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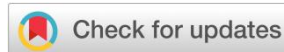
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Review Article

Artificial Intelligence in Drug Delivery for Infectious Diseases: A Critical Synthesis of Machine Learning Architectures, PBPK Modeling, and Antimicrobial Resistance

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Abstract

Objective: This paper provides a critical synthesis of the state-of-the-art AI methodologies applied to drug delivery systems for infectious diseases. This review aims to evaluate the integration of artificial intelligence (AI) and machine learning applications across four convergent pillars of drug delivery for infectious diseases: ML-guided drug formulation optimization; AI-driven targeted drug delivery system design; AI-augmented physiologically based PBPK modeling; ML and deep learning-based antimicrobial resistance profiling and management.

Data Sources and Study Selection: A comprehensive systematic search of peer-reviewed literature was conducted using databases including PubMed, Scopus, IEEE and Google Scholar. Search strategies involve combination of keywords such as “machine learning”, “drug delivery”, “antimicrobial resistance”, “deep learning”, “infectious diseases”.

Summary of the content of the article: The review aims to systematically map and categorize the principal AI and ML architectures according to their application and performance in drug delivery research. To critically assess the role of ML and DL based computational tools in drug formulation, AMR detection, susceptibility prediction, and resistance, their translational readiness, and contribution to broader AMR management strategies. To synthesize the current evidence on AI-integrated PBPK (Physiologically based Pharmacokinetic) modelling as a mechanism for improving the prediction of pharmacokinetic parameters in drug delivery systems. To identify the principal translational, regulatory, and methodological barriers to clinical deployment of AI-driven drug delivery tools for infectious diseases.

Conclusion: Infectious diseases frequently induce rapid, dynamic pathophysiological shifts in the host, complicating precise drug dosing and increasing the risk of therapeutic failure due to antimicrobial resistance. Artificial intelligence represents the most cost-effective methodological advance available to infectious disease drug-delivery research. Deep neural networks and ensemble architectures consistently outperform classical computational models across drug optimization, nanoparticle delivery prediction, and AMR phenotype classification. Hybrid ML-PBPK frameworks achieves 65% accuracy as compared to 47.5% for conventional PBPK models. The transition from static to dynamic AI-enhanced PBPK modeling represents a vital advancement towards precision dosing, offering a robust paradigm to optimize therapeutic indices and improve patient survival rates in severe infections.

Keywords: Drug delivery, Drug formulation, Artificial intelligence, Neural Networks, PBPK modelling, Anti-microbial resistance (AMR)

1. Introduction

Infectious diseases continue to be one of the greatest threats to public health around the world. The World Health Organization (WHO) estimates that 13.7 million deaths annually are due to communicable diseases, with the low-income population carrying a far greater burden due to limited access to therapeutics and health facilities. Despite decades of scientific progress, the development of safe, effective, and deliverable

pharmacological interventions remains hindered due to pharmacokinetic limitations of traditional drug delivery systems, the complexity of biological pathogens, and the increasing crisis of global antimicrobial resistance (AMR). The drug delivery, defined as the design, formulation, and administration of therapeutic agents to produce the intended pharmacological effects at the targeted site, lies at the confluence of pharmaceutical chemistry, material science, and clinical medicine. Over time, advances in drug delivery have led to

improvements in drug efficacy, safety, and patient adherence. Due to the empirical, resource-intensive, and trial-and-error nature of drug formulation and drug delivery, it is ill-suited to the demand and complexity of infectious disease challenges.

It is within this context that artificial intelligence (AI) is becoming more and more crucial to exert a transformative influence on drug discovery and development, patient care, and pharmacy operations. AI, a branch of computer science that focuses on the development of robots or computational methods, can perform a variety of cognitive activities at a level that is comparable or perhaps higher than human intelligence¹. Artificial intelligence can expedite and reduce the cost of complicated and costly drug delivery procedures. Recently, the integration of AI has emerged as a transformative force, revolutionizing the drug delivery processes. Designing a drug delivery system generally involves a number of difficulties, including forecasting the emergence of unforeseen occurrences and the link between formulation parameters and the outcome of the treatment. The effectiveness of the drug delivery is crucial as it increases the bioaccessibility and drug bioavailability, and can lessen adverse effects. The development of computational pharmaceuticals and the combined use of artificial intelligence and massive amounts of biological data have improved the pharmaceutical industry.

The use of AI-driven tools in the domain of drug delivery faces several persistent and interrelated challenges. First, the design of a drug delivery system for infectious diseases demands considering the competing parameters like bioavailability, targeted delivery, controlled release kinetics, and patient-specific pharmacokinetic profiles amidst rapidly increasing microbial targets. The conventional computational approaches, like QSAR and PBPK modeling, are limited in modeling the dynamic, nonlinear, and patient-heterogeneous nature of drug behavior. Second, the greatest challenge is the global trajectory of antimicrobial resistance. The traditional methods for identifying effective therapeutic agents are slow and costly, underscoring the importance of AI strategies in minimizing resistance induction. Third, the integration of diverse AI methodologies into a coherent and application-specific framework for infectious disease drug delivery has not yet been achieved.

The review of literature shows that several studies involving AI applications in drug delivery and discovery by Colombo (2020), the extensive use of AI in drug discovery by Chen *et al.* (2023), the comprehensive survey of AI in pharmaceutical technology by Vora *et al.* (2023), and the role of AI in drug discovery and drug delivery by Serrano *et al.* (2024) report the applications of AI in pharmaceutical sciences²⁻⁵. However, critical analysis of these studies indicates that there are several significant and interrelated gaps. First, there is no systematic and critically synthesized review on the interrelated four pillars that collectively define the AI-driven drug delivery domain for infectious diseases: (i)

ML-guided drug formulation; (ii) AI-targeted drug delivery system design; (iii) AI-integrated PBPK modeling; and (iv) ML (Machine learning) and DL (Deep learning) based AMR profiling. Second, the earlier reviews have omitted the comparative predictive performance of AI architectures across drug delivery applications. Finally, the translational and regulatory barriers to clinical implementation of AI-driven drug delivery tools have not been systematically synthesized in relation to infectious diseases.

