall, continued interdisciplinary collaboration will be essential to fully realize the potential of machine learning in accelerating safe and effective drug development.

ABBREVIATIONS

- ADME – Absorption, Distribution, Metabolism and Excretion
- ADMET – Absorption, Distribution, Metabolism, Excretion and Toxicity
- AI – Artificial Intelligence
- ANN – Artificial Neural Network
- BBB – Blood–Brain Barrier
- CNN – Convolutional Neural Network
- DTI – Drug–Target Interaction

- EC50 – Half Maximal Effective Concentration
- Emax – Maximum Drug Effect
- GBM – Gradient Boosting Machine
- HBA – Hydrogen Bond Acceptors
- HBD – Hydrogen Bond Donors
- LSTM – Long Short-Term Memory
- ML – Machine Learning
- MW – Molecular Weight
- NLP – Natural Language Processing
- PCA – Principal Component Analysis
- PD – Pharmacodynamics
- PK – Pharmacokinetics
- QSAR – Quantitative Structure–Activity Relationship
- RF – Random Forest
- RNN – Recurrent Neural Network
- RWE – Real-World Evidence
- SAR – Structure–Activity Relationship
- SMILES – Simplified Molecular Input Line Entry System
- SVM – Support Vector Machine
- XAI – Explainable Artificial Intelligence

REFERENCES

1. Caldwell J, Gardner I, Swales N. An introduction to drug disposition: the basic principles of absorption, distribution, metabolism, and excretion. Toxicologic pathology. 1995 Mar;23(2):102-14.
2. Vrbanac J, Slauter R. ADME in drug discovery. InA comprehensive guide to toxicology in nonclinical drug development 2017 Jan 1 (pp. 39-67). Academic Press.
3. Al-Kabani, A., Huda, B., Haddad, J., Yousuf, M., Bhurka, F., Ajaz, F., Patnaik, R., Jannati, S. and Banerjee, Y., 2025. Exploring experimental models of colorectal cancer: a critical appraisal from 2D cell systems to organoids, humanized mouse avatars, organ-on-chip, CRISPR engineering, and AI-driven platforms—challenges and opportunities for translational precision oncology. Cancers, 17(13), p.2163.
4. Turkarslan S, He Y, Hothi P, Murie C, Nicolas A, Kannan K, Park JH, Pan M, Patel A, Cobbs C, Baliga NS. EPCO-42. A SYSTEMS SCALE MODEL FOR PERSONALIZED PRECISION ONCOLOGY APPLICATIONS TO GBM. Neuro-Oncology. 2023 Nov 10;25(Suppl 5):v133.
5. Patel MP, Patel KM, Vhora SZ, Gajjar AK, Patel JK, Patel AK. Model-Based Pharmacokinetic Approaches. Basics and Clinical Applications of Drug Disposition in Special Populations. 2025 Mar 7:11-51.
6. Pavlyshyn V, Manziuk E, Barmak O, Radiuk P, Krak I. An Adaptive Machine Learning Approach to Sustainable Traffic Planning: High-Fidelity Pattern Recognition in Smart Transportation Systems. Future Transportation. 2025 Oct 28;5(4):152.
7. Bruce JL. An Overview of Supervised Machine Learning in Drug Discovery, PK/PD Modeling and Precision Pharmacogenomics. Medi Clin Case Rep J. 2025 Oct 13;3(4):1439-45.
8. Russell C, Rahman A, Mohammed AR. Application of genomics, proteomics and metabolomics in drug discovery, development and clinic. Therapeutic delivery. 2013 Mar 1;4(3):395-413.
9. Baptista D, Ferreira PG, Rocha M. Deep learning for drug response prediction in cancer. Briefings in bioinformatics. 2021 Jan;22(1):360-79.
10. Poweleit EA, Vinks AA, Mizuno T. Artificial intelligence and machine learning approaches to facilitate therapeutic drug management and model-informed precision dosing. Therapeutic drug monitoring. 2023 Apr 1;45(2):143-50.

