World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Review Article
ISSN: 2583-6579
SJIF Impact Factor: 6.916
Year - 2026
Volume: 5; Issue: 4
Page: 494-504

# MACHINE LEARNING APPROACHES FOR PREDICTING DRUG RELEASE FROM NOVEL DRUG DELIVERY SYSTEMS

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***Article Received: 17 February 2026*** || ***Article Revised: 9 March 2026*** || ***Article Accepted: 30 March 2026***

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**How to cite this Article:** Abhishek Ghosh, Sarmili Sahoo, Piyasa Chakraborty, Chintada Sowjanya, Dr. K. Sudheer Kumar, Seetaramswamy Seepena, Animesh Kumar Tiwari, Indeevar, Saksham Pathak and Kuldeep Singh (2026) MACHINE LEARNING APPROACHES FOR PREDICTING DRUG RELEASE FROM NOVEL DRUG DELIVERY SYSTEMS. World Journal of Pharmaceutical Science and Research, 5(4), 494-504.



**ABSTRACT**

This paper aims to present how machine learning methods can be used to predict drug release from novel drug delivery systems, which is one of the most crucial problems in pharmaceutical sciences. The goal therefore is to explain how different machine learning methods can enhance the predictive capabilities for drug release kinetics compared to traditional mechanistic modelling approaches. To achieve this goal, the basic concepts underlying drug release and presentation of data-based approaches are given in detail to provide background knowledge to the interdisciplinary modelling approach. The main outcomes of the paper are that machine learning algorithms make the prediction process easier which also facilitates more tailored formulation design due to the identification of various relations in complex datasets. To conclude, the successful application of machine learning in predictive modelling is presented to have the potential to create disruption in traditional modelling in pharmaceutical science that will lead to more efficient design and optimisation of innovative drug delivery systems.

**KEYWORDS:** Machine Learning, Drug Release Prediction, Drug Delivery Systems, Controlled Drug Release, Predictive Modeling.

## INTRODUCTION

Accurate drug release prediction is a critical issue in pharmaceutical sciences since relevant prediction highly determines the success of the therapy and safety of the patient. Novel technologies in drug delivery systems, such as innovative nanoparticles, hydrogels and implantable devices, have been designed to satisfy the drawbacks of classic formulations and to provide effects with controlled release. These advanced drug delivery platforms exhibit new challenges in drug release predictions due to their novel material properties and mechanisms. Significant traditional models, which highly depend on various mathematical equations, might not be successful in defining the drug release effects in complex systems where so many parameters are effective simultaneously. Applying machine learning, as a way of data extraction, might be a promising approach for the next generation decades combining methodologies for drug delivery systems due to its proficiency in defining complex relationships and correlations and its prediction capability.

### Background on Drug Delivery Systems

The switch from traditional drug delivery systems to advanced controlled and targeted drug delivery systems during the last few decades has driven drug delivery field to flourish. Nanoparticles, hydrogels, and micelles serve as examples for these drug delivery systems with their unique characteristics in adjusting release rate and enhancing drug bioavailability. The development of these delivery systems has been largely focused on nanocarriers, which have been characterized through systematic understanding of various parameters such as particle size, structure, and zetapotential, which can play a significant role in the stability, effect and success of the drug during in vivo conditions (Alshawwa et al., 2022). Principle of their functionality has been analyzed by applying characterization technologies including dynamic light scattering and electron microscopy, drug entrapment and release, which are crucial for the reliability and reproducibility of the drug delivery system (Alshawwa et al., 2022). The emergence of numerous delivery systems symbolize a successful effort to remove the barriers of controlled drug deliveries that lasted for years and represents one of the significant milestones in drug delivery research and development.

The predicted release profiles of the drug from novel delivery systems are mainly perturbed due to additional complexities of almost all these systems. The variability between materials, structure and is further complicated with time and the complexity of in vivo biological systems result in numerous limitations in utilizing current models which needs a huge effort to accomplish the nonlinearities possibly involved. Novel analysis like machine learning is also faced with challenges including overfitting due to the high data dimension, actual physical and chemical interaction characterization is incomplete, noise associated with experimental and measurement errors (Alshahrani et al., 2024). In addition, the complex choice of architecture and hyperparameter tuning is made evident based on the results of different regression performances using Gradient Boosting and Gaussian Process Regression models (Alshahrani et al., 2024). These factors appeal for careful measures for method choices with ideas on materials and processes utilized in these new delivery systems for model prediction.