The disciplinary siloing of the four pillars described above hinders the pace of methodological innovation and increases the risk of duplicated efforts. At the clinical and public health level, the stakes are more immediate. Without a clear, evidence-supported map of which AI tools are most effective, most mature, and most ready for clinical translation, the regulatory bodies, clinicians, and funding agencies are ill-equipped to make informed strategic decisions. Furthermore, the rapid growth of AI methodologies means that the field is at genuine risk of being surveyed only in fragmentary, discipline-specific ways that fail to capture the systemic potential of AI integration across the full drug delivery pipeline.

The present review aims to address the identified gaps by providing an integrative synthesis of AI and machine learning applications across the four convergent pillars of drug delivery discussed above. First, the review aims to systematically map and categorize the principal AI and ML architectures according to their application and performance in drug delivery research. To evaluate the comparative strength, limitations, and accuracy of these architectures across drug formulation, targeted drug delivery, and controlled release systems with particular reference to infectious diseases. Second, to critically assess the role of ML and DL based computational tools in drug formulation, AMR detection, susceptibility prediction, and resistance, their translational readiness, and contribution to broader AMR management strategies. Third, to synthesize the current evidence on AI-integrated PBPK (Physiologically based Pharmacokinetic) modelling as a mechanism for improving the prediction of pharmacokinetic parameters in drug delivery systems. Finally, to identify the principal translational, regulatory, and methodological barriers to clinical deployment of AI-driven drug delivery tools for infectious diseases. The present review seeks not merely to catalogue the current state of the art but to provide the analytical scaffolding through which AI-driven drug delivery for infectious diseases can be more efficiently, coherently, and translationally oriented.

2. Principal AI and Machine Learning Architectures in Drug Delivery Research:

The application of Artificial Intelligence and machine learning to pharmaceutical drug delivery encompasses a

diverse and rapidly expanding field of computational architecture. AI/ML represents an assembly of intricate algorithms created to mimic the functioning of the human mind by gaining knowledge from experiences and/or the environment. This section provides a detailed integrated analysis of the principal architectures employed across the three application

domains, i.e., drug formulation optimization, targeted drug delivery system, and controlled drug release engineering⁶. The primary types of machine learning are supervised learning, unsupervised learning, semi-supervised learning, deep learning, and reinforcement learning. Figure 1 shows commonly explored machine learning models and their classification.

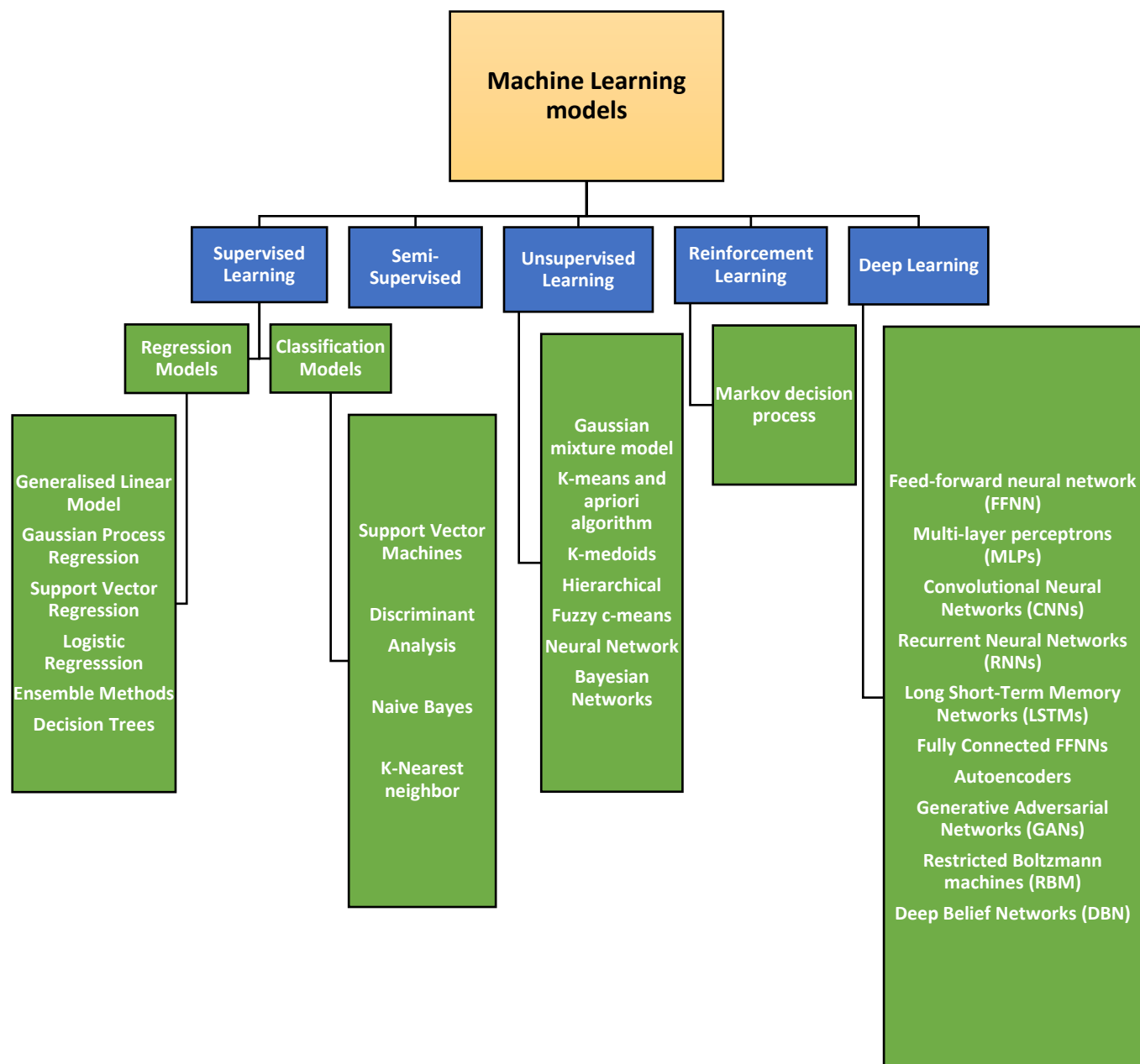


Figure 1: Different AI machine learning models used in pharmaceuticals.