11. Ghani S, Khan N, Sable H, Yao F, Shafiq M. Computational techniques for enhancing PK/PD modeling and simulation and ADMET prediction. InComputational Methods in Medicinal Chemistry, Pharmacology, and Toxicology 2025 Jan 1 (pp. 153-174). Academic Press.
12. Dudarski L. Harnessing machine learning for predictive pharmacokinetics: revolutionizing drug development and personalized medicine. Current Issues in Pharmacy and Medical Sciences. 2025 May 21;38(2):125-31.
13. Chou WC, Lin Z. Machine learning and artificial intelligence in physiologically based pharmacokinetic modeling. Toxicological Sciences. 2023 Jan 1;191(1):1-4.
14. Arav Y. Advances in modeling approaches for oral drug delivery: Artificial intelligence, physiologically-based pharmacokinetics, and first-principles models. Pharmaceutics. 2024 Jul 24;16(8):978.
15. Paliwal A, Jain S, Kumar S, Wal P, Khandai M, Khandige PS, Sadananda V, Anwer MK, Gulati M, Behl T, Srivastava S. Predictive Modelling in pharmacokinetics: from in-silico simulations to personalized medicine. Expert Opinion on Drug Metabolism & Toxicology. 2024 Apr 2;20(4):181-95.
16. Altynova S, Saliev T, Asanova A, Kozybayeva Z, Rakhimzhanova S, Bolatov A. Artificial Intelligence and Predictive Modelling for Precision Dosing of Immunosuppressants in Kidney Transplantation. Pharmaceuticals. 2026 Jan 16;19(1):165..
17. Kantesaria R, Panda HS. A Review on AI-Based Data-Driven Models for Optimization of Nanocarriers as Drug Delivery Systems. ACS Biomaterials Science & Engineering. 2026 Feb 10.
18. D'Souza S, Prema KV, Balaji S. Machine learning models for drug–target interactions: current knowledge and future directions. Drug Discovery Today. 2020 Apr 1;25(4):748-56.
19. You J, McLeod RD, Hu P. Predicting drug-target interaction network using deep learning model. Computational biology and chemistry. 2019 Jun 1;80:90-101.
20. Ma J, Sheridan RP, Liaw A, Dahl GE, Svetnik V. Deep neural nets as a method for quantitative structure–activity relationships. Journal of chemical information and modeling. 2015 Feb 23;55(2):263-74.
21. Soares TA, Nunes-Alves A, Mazzolari A, Ruggiu F, Wei GW, Merz K. The (Re)-Evolution of Quantitative Structure–Activity Relationship (QSAR) studies propelled by the surge of machine learning methods. Journal of Chemical Information and Modeling. 2022 Nov 28;62(22):5317-20.
22. Esposito EX, Hopfinger AJ, Madura JD. Methods for applying the quantitative structure-activity relationship paradigm. InChemoinformatics: Concepts, methods, and tools for drug discovery 2004 Jan 1 (pp. 131-213). Totowa, NJ: Humana Press.
23. Guan S, Xu Z, Yang T, Zhang Y, Zheng Y, Chen T, Liu H, Zhou J. Identifying potential targets for preventing cancer progression through the PLA2G1B recombinant protein using bioinformatics and machine learning methods. International journal of biological macromolecules. 2024 Sep 1;276:133918.
24. Li R, Li L, Xu Y, Yang J. Machine learning meets omics: applications and perspectives. Briefings in Bioinformatics. 2022 Jan;23(1):bbab460.
25. Jamshidi M, Moztarzadeh O, Jamshidi A, Abdelgawad A, El-Baz AS, Hauer L. Future of drug discovery: The synergy of edge computing, internet of medical things, and deep learning. Future Internet. 2023 Apr 7;15(4):142.