### Fundamentals of Drug Release Kinetics

Kinetic modeling and understanding the principles of drug release is important to characterize the therapeutic activity and performance of drug formulations. The most known and reliable kinetic models, such as zero-order, first-order, Higuchi, and Korsmeyer-Peppas included describe various drug release mechanisms from the delivery system and, consequently, are important tools for experimental data interpretation. For example, zero-order kinetics and constants

relate to the zero-order model characteristics, first-order kinetics and constants are related to the drug concentration effects, and Higuchi and Korsmeyer-Peppas models included diffusion process and polymer relaxation effects, respectively. The kinetic models are determined by different factors affecting drug release rate including drug and carrier physicochemical properties; surrounding factors and delivery system structure characteristics (Alshahrani et al., 2024). The data and parameters used can result in the exact and predictive drug release kinetic models, if then applied through the polymer-drug relations and results of their parameters and geometry (Alshahrani et al., 2024).

However, the traditional kinetic models have serious drawbacks in the application to modern drug carrier design because of the increasing system complexity. Although the traditional models yield acceptable descriptions for the simple matrices, these models cannot handle the non-linear multi-variable effects of advanced carriers with a variety of factors, including variable microenvironments or complex material composition. In fact, the deterministic equations of the Higuchi's or Korsmeyer-Peppas models cannot provide realistic descriptions to non-homogeneous release behaviors caused or greatly influenced by multi-component matrices and interacting excipients, which are acquired from most present-day formulations. Furthermore, it has been documented that most of these traditional models provide poor predictive capabilities across multiple conditions for different drug formulations, which mainly consist of the different active pharmaceutical ingredients and types of excipients (Protopapa et al., 2025). Consequently, it has become evident that researchers have advocated further the use of alternative approaches that have the ability to deal with big, heterogeneous datasets and capture the complex relationships underlying drug release from modern delivery technologies (Protopapa et al., 2025).

**Introduction to Machine Learning in Pharmaceutics**

Unlike previous analytical technology of gastric release methods and dissolution tools, machine learning has brought a paradigm shift to the pharmaceutical research and development industries, especially in the predictive modeling studies of release from complex drug delivery systems. In this era of complex formulation, where the traditional approaches are faced with the curse of dimensionality, machine learning offers the unprecedented opportunity to practitioners to deal with and interrogate the complex and multifactorial data sets to uncover the hidden structure–function relationships (Gormley, 2024). The adoption of cutting-edge data science tools may allow scientists to quit their ineffective high-throughput screening days and ultimately yield empirically predictive but quantitative models to describe each drug-material combination accurately from the process. When coupled with automation processes, machine learning could make formulation development a streamlined process by designed experiments and accelerate the optimization of novel delivery systems to formulation labs (Gormley, 2024). Therefore, while machine learning is in its infancy stages in the field of pharmaceutics, incorporating machine learning into modeling and simulation can unravel the analytical challenges expected from contemporary drug delivery systems while improving the scientific knowledge and creativity within the discipline.

The machine-learning-based model for prediction of successful drug release profiles also integrates the choice of multiple forms of data.Concurrent with the machine-learning-based model and the machine- learning training inputs, the model inputs drug formulation includes formulation parameters such as polymer type (e.g. PLGA), drug loading amount (e.g. 200 µg/mL), excipient type and amount (e.g. 250 µg/mL of surfactant for control), particle geometry (e.g. rod, spheres), physicochemical properties including solubility (e.g. α, 490 mg/L), molecular weight (e.g. 12 Kg/mol of PLGA, 9000 g/mol), surface-to-volume (e.g. 0.1), and experiment release data taken from in vitro release experiments

conducted varying parameters such as pH scales (e.g. 5.5 – 7.4) , temperature (e.g. 37º C, 39º C).Importantly, the experimental probe of data gathered from these processes teach the model data about the characterizing elements of the defining underlying multiple input variables to the variable output (i.e. drug-release) behavior of the chosen delivery system in the different environments and conditions. The model subsequently integrates this information and helps to determine the relationships of release behavior and its posited contributory factors (i.e. drug anthropometrics, delivery system loading and drug-excipient-geometric interactions, etc.). In this way, machine-learning of probe-based data can define new methods for making observations about the drug-delivery behavior process and how its outcomes are influenced by structural characteristics, compositional information, and environmental considerations. In this way, the machine learning process facilitates the generation od more precise data-driven models and predictive outputs where classical inference methods simply cannot provide (Sun et al., 2025).