Supervised Learning is trained on labelled data and is used to predict new supplied data. It includes 'Regression' models, which involve predicting a quantity (e.g. Linear regression or a generalized linear model, Gaussian process regression, ensemble methods, logistic regression, support vector regression, and decision trees) and 'Classification' models which involves predicting a label (e.g. discriminant analysis, support vector machines (SVMs), Naive Bayes and nearest Neighbor like K-nearest Neighbor (KNN)). Backpropagation neural network and random forest models also fall under supervised learning⁷. Unsupervised learning finds associations among data points using the unlabelled data clusters to identify patterns and sequences of recurring patterns. This approach of classification, also known as 'Data-driven methodology', is repetitive and does not involve a target. Gaussian mixture model, Apriori algorithm, and K-means clustering algorithm⁸, K-medoids, hierarchical, fuzzy c-means⁹, neural networks, and Bayesian networks¹⁰ are some of the popular examples. Using both labelled and unlabelled data inputs, semi-supervised learning combines supervised and unsupervised learning. In reinforcement learning, a model is trained to interact with its surroundings to increase the algorithm's accuracy. Unlike supervised learning, which uses trained datasets, reinforcement learning uses trial and error to train itself to make predictions in the midst of unclear information, such as using a Markov decision process¹¹.

Deep learning (DL) or neural network is defined as a multi-layered learning module. A deep neural network (DNN) serves as the foundation of DL. A DNN is fundamentally an artificial neural network (ANN) with a large number of hidden layers¹². Non-linear modules make up a neural network, which converts and transfers data between its layers. These non-linear modules, known as activations or analogous to the activation potential of a biological neuron, determine the strength with which information flows through the network. Activation functions determine the activations in a neural network, and these activations then serve as a system parameter. Convolutional neural networks (CNNs)¹³, recurrent neural networks (RNNs)¹⁴, long short-term memory networks (LSTMs)¹⁵, autoencoders (sparse autoencoder, denoising autoencoder, contractive

autoencoder, variational autoencoder)¹⁶, generative adversarial networks (GANs)¹⁷, restricted Boltzmann machines¹⁸, and deep belief networks (DBN)¹⁹ are some examples of DL algorithms. Table 1 shows the comparative summary of principal AI/ML architectures across drug delivery applications in Infectious disease management

There are several innovative opportunities to enhance drug delivery through the application of AI and machine learning techniques in biomedical research. Artificial intelligence (AI) has the capacity to improve drug delivery systems and create stable correlations between formulation parameters and release kinetics²⁰. In order to completely understand the potential of artificial intelligence in drug delivery, additional investigation is required to improve interpretability, offer guidance for choosing machine learning models, and enhance the quality of the data gathered. A cross-cutting finding of this comparative analysis is that the performance hierarchy among architectures is strongly modulated by dataset size, data modality, and the complexity of the relation between inputs and outputs. Several cross-cutting challenges restrict the deployment of AI/ML methods in drug delivery.

First, the issue of data quality and representativeness is pervasive. AI models are basically bounded by the quality of their training data, which are characterized by class imbalance, high measurement noise, and compositional bias towards well-studied drug classes and pathogens. The models trained on such data give excellent results on the training distribution but fail to generalize to novel compounds, resistant mutants, and less represented patient populations. Second, the black box nature of high-capacity deep learning models remains a substantive barrier to regulatory acceptance and clinical trust. This becomes acute in drug delivery for infectious diseases, where the consequences of erroneous model prediction can lead to treatment failure and induction of antimicrobial resistance. Third, the integration of multiple data modalities like molecular structure, formulation composition, and biological activity into a predictive framework remains methodologically underdeveloped for drug delivery applications. Addressing these gaps is a prerequisite for the responsible deployment of AI-driven drug delivery tools in infectious disease management.

Table 1: Comparative Summary of principal AI/ML architectures across drug delivery applications in Infectious disease management.

AI/ML Architectures	Algorithm	Description/Key Strengths	Application Domain	Principal Limitations	Infectious Disease Relevance
Supervised Learning Regression Models	Generalized linear model or linear regression ⁷	The relation between the dependent and independent variables is assumed to be linear.	Drug release rate prediction or plasma drug concentrations over time.	Assumes linearity, poorly interacting variables	Baseline modelling of antibiotic plasma profiles; toxicity screening
	Gaussian process regression ²¹	Non-linear, non-parametric techniques capture uncertainty in predictions.	Drug absorption prediction across biological barriers: formulation uncertainty	Restricted to small data sets	Barrier penetration modelling for intracellular pathogens, to estimate growth rates
	Ensemble algorithms (boost types) ²²	An additive model to create an efficient predictive framework	Predict drug-drug interactions by integrating several weak learners and pharmacokinetic parameters.	Low interpretability, lack of adaptability	Predictive accuracy in diagnostics, Forecasting outbreaks.
	Support Vector Regression (SVR) ²³	Handles both linear and non-linear variables.	Predicts drug release kinetics from polymeric matrices.	Computationally intensive, poor scaling	Stimuli-responsive antimicrobial delivery, Drug target interaction
	Random Forest models (RFM) ²⁴	Constructs decision trees and aggregates their predictions to increase reliability and generalizability.	Predicts drug solubility and permeability.	Limited temporal modelling	Skin antibiotic permeability, AMR prediction
	Logistic Regression ²⁵	Models binary outcomes	Predicts drug toxicity, efficacy, or response.	Inability to model highly complex non-linear interactions	Toxicity screening
	Decision tree ²²	Every internal node represents a feature-based decision, every branch denotes the decision's result, and every leaf node denotes a tag or numerical data.	In the development of drug formulations, drug release profiles.	Overfitting, Unable to model complex linear relationships	Analyse clinical symptoms, identify predictors of AMR
	Backpropagation neural network ²⁷	Adjusts the connection between neurons in a neural network and reduces the gap between predicted output and actual target output.	Drug formulation optimization, toxicity prediction, and pharmacokinetic modelling.	Overfitting risk in small datasets, interpretability deficit	PBPK input estimation