26. Muratov EN, Amaro R, Andrade CH, Brown N, Ekins S, Fourches D, Isayev O, Kozakov D, Medina-Franco JL, Merz KM, Oprea TI. A critical overview of computational approaches employed for COVID-19 drug discovery. Chemical Society Reviews. 2021;50(16):9121-51.
27. Zhou Y, Wang F, Tang J, Nussinov R, Cheng F. Artificial intelligence in COVID-19 drug repurposing. The Lancet Digital Health. 2020 Dec 1;2(12):e667-76.
28. Tripathi RK. Data analytics and AI for predictive maintenance in pharmaceutical manufacturing. InData analytics and artificial intelligence for predictive maintenance in smart manufacturing 2024 Oct 23 (pp. 117-149). CRC Press.
29. Rajesh MV, Elumalai K. The transformative power of artificial intelligence in pharmaceutical manufacturing: enhancing efficiency, product quality, and safety. Journal of Holistic Integrative Pharmacy. 2025 Jun 1;6(2):125-35.
30. Caldwell GW. ADME optimization and toxicity assessment in drug discovery. InFrontiers in Medicinal Chemistry: Volume 8 2016 Jan 26 (pp. 3-60). Bentham Science Publishers.
31. Naik K, Goyal RK, Foschini L, Chak CW, Thielscher C, Zhu H, Lu J, Lehár J, Pacanoswki MA, Terranova N, Mehta N. Current status and future directions: the application of artificial intelligence/machine learning for precision medicine. Clinical Pharmacology & Therapeutics. 2024 Apr;115(4):673-86.
32. Patel AA. Hands-on unsupervised learning using Python: how to build applied machine learning solutions from unlabeled data. O'Reilly Media; 2019 Feb 21.
33. Johnston B, Jones A, Kruger C. Applied Unsupervised Learning with Python: Discover hidden patterns and relationships in unstructured data with Python. Packt Publishing Ltd; 2019 May 28.
34. Valkenborg D, Rousseau AJ, Geubbelmans M, Burzykowski T. Unsupervised learning. American Journal of Orthodontics and Dentofacial Orthopedics. 2023 Jun 1;163(6):877-82.
35. Gahane, S., Verma, P., Khode, P., Sharma, D. and Anawade, P., 2024, December. Innovating supervised and semi supervised learning: reducing label dependency, enhancing data efficiency and developing scalable, adaptive models for real time applications. In International Conference on Information and Communication Technology for Competitive Strategies (pp. 133-143). Singapore: Springer Nature Singapore.
36. Yan J, Wang X. Unsupervised and semi-supervised learning: the next frontier in machine learning for plant systems biology. The Plant Journal. 2022 Sep;111(6):1527-38.
37. Williamson B, Bonn B, Lindmark B, Colclough N, Harlfinger S, Llinas A, Hilgendorf C. Metabolism and Pharmacokinetic Optimization Strategies in Drug Discovery. Drug Discovery and Development E-Book: Technology in Transition; Elsevier: Amsterdam, The Netherlands. 2021 May 16;134:134-58.
38. Rane NL, Paramesha M, Choudhary SP, Rane J. Machine learning and deep learning for big data analytics: A review of methods and applications. Partners Universal International Innovation Journal. 2024 Jun 25;2(3):172-97.
39. Boppiniti ST. Big data meets machine learning: Strategies for efficient data processing and analysis in large datasets. International Journal of Creative Research In Computer Technology and Design. 2020;2(2).
40. Mishra P, Varadharajan V, Tupakula U, Pilli ES. A detailed investigation and analysis of

using machine learning techniques for intrusion detection. IEEE communications surveys & tutorials. 2018 Jun 15;21(1):686-728.
41. Butina D, Segall MD, Frankcombe K. Predicting ADME properties in silico: methods and models. Drug discovery today. 2002 May 6;7(11):S83-8.
42. Chou WC, Canchola A, Zhang F, Lin Z. Machine learning and artificial intelligence in nanomedicine. Wiley interdisciplinary reviews: Nanomedicine and nanobiotechnology. 2025 Jul;17(4):e70027.
43. Chuntakaruk H, Boonpalit K, Kinchagawat J, Nakarin F, Khotavivattana T, Aonbangkhen C, Shigeta Y, Hengphasatporn K, Nutanong S, Rungrotmongkol T, Hannongbua S. Machine learning-guided design of potent darunavir analogs targeting HIV-1 proteases: A computational approach for antiretroviral drug discovery. Journal of Computational Chemistry. 2024 May 15;45(13):953-68.
44. Kosugi Y, Hosea N. Prediction of oral pharmacokinetics using a combination of in silico descriptors and in vitro ADME properties. Molecular Pharmaceutics. 2021 Jan 29;18(3):1071-9.
45. Sharma AK, Srivastava GN, Roy A, Sharma VK. ToxiM: a toxicity prediction tool for small molecules developed using machine learning and chemoinformatics approaches. Frontiers in pharmacology. 2017 Nov 30;8:880.
46. Elsayad AM, Zeghid M, Elsayad KA, Khan AN, Baareh AK, Sadig A, Mukhtar SA, Ali HF, Abd El-kader S. Machine learning model for random forest acute oral toxicity prediction. Global Journal of Environmental Science and Management. 2025;11(1):21-38.
47. Zhang Y, Haghani A. A gradient boosting method to improve travel time prediction. Transportation Research Part C: Emerging Technologies. 2015 Sep 1;58:308-24.
48. Butina D, Segall MD, Frankcombe K. Predicting ADME properties in silico: methods and models. Drug discovery today. 2002 May 6;7(11):S83-8.
49. Li Z, Jiang M, Wang S, Zhang S. Deep learning methods for molecular representation and property prediction. Drug Discovery Today. 2022 Dec 1;27(12):103373.
50. Mswahili ME, Jeong YS. Transformer-based models for chemical SMILES representation: A comprehensive literature review. Heliyon. 2024 Oct 30;10(20).
51. Niazi SK, Mariam Z. Recent advances in machine-learning-based chemoinformatics: a comprehensive review. International Journal of Molecular Sciences. 2023 Jul 15;24(14):11488.
52. Raevsky OA. Physicochemical descriptors in property-based drug design. Mini reviews in medicinal chemistry. 2004 Dec 1;4(10):1041-52.
53. Meanwell NA. Improving drug candidates by design: a focus on physicochemical properties as a means of improving compound disposition and safety. Chemical research in toxicology. 2011 Sep 19;24(9):1420-56.
54. Hansch C. The physicochemical approach to drug design and discovery (QSAR). Drug Development Research. 1981;1(4):267-309.
55. Wang Y, Li Y. Machine learning prediction of dioxin lipophilicity and key feature Identification. Computational and Theoretical Chemistry. 2025 Feb 1;1244:115032.
56. Decherchi S, Cavalli A. Thermodynamics and kinetics of drug-target binding by molecular simulation. Chemical Reviews. 2020 Oct 2;120(23):12788-833.
57. Ning X, Karypis G. In silico structure-activity-relationship (SAR) models from machine learning: a review. Drug