**Types of Machine Learning Approaches**

As the major machine learning methods employed in drug release prediction, recent findings have reported a variety of supervised learning algorithms: regression methods, decision trees, and support vector machines. Regression algorithms, both linear and non-linear models, are utilized to model the direct dependencies between formulation variables and drug release. Regression methods can directly analyze the continuous dependent variables which are often encountered in drug release studies. Similarly, decision-tree based algorithms which recursively divide the input variable into the leave nodes with interpretable rules are also widely combined with boosting learned algorithms such as AdaBoost or used as a modular component in more advanced stacked models, e.g. multilayer perceptron networks.

This is mainly done to further improve accuracy in drug release prediction for high multidimensional datasets (Yadav et al., 2025). High dimensionality and complex classification problems characteristic of pharmaceutical data can also incurred by support vector machines, which is often used to produce optimal hyperplanes to separate classes either for classification or regression. Interestingly, hybrid algorithm such as dimensionality reduction techniques or optimization algorithms in combination with other methods have also exhibited improved model performances in predicting complex drug releasing patterns for targeted delivery systems (Yadav et al., 2025).

**Table 1: Types of Machine Learning Algorithms Used in Drug Release Prediction.**

| Machine Learning Method | Type | Key Principle | Application in Drug Release Prediction | Advantages | References |
|---|---|---|---|---|---|
| Linear / Non-Linear Regression | Supervised Learning | Models relationships between formulation variables and drug release values | Predict continuous drug release profiles based on formulation parameters | Simple, interpretable, suitable for regression data | Yadav et al., 2025 |
| Decision Tree & Random Forest | Supervised Learning | Splits dataset into decision nodes to model variable interactions | Predict cumulative drug release from complex formulations | Handles non-linear data and multiple variables effectively | Protopapa et al., 2025 |
| Support Vector Machine (SVM) | Supervised Learning | Creates optimal hyperplanes for regression or classification tasks | Used for predicting release kinetics and complex pharmaceutical datasets | High accuracy in high-dimensional datasets | Yadav et al., 2025 |
| Gradient Boosting Algorithms | Supervised Learning | Combines multiple weak models to improve prediction accuracy | Predicts drug release kinetics in complex systems | High predictive performance | Alshahrani et al., 2024 |
| Artificial | Deep | Multi-layer networks | Predict drug release | Captures complex | Husseini et |

| | | | | | |
|---|---|---|---|---|---|
| Neural Networks (ANN) | Learning | that learn nonlinear relationships | behavior in nanocarriers and advanced DDS | nonlinear relationships | al., 2024 |
| Clustering (e.g., K-means) | Unsupervised Learning | Groups data based on similarity without predefined labels | Identifies patterns in drug release profiles and formulation datasets | Useful for exploratory data analysis | Liu et al., 2023 |

Table 1 summarizes the major machine learning algorithms used for predicting drug release from novel drug delivery systems. Various supervised learning approaches such as regression models, decision trees, and support vector machines are commonly applied to model the relationship between formulation variables and drug release profiles. In addition, ensemble techniques like gradient boosting and deep learning models such as artificial neural networks have demonstrated improved predictive performance for complex datasets. Unsupervised learning methods, including clustering algorithms, are also useful for identifying hidden patterns within drug release data. These approaches enable the analysis of multidimensional pharmaceutical datasets and enhance the accuracy of drug release prediction compared with traditional modeling techniques (Yadav et al., 2025; Protopapa et al., 2025; Liu et al., 2023).