Supervised Learning Classifications Models	Instance-based algorithms/Support Vector Machines (SVMs) ²⁸	Handles high-dimensional data and nonlinear decision boundaries.	Predict and model the relationship between formulation variables, identifying drug delivery systems with specific targeting capabilities.	Fails for small datasets	Drug target interaction prediction, Toxicity classification
	Discriminant Analysis ²⁹	Statistical classification technique	Predict drug toxicity, drug formulation, and patient stratification.	Sensitive to outliers, unfit for non-linear data	Patient satisfaction
	Naive Bayes ³⁰	Performs well with high-dimensional data	Predict drug toxicity, drug formulation, optimize drug dosing regimen, and patient stratification	Low predictability	Rapid risk assessment
	Nearest Neighbor, like K-nearest Neighbor ³¹⁻³²	Compound classification algorithm, non-parametric nature	Toxicity prediction, drug formulation classification, and drug-drug interactions.	Sensitive to the curse of dimensionality and noisy data, computational cost	Predict outbreaks and patient conditions
Unsupervised Learning	Gaussian mixture model (Clustering Algorithm) ³³	Uses Gaussian distributions to represent data; Expectation-Maximization (EM) algorithm to calculate parameters.	Patient stratification, compound classification, and predicting time series drug release profiles	Sensitive to initialisation, computational expense	Pattern recognition, disease subtyping
	K-means and Apriori algorithm ³⁴	Partitions data into K clusters based on similarity measures.	Identifies similar groups of similar drug formulations. Patient clustering based on drug response patterns.	Sensitive to outliers, Computational Inefficiency	Pattern mining, patient segmentation
	Hierarchical Clustering ³⁵	Builds a tree-like hierarchy of clusters, which can be agglomerative and divisive.	Target identification, patient stratification, drug formulation optimization, and pharmacovigilance.	Scalability, Sensitive to outliers and noise	Phylogenetic tracking, patient stratification
	Fuzzy C-Means ⁹	FCM allows for fuzzy clustering of data points into multiple clusters.	Patient stratification, drug formulation optimization, and pharmacokinetic modelling.	Sensitive to outliers and noise	Patient risk stratification, Segmenting infections
	Bayesian Network ³⁶⁻³⁷	Probabilistic reasoning, causal modelling	Evaluate risks, optimize experimental designs, and make probabilistic predictions.	Scalability challenges, manual graph construction	AMR risk modelling, Dosing optimisation

Semi-Supervised Learning		Leverages both labelled and unlabelled data.	Anti-microbial drug delivery development	-	-
Reinforcement Learning	Markov decision process ¹¹	Regression-based pharmacokinetic modelling	Create personalized treatment programs and optimize medication dosage regimes.	Data inefficiency and quality, safety constraints	Balance competing objectives like reducing infections vs limiting lockdown
Deep learning	Artificial neural network (ANNs) ¹²	Captures complex nonlinear relationships between variables; Capable of learning from large datasets.	Predicts drug release profiles from nanoparticles or microparticles; Formulation optimisation	Overfitting risk on small datasets; Interpretability deficit	PBPK input estimation; Sustained release antimicrobial formulation
	Deep Convolutional Neural Network (CNNs) ¹³	Performs efficiently in image-based applications	Predicting characteristics and evaluating chemical structure.	Requires large labelled datasets; limited to spatial data	Tablet defect detection
	Recurrent Neural Networks (RNNs) ¹⁴	Generates new sequences using learned patterns	Predicting protein structure or designing a peptide sequence	Sequential processing limits scalability	Drug concentration profiling; Antimicrobial peptide generation
	Long Short-Term Memory Networks (LSTMs) ¹⁵	Type of RNNs with enhanced modelling and temporal dependency prediction capabilities	Forecast drug concentration-time profiles and assess the effectiveness of drugs	Computational complexity	Analyse time series data
	Autoencoders ³⁸	Autoencoders are utilized for obtaining features and decreasing dimensionality	Virtual and compound screening: Capturing key characteristics of molecules	High computational cost; low interpretability	Novel antibiotic scaffold design
	Generative Adversarial Networks (GANs) ¹⁷	A discriminator network that verifies quality and a generator network that produces new molecules.	Used in drug product development.	Training instability; Low interpretability	Data augmentation
	Restricted Boltzmann Machines (RBMs) ¹⁸	A neural network model suited for modelling complex relationships in high-dimensional data.	Molecule representations; drug formulation optimization; predictive modelling, drug-target interaction	Sensitivity to parameters; Limited interpretability	Drug target identification: Predicting outbreaks
	Deep Belief Networks (DBN) ¹⁹	Feature extraction from complex high-dimensional data	Drug formulation optimization; toxicity prediction; pharmacokinetic modelling; drug-target interaction analysis.	Sensitivity to parameters; Limited interpretability	Anomaly detection, surveillance, and forecasting

3. Role of AI/ML in Drug Formulation Design

Drug Formulation design is one of the most important, resource-intensive, and empirically demanding stages in pharmaceutical development. The conventional formulation science is statistically rigorous, are constrained in its capacity to model high-dimensional, non-linear interactions between the dozens of material and process variables as compared to modern AI/ML tools. One of the key advantages of integrating AI into medicine delivery systems is its capacity to handle and evaluate massive amounts of data. By leveraging large datasets, AI systems can identify patterns and correlations in drug formulations that would not be visible using more traditional methods³⁹. The connections between various formulation ingredients, their concentrations, and their effects on drug delivery performance can all be better understood by researchers owing to this data-driven approach. By examining a range of data sources, including physicochemical characteristics, chemical structures, and biological activity data, AI systems are able to uncover hidden correlations. By identifying patterns and trends, AI can assist in improving medication delivery systems for safety, greater stability, and efficacy⁴⁰. All these factors should be considered for drug formulation, such as whether the drug should be in the form of a tablet or capsule (due to its regulated distribution into the bloodstream and ease of usage), an injectable formulation (for better and targeted delivery), inhalers (for respiratory ailments), or topical treatments (which, for localized treatment, can be administered directly to the skin) to enhance its stability, safety, and efficacy. This section critically evaluates the evidence for AI/ML and DL applications across three interconnected dimensions of drug formulation design: (i) the prediction and optimization of formulation composition and performance, (ii) integration of AI into the manufacturing process, and (iii) the application of deep learning to particulate and advanced drug delivery design.