Development Research. 2011 Mar;72(2):138-46.
58. Zhang R, Nolte D, Sanchez-Villalobos C, Ghosh S, Pal R. Topological regression as an interpretable and efficient tool for quantitative structure-activity relationship modeling. Nature Communications. 2024 Jun 13;15(1):5072.
59. Vaishnav Y, Verma S, Mishra A. The Role of Structure-Activity Relationship (SAR) In Drug Discovery. Indian Journal of Pharmaceutical Chemistry and Analytical Techniques. 2025 Jun 2:67-83.
60. Staszak M, Staszak K, Wieszczycka K, Bajek A, Roszkowski K, Tylkowski B. Machine learning in drug design: Use of artificial intelligence to explore the chemical structure–biological activity relationship. Wiley Interdisciplinary Reviews: Computational Molecular Science. 2022 Mar;12(2):e1568.
61. Wu JN, Wang T, Chen Y, Tang LJ, Wu HL, Yu RQ. t-SMILES: a fragment-based molecular representation framework for de novo ligand design. Nature Communications. 2024 Jun 11;15(1):4993.
62. Li C, Feng J, Liu S, Yao J. A Novel Molecular Representation Learning for Molecular Property Prediction with a Multiple SMILES-Based Augmentation. Computational Intelligence and Neuroscience. 2022;2022(1):8464452.
63. Stevens J, Ploeger BA, Hammarlund-Udenaes M, Osswald G, van der Graaf PH, Danhof M, de Lange EC. Mechanism-based PK–PD model for the prolactin biological system response following an acute dopamine inhibition challenge: quantitative extrapolation to humans. Journal of pharmacokinetics and pharmacodynamics. 2012 Oct;39(5):463-77.
64. Mei S, Zhang K. A machine learning framework for predicting drug–drug interactions. Scientific Reports. 2021 Sep 2;11(1):17619.
65. You J, McLeod RD, Hu P. Predicting drug-target interaction network using deep learning model. Computational biology and chemistry. 2019 Jun 1;80:90-101.
66. Qureshi R, Basit SA, Shamsi JA, Fan X, Nawaz M, Yan H, Alam T. Machine learning based personalized drug response prediction for lung cancer patients. Scientific Reports. 2022 Nov 7;12(1):18935.
67. Ietswaart R, Arat S, Chen AX, Farahmand S, Kim B, DuMouchel W, Armstrong D, Fekete A, Sutherland JJ, Urban L. Machine learning guided association of adverse drug reactions with in vitro target-based pharmacology. EBioMedicine. 2020 Jul 1;57.

HOW TO CITE: Sakshi Jagtap, Srushti Gaikwad, Rasika Kadam, Prajakta Patil, Machine Learning in Pharmacokinetics and Pharmacodynamics, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 4, 2436-2452. https://doi.org/10.5281/zenodo.19595366