Recently, deep-learning methods, especially neural networks, also appeared as appropriate alternatives to predict drug release from the next generation delivery systems. Their typical features for layered non-linear function approximations enables deep-learning models to learn complex relationships between numerous internal composition- and external environment-related parameters. A study explored the use of deep-learning algorithms for the prediction of triggered drug release applications from nanocarrier systems, namely liposomes and metal-organic frameworks, under various physical and chemical parameters (Husseini et al., 2024). In this work, deep-learning neural networks outperformed traditional linear models to model triggered release processes by intrinsic and extrinsic stimuli, such as pH change and ultrasound or ultraviolet-light stimulation. In brief, employing deep-learning models allow a better, and also scalable, expansion of the predictive model to be utilized for a more accurate optimization and control of drug-delivery systems implementation in modern clinical practices (Husseini et al., 2024)

In addition, unsupervised methods, such as clustering, have been increasingly applied for analysis of drug release data to extrapolate hidden information that is common for cases where predefined output classes or labels are unavailable (Liu et al., 2023). Clustering of drug release profiles, formulation parameters, and environmental conditions can help recognize data structure and variability, which can be indicative of release kinetics associated with minor formulation factors or batching errors, otherwise non-recognizable through standard analysis (Liu et al., 2023). The implementation of deep learning-based quantitative methods into unsupervised techniques has contributed to recognition of prevailing temporal trends and subpopulations among wide-scaled in vitro studies (Liu et al., 2023). These analytics can provide an important data background for model building, formulation knowledge, and delivering advanced drug carriers for matching multiple clinically-relevant demands.

**Data Preparation and Feature Engineering**

The critical role of data preparation and feature engineering in the development of reliable ML-based drug release prediction involves the use of proper preprocessing, such as normalization and outlier detection, to allow recognition of the different formulation and experimental conditions during model training or application. Proper features selection identifies the parameters that have the greatest influence on the release kinetics, such as drug loading, polymer type and content as well as environmental factors. The identification process should also aim to remove highly-correlated or unimportant parameters that may increase the risk of overfitting or prolong computation time (Al-Rajabi et al., 2025).

Feature engineering involves the derivation of new input variables or the transformation of available variables to allow the modeling process to discover complex relationships in the present data, such as nonlinear dependences on temperature as well as compositional factors, which are present in sophisticated drug delivery systems. According to the recent research utilizing temperature-sensitive hydrogels, the application of these techniques has allowed hybrid ML models to achieve a superior level of predictive performance based on the inclusion of physical and compositional data that are significant for the underlying drug release phenomena (Al-Rajabi et al., 2025).

**Table 2: Key Factors and Data Inputs Used for Machine Learning Models in Drug Release Prediction.**

| Category | Input Parameters | Example Values | Importance in Prediction | References |
|---|---|---|---|---|
| Drug Properties | Solubility, molecular weight, chemical structure | Solubility: 490 mg/L | Determines drug diffusion and dissolution rate | Sun et al., 2025 |
| Formulation Parameters | Polymer type, drug loading, excipient concentration | PLGA polymer, drug loading 200 µg/mL | Influences drug encapsulation and release kinetics | Sun et al., 2025 |
| Carrier Characteristics | Particle size, shape, surface-to-volume ratio, zeta potential | Nanoparticles, spheres or rods | Affects drug stability and release mechanism | Alshawwa et al., 2022 |
| Environmental Conditions | pH, temperature, biological environment | pH 5.5–7.4, temperature 37°C | Controls degradation and diffusion processes | Sun et al., 2025 |
| Experimental Data | In-vitro drug release profile, dissolution rate | % drug released over time | Used to train ML models and validate predictions | Protopapa et al., 2025 |
| Derived Features | Normalized variables, interaction terms | Temperature–polymer interaction | Enhances model learning and predictive accuracy | Al-Rajabi et al., 2025 |

Table 2 presents the key input parameters commonly used in machine learning models for predicting drug release behavior from advanced drug delivery systems. These parameters include physicochemical properties of the drug, formulation variables such as polymer type and drug loading, carrier characteristics like particle size and surface properties, environmental conditions such as pH and temperature, and experimentally generated drug release data. The integration of these variables allows machine learning algorithms to capture complex interactions between formulation composition and environmental factors, thereby improving the predictive accuracy of drug release models and supporting the optimization of novel drug delivery systems (Sun et al., 2025; Alshawwa et al., 2022; Al-Rajabi et al., 2025).