Artificial neural networks trained on formulation composition and process parameter inputs have demonstrated consistent performance. ANN- based multilayer perception (MLP) models have been applied to predict and tailor drug release profiles as a function of polymer concentration, drug loading, and compaction pressure. ANN using an MLP model trained on sustained-release formulations of metformin hydrochloride, attained accurate prediction of dissolution profiles⁴¹. The integration of ANN models with quality-by-design (QbD) frameworks represents a more recent and architecturally sophisticated development. ANN-genetic programming hybrid systems have been applied to tablet manufacture by direct compression, constructing multivariate models of

the causal relationships between formulation input variables and multiple product quality attributes within a single predictive architecture⁴². Another study utilized CNN to apply deep learning to the detection of internal tablet faults with high throughput, accuracy, and adaptability. Errors in tablet formulations that arise during production can lead to delays in the schedule, increased expenses, and quality issues. The computer program achieves 94% average accuracy in robustly quantifying interior tablet cracks⁴³.

A critical impediment to the clinical translation of cancer nanomedicine is the low delivery efficiency of nanoparticles (NPs) to tumor tissue, for which the physicochemical and biological determinants remain incompletely characterized. Lin *et al* (2022) conducted a systematic, multi-algorithm study drawing on the Nano-Tumor Database, a curated repository of 376 PBPK model-derived datasets encoding NP physiochemical descriptors, cancer models, and tumor morphology⁴⁴. Comparative evaluation of five ML architectures (DNNs, SVMs, RFs, Linear regression, and ensemble models) revealed that DNN architectures achieved consistently superior predictive performance. It demonstrates that the non-linear high-dimensional feature interactions governing NP tumor accumulation are more effectively captured by deep learning representations than by linear constrained models. DNN predicted tumor delivery efficiency ranged from 19% to 29% across, with the performance substantially modulated by tumor type. Beyond its immediate mechanistic insights, this work demonstrates the feasibility and analytical value of integrating AI-driven ML with PBPK modeling frameworks for quantitative nanomedicine characterization.

4. Artificial Intelligence in the development of Drug Delivery Systems/modes of delivery

The drug delivery workflow functions as a data-driven, self-improving pipeline that accelerates the convergence of therapeutic application, functional evaluation, and material design. This method reduces experimental costs while enabling the rapid identification of high-performance, customized medication delivery options by utilizing AI's ability to assess and integrate high-dimensional data. It provides the operational basis for the nanoarchitectonic approach in precision nanomedicine. The practical tactics covered in the ensuing parts are supported by the general framework presented here. These include model-driven nanocarrier design, AI-guided material selection, and iterative experimental validation, all of which cooperate to implement and improve the suggested design loop⁴⁵. Figure 2 illustrates the general workflow for a drug delivery system using an AI approach.

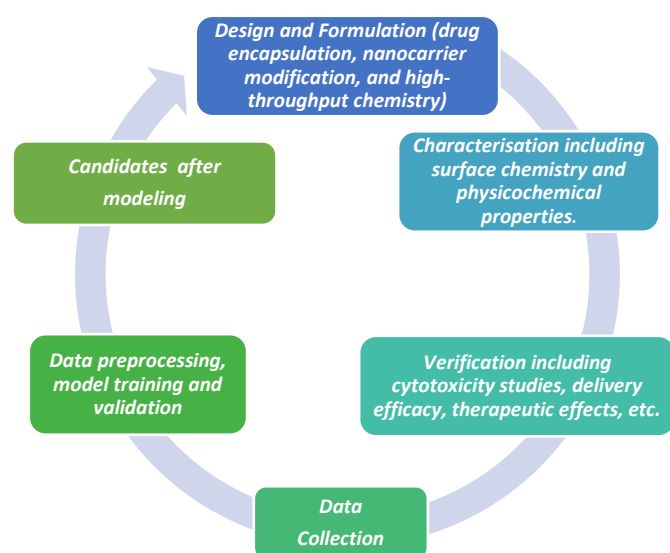


Figure 2: General workflow of a drug delivery system using Artificial Intelligence (AI).

The main elements in the design of different intelligent drug delivery systems are the on-demand dose modification, the rates of drug distribution, targeted release, and drug stability. Appropriate algorithms are useful for controlling the volume and duration of drug release in automatic drug delivery systems. As a result, the potential and effectiveness of various drug delivery dosage forms, including tablets, emulsions, solid dispersions, and microemulsions, and multi-particulates (beads, microparticles, nanoparticles, and beads) can be predicted using artificial intelligence (AI) approaches. Table 2 shows the comparative analysis of different modes of delivery and the AI/ML tools used. Across dosage form types, particularly ANN-based models consistently outperform classical regression models when formulation design space involves non-linear, high-order interactions between multiple variables. A second point of convergence is that the ensemble methods and ANN architectures are the best-performing models for structured pharmaceutical tabular data, with performance advantage increasing with dataset size and input dimensionality⁴⁶.

Table 2: Different modes of delivery, the AI tool used, and their application.

S. No	Modes of delivery/Drug Delivery System	AI tool/ Database	Key Reported Outcome
1	Nanoparticle	ANN	Predict and forecast the biosynthesis of chitosan nanoparticles; Reduced error values and increased prediction efficacy ⁴⁷ .
2	3D printed capsule scaffold	ANN	Printing parameters' optimization, namely printing speed and temperature ⁴⁸ .
3	Tablet compression	ANN + Genetic Engineering	Simultaneous prediction of hardness: Integrated multivariate method for examining the causal relationship between the components of the formulation and the characteristics of the final product ⁴⁹ .
4	Crystallization Process	RNN and auto-encoder RNN (AERNN)	Simultaneous optimization of energy consumption, quantity of particles in the final product, crystal size, and product yield ⁵⁰ .
5	Protein Therapeutics	CNN	Construction of a classification model to effectively differentiate silicone droplets of oil from protein aggregates ⁵¹ .
6	Particle size detection	R-CNN, k-means clustering algorithm, RF classifier.	Multiple foreign particles detected using a Faster R-CNN; Clustering of pathways by k-means clustering algorithm; Differentiation of the foreign particles and noises by RF classifier ⁵² .
7	Film-coated tablets	Deep learning (image analysis)	Automated recognition and classification of the errors in the film-coated tablets ⁵³⁻⁵⁴ .
8	Transdermal iontophoresis	Gaussian mixture model	Multi-modal time series drug release profile prediction; uncertainty quantification ⁵⁵ .
9	Carrier surface design in dry powder inhalation	ANN + Genetic Algorithm	Evaluates the dry powder inhalation design and operation efficiency characteristics; Final particle fraction and released dose ⁵⁶ .
10	Granulation and tableting processes	ANN, k-NN, Cubist model, RF	For forecasting granulation and tableting process outcomes, analyze data and resolve challenges related to tablet production, including input and output requirements ⁴⁶ .
11	Immediate-release tablet	ANN + Near IR/Raman Spectroscopy	Accurate real-time dissolution profile prediction; eliminates offline testing ⁵⁷ .
12	Fast-disintegrating tablet	Deep neural network	99% tablet hardness and 73% disintegration time accuracy in the prediction formulation ⁵⁸ .
13	Delivery of nanoparticles	Deep learning, SVM, and RF	Transport efficiency of nanoparticles to various cancers ⁵⁹ .
14	Microparticles	Artificial Neural Network	Predict particle sizes across microfluidic systems and build a single in silico model ⁶⁰ .