Nevertheless, difficulties with data quality often obstruct the feasibility of the effective model building, particularly, when the missing values and data sparsity create an insurmountable problem. Due to trial-and-error methodology of the machine learning paradigm, the drug loading estimation is vulnerable to the misestimations arising with truncation of the completion path or variation in the measurements, while the sporadically available data subsets may result in biased predictions, loss of statistical significance guarantees, and compromise the model interpretability. Data sparsity is a chronic disease for the pharmaceutical fields as the in vitro studies are time- and resource- consuming experiments, and the drug release profiles compilation is frequently costly, thus, the inferences from statistical models cover a limited variety of made formulations. To date, multiple loss recovery techniques with data imputation methods and synthetic data generation for the existing models, and for model-specific estimation procedures as in the cases of production of the Gaussian process regression workflows which are robusters to the sparsity and noising with efficient prediction

(Woodring et al., 2025), have been employed to overcome the data loss. Hence, building generalizable machine learning models which are capable of reproducible estimations of drug release profiles from the respective advanced drug delivery systems will benefit from treating data quality issues.

**Model Training and Validation**

The majority of drug release predictions are based on model training and validation where adequate partitioning of pharmaceutical data into test and training sets is designed to avoid overfitting and assessment of generalization. Cross-validation processes, such as k-fold and leave-one-out, are popularized among scientists to allow sequential model access for different data subsets, particularly for limited availability of datasets {Ref-s175849}. Hyperparameter tuning, the optimization process to determine the best-performing configuration settings for global drug release prediction models (e.g. Sailfish Optimizer) provides significant performance increase based on complex, large datasets such as the profiles obtained from Raman spectroscopy {Ref-s175849}. Furthermore, dimensionality reduction techniques, for example, Principal Component Analysis (PCA), are also integrated in the model before fitting to enable computational efficiency catering to the thousands of dataset features while retaining important information regarding the kinetics of drug release. Kernel Ridge Regression coupled with SFO model training and PCA dimensionality reduction exhibited highly accurate results on those independent test datasets made evident that model validation principles are intricate in certain pharmaceutical applications {Ref-s175849}.

Moreover, the assessment of machine learning practitioners for drug release models must be accompanied with the appropriate metrics to estimate their precision and explanatory power in regression. Specifically, mean squared error (MSE) is a metric used to determine the average squared distance between the observed and predicted drug release values. It directly reflects the predictive precision of models based on the provided test set. The coefficient of determination ($R^2$) reflects the percentage of variance in the drug release data that is accounted for by models, giving an indication of model fit in complex scenarios of formulation development (Alshahrani et al., 2024). Other metrics, including mean absolute error (MAE) and root mean squared error (RMSE), may be explored to give alternatives with unique characteristics with respect to outlier sensitivity or direct interpretability for practitioners. The application of such quantitative assessment techniques is indispensable to strengthen the validation of predictive frameworks and their distinguishing impacts even with minor changes driven by integrated or advanced modeling techniques in pharmaceutical development (Alshahrani et al., 2024).

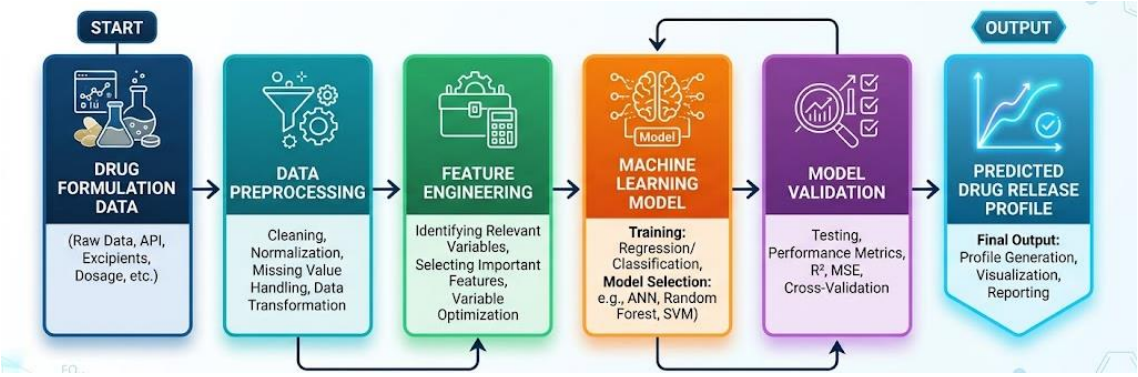


**Figure 1: Workflow of machine learning modeling for predicting drug release from novel drug delivery systems.**

Figure 1 illustrates the general workflow of a machine learning framework used for predicting drug release from novel drug delivery systems, including data collection, preprocessing, feature engineering, model training, validation, and prediction of release profiles (Gormley, 2024; Sun et al., 2025).