5. Targeted drug delivery systems (TDDS)

TDDS represents a fundamentally distinct pharmaceutical engineering challenge. The design objective is not merely to achieve a desired release profile under controlled conditions, but to engineer site-specific pharmacological action, i.e., directing therapeutic payloads to defined cellular, tissue, or subcellular compartments while preserving systemic safety. Pathogenic microorganisms occupy a range of biologically protected niches that are inaccessible to conventionally administered antimicrobials at concentrations sufficient to achieve therapeutic effect without toxicity. The convergence of ML and DL with targeted drug delivery system engineering has the potential to address this challenge at multiple levels simultaneously. This section critically evaluates the evidence of ML and DL contributions across the targeted delivery research relevant to infectious diseases.

Random forests (RF), Support vector machines (SVM), and neural networks (NN) are examples of AI algorithms that enable the nanoengineering of a wide variety of novel peptide materials for therapeutic administration across diverse applications⁶¹. Natural protein sequences can be the source of amphiphilic cell-penetrating peptides (CPP), which can self-assemble into nanocarriers with improved cellular absorption. Because of their innately low immunogenicity, therapeutic molecules can be safely delivered across biological boundaries. A field of study that is gaining popularity is the advancement of innovative drug distribution techniques that increase the absorption and utilization of medicines and reduce serious adverse effects. Polymers, lipids, peptides, carbohydrates, surfactants, and other amphiphilic substances constitute drug-delivery nanoassemblies⁶²⁻⁶³.

CPPs are short amino acid sequences, typically up to 35 amino acids long, that may pass through biological bilayer membranes without causing any harm. The study of CPPs revealed that components of certain proteins, such as signal sequences, transcription activating factors, and homeoproteins, may facilitate their passage through the plasma membrane and towards cellular compartments. CPPs can be synthesized or generated from proteins. Different bioactive molecule types, such as proteins, RNA, DNA, or anticancer drugs, may be transported and delivered into living cells via CPP⁶². Because of their low immunogenicity and ability to self-assemble, CPPs that are generated from native proteins and exhibit amphiphilicity may be more effective as drug delivery vehicles. Quantitative structure-activity relationships, or QSAR, investigations have served as the foundation for CPP predictions in the initial generation of *in silico* algorithms⁶⁴. The results demonstrated that cell-penetrating features are present in 95% of known CPPs. Ten amino acid sequences represent the new CPPs,

which were generated from the biosurfactant protein Ki-67. The transition from QSAR to ML and DL architectures for CPP prediction has substantially expanded predictive capability by replacing fixed descriptor vectors with learned, task-specific feature representations.

In order to discover amphiphilic peptides as potential drug delivery agents, Feger et al. combined newly acquired CPPs with amphiphilic peptides to discover potential drug delivery agents, as the latter might not be able to reach intracellular membranes' lipid plasma membranes⁶¹. Cancer therapy approaches represent one of the most promising areas of peptide amphiphile study⁶⁵. According to recent reports, linking the active medicinal molecule to CPPs may improve treatment for breast cancer⁶⁶. The attachment of an anticancer carrier to a CPP can enhance *in vivo* drug transport and tumor targeting, thereby mitigating the therapeutic side effects⁶⁷. The most widely used and researched self-assembled peptide nanostructures at this time are hydrogels based on peptides, which have been utilized for regulated medication release. When applied topically, peptide amphiphile hydrogels have allowed for the prolonged release of therapeutic proteins (such as trophic factors)⁶⁸. Hydrogels made of peptide amphiphile nanofibers have been studied for their capacity to regenerate in a variety of applications, including spinal cord injuries, bone regeneration, and neurite production⁶⁹.

The ML-guided design of targeting ligand-receptor pairs for infectious disease delivery has received comparatively limited attention relative to oncology applications. For infection-specific targeting, the relevant receptor landscape includes pattern recognition receptors on macrophages as well as pathogen-specific surface structures. A notable example of ML-informed surface engineering is the design of amphiphilic iRGD peptide nanocarrier conjugates for enhanced tumor accumulation and tissue penetration. The integration of computational peptide design with self-assembly nanovesicle fabrication achieved improved penetration depth and photosensitizer delivery compared to non-targeted controls⁶⁷. The protein corona presents a specific and formidable challenge for ML-guided surface design. Protein corona composition is determined by a complex, concentration-dependent competitive adsorption process that depends on NP surface chemistry, size, curvature, and charge in ways that empirical studies have characterized only partially. ML models trained on NP-protein corona datasets predict corona composition from NP physiochemical descriptors with RF and neural network architectures, demonstrating the strongest correlation between predicted and experimental corona protein identities⁴⁰.

6. Emergence of anti-microbial resistance (AMR)

One of the major risks to food security, social progress, and global health today is antimicrobial resistance (AMR). The World Health Organization (WHO) has listed antimicrobial resistance (AMR) as one of the top ten global public health issues, underscoring the critical need for innovative solutions to halt its spread⁷⁰. AMR has led to a steady rise in the prevalence of multidrug-resistant germs that are resistant to standard antibiotic therapies. Microorganisms such as bacteria, viruses, fungi, and parasites cause infectious diseases⁷¹. With the increasing global momentum of antibiotic resistance, infectious illnesses are now regarded as the primary cause of morbidity and mortality globally⁷². Finding the active therapeutic agent(s) for each unique treatment is now essential due to the rising prevalence of antimicrobial resistance (AMR) across various microbial species. Inadequate medication dosage may result in undesirable side effects, exacerbation of symptoms, and, additionally, the creation of antimicrobial resistance⁷³⁻⁷⁴. As drug-resistant bacteria continue to evolve and spread, it is predicted that by 2050, the yearly global death toll through AMR will approach 10 million, with a \$100 trillion cost if nothing is done. The inadequacy of current countermeasures creates an urgent imperative for computational approaches that can operate at the scale, speed, and integrative complexity that the AMR problem demands⁷⁵. The development of artificial intelligence (AI) techniques might significantly ease these issues.

The conventional antimicrobial susceptibility testing (AST) is confined to cultivable microorganisms, takes a long time, and has minimal productivity⁷⁰. AST is a scientific technique used to assess how well a certain antimicrobial agent works against bacteria or other pathogens. In order to treat bacterial infections, it aids medical practitioners in choosing the right antibiotics⁷⁶. AI possesses the ability to improve medication distribution while facilitating efficient treatment of infectious diseases, as evidenced by recent research findings. Without the use of tedious biological experiments, it can generate accurate predictions by locating the appropriate elements in large and complex datasets. Therefore, it could serve as a helpful tool for medication research, selecting combinations of drugs, and optimizing therapeutic dosage, all of which require an extremely broad experimental scope, encompassing a wide variety of pathogenic strains, potential medicinal chemicals, screening concentration matrices, and additional replicates⁷⁷. Deep learning algorithms have also demonstrated significant interest in discovering AMR genes, detecting AMR peptides, and forecasting novel antibiotic medications⁷⁸⁻⁷⁹ and machine learning for automated AMR prediction. AMR-related problems can now be effectively addressed with machine learning approaches⁸⁰. Nowadays, DL and ML are effectively used to predict the accurate AMR results⁷⁰. These cutting-edge techniques are establishing the foundation for better predictive outcomes and useful insights by

combining sequencing techniques with existing databases and AMR phenotypic data^{76,81}.

Novel ways to address this worldwide health concern are provided by the incorporation of artificial intelligence (AI) into antimicrobial resistance (AMR) management plans⁸². Systems utilizing AI greatly accelerate the early stages of drug discovery by analyzing enormous chemical libraries to identify molecules with possible antibacterial properties. For identifying candidates that might be efficient against resistant bacteria, deep learning methods, for instance, can detect structural properties of molecules that correlate with antimicrobial activity⁸³. AI can accurately predict patient responses, discover a variety of potential drug candidates, and offer an extensive patient sample to enhance the strategy of clinical trials for novel antibiotics⁸⁴. Thus, AI is transforming healthcare by improving accuracy and efficiency. In research, AI helps to uncover novel drugs at a faster rate and eliminate arduous conventional drug development techniques. Overall, it enhances patient care, streamlines hospital management, improves diagnosis efficiency, and reduces healthcare costs (see Figure 3).

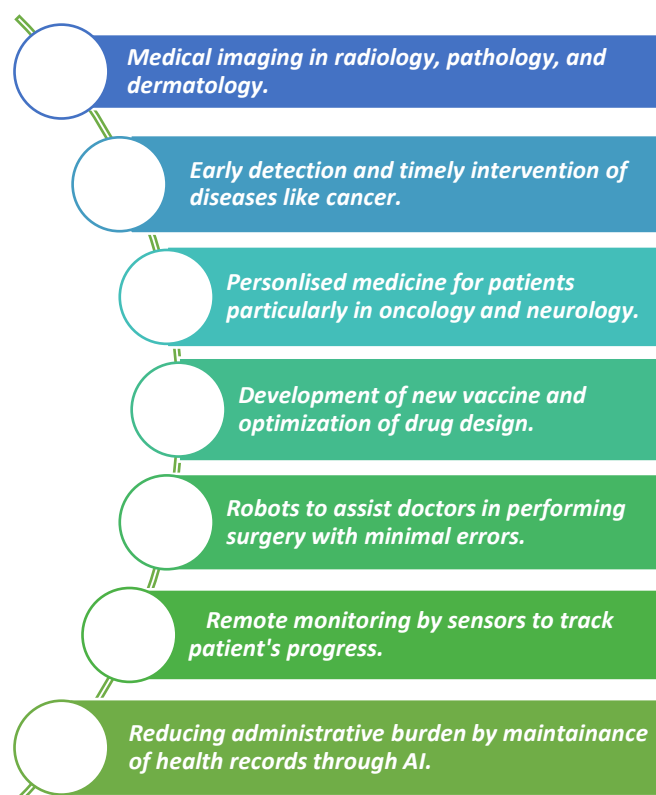


Figure 3: A schematic illustration of how artificial intelligence is being used in several healthcare areas to improve the speed and precision of diagnosis and treatment procedures.

7. Physiologically based pharmacokinetic (PBPK) modelling

PBPK modeling acts as a useful computational approach for evaluating pharmacokinetics or toxicokinetics. PBPK models partition the body into discrete physiologically defined tissue compartments and simulate drug absorption, distribution, metabolism, and excretion (ADME) through mechanistic differential equations that encode tissue-specific flow rates, volume fractions, and biochemical activity parameters in both humans and animals. This approach can be useful for drug development and environmental chemical hazards analysis. It can take a lot of resources and time to gather the particular species' physiological and chemical ADME data for PBPK model development⁸⁵. Recent developments in ML/AI-based methods for the structure-based prediction of critical PK (pharmacokinetic) parameters have led several researchers to develop a PBPK model. Researchers highlight the requirement to develop computational models that can forecast PBPK model input parameter values, particularly for novel chemicals. In the manufacturing of drugs, PBPK models are often utilized to support dose recommendations and facilitate clinical trial design⁸⁶. Basic PBPK models require various molecule-specific parameters from in vitro studies, which reduces their accuracy and efficiency.