**Case Studies and Applications**

An interesting use case of machine learning in modeling drug release is also available, based on the estimation of dissolution profiles of tablets made by direct compression using tree-based models. Using Random Forest and Extreme Gradient Boosting algorithms, investigators have attempted to estimate the cumulative drug release at various time points for 377 formulations containing different active pharmaceutical ingredients and excipients (Protopapa et al., 2025). The developed models exhibited satisfactory prediction performance ($R^2$, 0.635 and 0.601), which rose further when initial dissolution time points were included as a model input. The investigators also implemented a complementary modeling approach involving machine learning to generate estimates for kinetic parameters either obtained from the conventional release models or marching with them. Such models connect mechanistic understanding with data-driven predictions. Overall, using a rich drug release dataset of diverse systems and excipient classes, the study is an example showing how machine learning methods can potentially be useful given a realistic scenario of pharmaceutical development (Protopapa et al., 2025).

Finally, machine learning-based predictive models can be used to optimize the drug release, which is a crucial part of the drug development stage, and to make decisions regarding drug formulation. The rapid virtual screening of candidate delivery systems is made possible due to the machine learning-powered models. The desired release profiles can be achieved by identifying the properties of nanocarriers through computational modeling and machine learning, allowing researchers to minimize the use of conventional trial-and-error methods (Gao et al., 2024). The combination of machine learning and computational modeling at the molecular level can also ensure precision during formulation development.

Simulating at an atomic level can determine, for example, the lipid materials to be used in the phaseseparation, ultimately ensuring optimized physical stability and performance. The machine learning-supported molecular modeling can allow the iterative design due to data generation and the proposed model replacements, which can enable the researchers to vary and modify the parameters in silico rapidly. This can lead to promising formulations for particular therapeutic applications. The increased predictive performance can make the drug delivery system experimental activities faster while allowing for rational decision-making throughout the formulation development pipeline for candidate drug delivery systems (Gao et al., 2024).

**Limitations and Challenges**

There are some limitations that hinder the application of ML in drug release prediction. One of the major concerns is the lack of data. Although there are multiple ML-based applications in drug delivery, the amount and resolution of drug release data are inadequate in comparison to the amount of resources needed to develop them, particularly if it involves advanced systems or patient-specific conditions (Geraili et al., 2021). Another concern is overfitting which occurs when a model fits the noise instead of the data. This could occur due to insufficient data. The use of succession or physics-based approaches must be modeled in order to generalize its prediction across unseen processes, such as drug formulations (Geraili et al., 2021). Furthermore, ML-based models are hard to interpret. This is especially important as regulatory bodies require mechanistic understanding before allowing the clinical application of advanced strategies such as smart delivery systems. Generalization over different materials is a big challenge for the application of ML for

personalized treatment. This is also due to the advancement in dosage forms such as 3D-printed pieces produced in patient-specific conditions (Geraili et al., 2021).

To this end, various promising routes have been proposed with the aim to alleviate problems of data availability, transferability and model interpretability in ML-based drug release forecast. The major data availability problems can be significantly alleviated via data augmentation techniques like generation of synthetic data and simulation-based experimental dataset augmentation, allowing the prototype predictive models to be trained more effectively when the physical quantities of samples are limited. Transfer learning strategies can further improve the availability of data to an extent, transferring the learned representations from similar tasks to the application from here, avoiding unnecessary acquisition of new data and allowing for fast adaptation for previously unexplored formulations. Related mechanistic knowledge, such as kinetic models and materials-based limitations, can be incorporated into ML methods in order to improve interpretability that the black box nature of ML approaches heavily lacks, while taking advantage of the explanatory power of the traditional approaches (Gormley, 2024). Such a compromise between data-oriented approaches and mechanistic understanding can allow the construction of models that are able to serve as faithful representatives of the drug-material interactions, thus improving the reliability and regulatory compliance of pharmaceutical design with predictive capabilities (Gormley, 2024).

**Future Perspectives**

Future advances in explainable artificial intelligence (AI) and digital twin technologies will revolutionize the landscape for predicting drug release from new delivery systems. Explainable AI, which effectively informs users of the logic behind a model's prediction, has emerged as means to address the "black box" problem, where AI-based algorithms can obscured the underlying rationale for an outcome to all stakeholders (Uddin et al., 2025). Digital twins – virtual replicas of actual drug delivery systems – will enable monitoring, simulation, and formulation process optimizations to improve quality iteratively throughout the product lifecycle based on real-time and empirical data and prediction models. Converging AI with machine learning and these advanced technologies will ultimately build and ensure trust, transparency, and model efficiency in the drug quality control process, as regulators demand risk-based assessments, and greater stakeholder understanding of model development (Uddin et al., 2025). As these technological advancement aims to reshape the future of drug delivery systems, it will require collective action between the industry, regulators, and academics to consider ethical implications and global standards for predictive modeling.

Moreover, models of the drug release using machine learning techniques are promising opportunities for personalized art of drug delivery through customized design of formulations based on patient-specific and situational factors. By successive fusion of instrumental in vitro data and algorithmic modeling patients' characteristics needed to predict drug release behavior, such as tissue pH or enzymatic activity, can be integrated into the model (Sun et al., 2025). Being trained on crucial features, such as drug solubility and molecular weight or particle size and shape, machine learning algorithms can predict an optimal formulation for a specific patient situation or treatment goal. For example, if the algorithm is able to predict an effect of the surface-to-volume ratio or pH on the release profile, the specific formulation could be designed ahead to account for changes in biological environment in-situ during the treatment period (Sun et al., 2025). The algorithm-driven analytical approach allows the clinicians and scientists to overcome a daily need to use a "one solution fits all" attitude and to design individualized delivery systems with improved safety and efficacy.

**Ethical and Regulatory Considerations**

As the practice of machine learning continues to prevail within the realms of innovative pharmaceutical advancement and drug release forecasting, ethical and regulatory implications are gaining traction and require essential discussion.

The primary concerns regarding this context pertain to the dilemmas of data privacy, as complex models may find it probable to re-identify depersonalized patient records based on demographics or clinical factors – this presents a certain risk to confidentiality (Alshehade et al., 2026). The second primary consideration is termed as algorithmic bias, where findings support that the performance of forecasting models reveals significant variations with patient population demographics. Should model bias not be addressed via diversified data collection alongside fairness objectives within governance strategies, the unequal profit gap between their effected populations may be aggravated (Alshehade et al., 2026). As a response to machine learning's growth in application, regulatory frameworks highlight the adoption of methodologies surrounding the context of explainable artificial intelligence, federated learning and ethical suggestive measures alongside predictive modelling approach – this correlates with effecting model transparency, patient data protection and minimising bias incidents through future deployment. Such mechanisms that encourage transparency, inter-agency cooperation and documentation through procedure deliverance are now recognised in the emergence of machine learning and posess the potential to ethically realise innovative pharmaceutical processes within fields such as drug release modelling (Husnain et al., 2023).

## CONCLUSION

In conclusion, this review presented the utilization of machine learning approaches in predicting the drug release of novel drug delivery systems, which would revolutionize development of DDS while having some challenges. The pros and cons of the ML models were discussed. It was shown that the predictive drug release performance, personalized formulation approach and efficient experimentation workflow can benefit from data-driven learning models compared to conventional modeling methods. Despite the progress in supervised, unsupervised and deep learning approaches, the availability of data, model interpretability and platform transferability remain major challenges. Explainable AI, digital twin and hybrid approaches are novel models with the potential to solve the difficulties in platform transferability, enhancing the prediction to experimental observation in clinically and commercially important settings. Further, interdisciplinary networking, reproducibility, validation based rigorous research and ethical responsibilities are decisive for the ML evolution in maximizing drug release and pharmaceutical progress.

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