In order to resolve this matter, Yuelin Li et al. found that early detection of drugs frequently uses PBPK models and ML models in combination to forecast drug characteristics⁸⁷. Additionally, it enables us to accurately anticipate molecular PK profiles of small compounds without relying on experimental data. Li et al. (2024) evaluated a combined ML-PBPK model in which ML-predicted parameter estimates served as inputs to a mechanistic PBPK structure across 40 different compounds. The hybrid framework achieved 65% accuracy for the area under the concentration-time curve (AUC), which demonstrated a 2-fold error range compared to 47.5% accuracy for conventional PBPK models⁸⁷. Another study focuses on integrating machine learning with PBPK modelling; this method not only enhances pharmacokinetic parameters but also establishes the groundwork for precision nanomedicine, NP optimization, and AI-assisted drug development. In different organs, PBPK models promote NP uptake, metabolism, and excretion; however, in challenging environments, their accuracy is limited by their dependence on oversimplified assumptions. Real-time absorption by cells or targeting induced by surface alterations are examples of dynamic changes in NP behavior that PBPK models struggle to account for effectively. Due to these difficulties, interest in AI-driven solutions is rising. In order to overcome the shortcomings of both PBPK and conventional machine learning techniques, models can more accurately represent NP pharmacokinetics by combining domain-specific NP characteristics with AI-driven methodologies⁸⁸. The pharmacodynamic (PD) model and AI-related algorithms were all merged into a single

platform using a web-based platform known as *B²O*simulator⁸⁹.

During the early stages of drug discovery, this platform helps researchers find a drug's PK profile with its intended PD effects. These models use mathematical equations to predict how drugs will behave in the human body. The ADME and other physicochemical characteristics are predicted using machine learning (ML) techniques, which are a subset of AI. This study uses graph neural networks (GNNs), a particular kind of machine learning technique, for analyzing chemical structures and forecasting structural PK parameters⁸⁹. Finding appropriate drug- or chemical-specific parameters is a major obstacle while creating a PBPK model, particularly for recently created drugs or chemicals, because calculated values for the majority of these parameters are unavailable. In order to close this scientific gap, several researchers combined an ML-based QSAR model with a PBPK model to estimate tissue and plasma concentrations, along with a number of PK characteristics. The successful design of efficient PBPK models for a wide range of compounds will continue to be made possible by ML/AI techniques, in spite of current difficulties⁹⁰. To predict toxicokinetic parameters, multiple in-silico models can be utilized as input variables for PBPK and high-throughput toxicokinetic (HTTK) framework, which were developed using a significant amount of data involving nonpharmaceutical compounds such as pesticides, environmental pollutants, and industrial chemicals⁹¹⁻⁹².

Despite these advancements, the integration of AI into PBPK modeling for infectious diseases presents substantial methodological and translational limitations. A predominant concern is the inherent tension between the transparency of classical PBPK models and the opaque "black-box" nature of advanced deep learning architectures. Regulatory bodies such as the FDA and EMA mandate high degrees of interpretability for models informing dosage guidelines. Thus, the lack of transparency in AI-derived parameter estimations remains a significant barrier to widespread clinical translation.

8. Challenges and limitations

Although AI presents great opportunities for drug formulation and delivery, several obstacles have been encountered, such as data availability and quality, given that thorough datasets and high-quality data are necessary for training efficient AI models. Another problem is model interpretability, which is crucial for improving model transparency for regulatory acceptability and clinical trust. This is because AI models are complicated and frequently operate as black boxes, thus making it difficult to understand how they make decisions. Regulatory frameworks for AI-augmented pharmaceutical tools are at an early stage globally. Regulatory agencies like the FDA and EMA mandate high degrees of interpretability tools that dictate drug dosage. Without clear visibility into how an

AI model weighs specific physiological covariates to arrive at a dosing recommendation, clinical adoption remains constrained by safety and liability concerns. Ethical dimensions, including data privacy, algorithm equity, and the responsible communication of AI predictions under uncertainty, are insufficiently addressed in current pharmaceutical literature.

9. Future perspective

AI-driven drug discovery is the most promising method in the coming years, reshaping the current drug discovery methods. Machine learning models will enable the rapid identification of novel drug candidates and help revolutionize healthcare. AI-guided design of nanocarriers and smart biomaterials will definitely improve treatment outcomes for AMR. Moreover, AI-powered epidemiological models are expected to support better and more personalized prophylaxis strategies by detecting infection risks at an early stage. As these technologies advance, the integration of AI with genomics and digital health tools will result in more efficient patient care and strengthen global readiness for future outbreaks. However, the main hurdles that must be addressed are biological issues, large-scale manufacturing, biocompatibility and protection, research and development, regulatory norms, and overall cost efficiency compared to current medications. Data privacy and security concerns further complicate the new techniques as sensitive patient information can be leaked. Interdisciplinary collaboration amongst data scientists, researchers, and engineers slows down the innovation process. Resource limitations may also restrict access to AI-driven healthcare solutions. Overcoming these drawbacks will undoubtedly enhance the incorporation of AI/ ML techniques into drug discovery and enhance healthcare practices.

10. Conclusion

AI/ML has emerged as a genuinely transformative methodological force in drug delivery for infectious diseases. DNN and ensemble architectures consistently outperform classical statistical and computational models in drug formulation, targeted drug delivery, and antimicrobial resistance. Hybrid ML-PBPK frameworks have demonstrated improvements in pharmacokinetic prediction accuracy over conventional models. These contributions collectively provide a strong justification for the integration of AI across the full drug delivery pipeline for infectious disease management. The review makes clear that three structural gaps define the boundaries of current AI-drug delivery translation. First, the compositional bias of trained datasets toward the non-antimicrobial pharmaceutical space limits the applicability of trained models. Second, the near-universal reliance on in vitro validation means that the true clinical accuracy prediction of drug delivery tools remains unverified. Third, the absence of regulatory frameworks for AI-augmented drug delivery tools creates governance uncertainty. Overcoming these gaps will require a coordinated action plan between research,

industry, and regulatory domains. The present review seeks not merely to catalogue the state of the art, but to provide the analytical scaffolding through which these investments can be directed most productively.

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