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Review Article

# Artificial Intelligence-driven Strategies and Modern Innovations to Surpass Biopharmaceutic Limitations in Traditional Drug Development

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## Abstract

Drug discovery is an exceptionally long and costly process, often taking over 10 years and costing billions of dollars. Despite these efforts, more than 90% of drug candidates fail, with most failures occurring during clinical trials due to issues related to efficacy, safety, or poor pharmacokinetics. A major contributor to these failures is biopharmaceutic barriers, including poor solubility, limited permeability, active efflux by transporters such as P-glycoprotein and breast cancer resistance protein, and extensive first-pass metabolism by CYP450 enzymes. These factors severely limit drug absorption and bioavailability, reducing therapeutic efficacy. Although traditional approaches, such as high-throughput absorption, distribution, metabolism, and excretion screening and improved chemical design, have achieved some progress, a major shift is now occurring through the use of in silico modeling, artificial intelligence (AI), and machine learning. These AI-driven tools enhance the prediction accuracy of absorption, distribution, metabolism, and excretion profiles, identify transporter interactions, and even simulate metabolic pathways. Additionally, modern formulation technologies, such as three-dimensional printing, lipid-based nanocarriers, and biodegradable delivery systems, are increasingly being integrated with AI-powered design platforms to personalize and optimize drug delivery. However, these promising advancements also raise regulatory and ethical concerns that must be addressed before widespread adoption. This review examines the major biopharmaceutic barriers responsible for drug development failures and explores how emerging AI-driven strategies and formulation innovations are being used to overcome these limitations. It also discusses current regulatory challenges and ethical considerations associated with adopting these technologies.

## Introduction

The path to discovering and developing a new drug is far from easy. It is a process that can take over a decade and cost upwards of 1 to 2 billion dollars,[1] yet the success rate remains shockingly low. More than 90% of drug candidates fail during clinical development, and if preclinical failures are included, the odds are even worse.[2] While many of these failures are attributed to lack of efficacy or safety issues such as toxicity, a substantial proportion are actually due to poor biopharmaceutic properties. In other words, a drug may appear promising in theory, but if it does not dissolve well, cannot cross biological membranes, is actively pumped out by efflux transporters, or is metabolized too quickly, it will not perform effectively in the body. These challenges fall under the domain of biopharmaceutics, the study of how a drug's formulation and physicochemical properties affect its absorption and bioavailability. Despite ongoing advances in medicinal chemistry and formulation science, many compounds with therapeutic potential fail due to unresolved issues related to solubility, permeability, transport, or metabolism.[3,4] The need for smarter, predictive strategies grows as drug molecules become more complex. Emerging technologies such as in silico modeling, machine learning (ML), and artificial intelligence (AI) now offer powerful tools to assess biopharmaceutical behavior early in development. Innovations in drug delivery systems, including lipid-based carriers, nanotechnology, and three-dimensional printing (3DP), have also reshaped the formulation of poorly bioavailable drugs. AI is playing a growing role in drug development, particularly in handling complex early-stage decisions. ML, one of the most widely used AI approaches, involves models that learn from data to make predictions about absorption, distribution, metabolism, and excretion (ADME),

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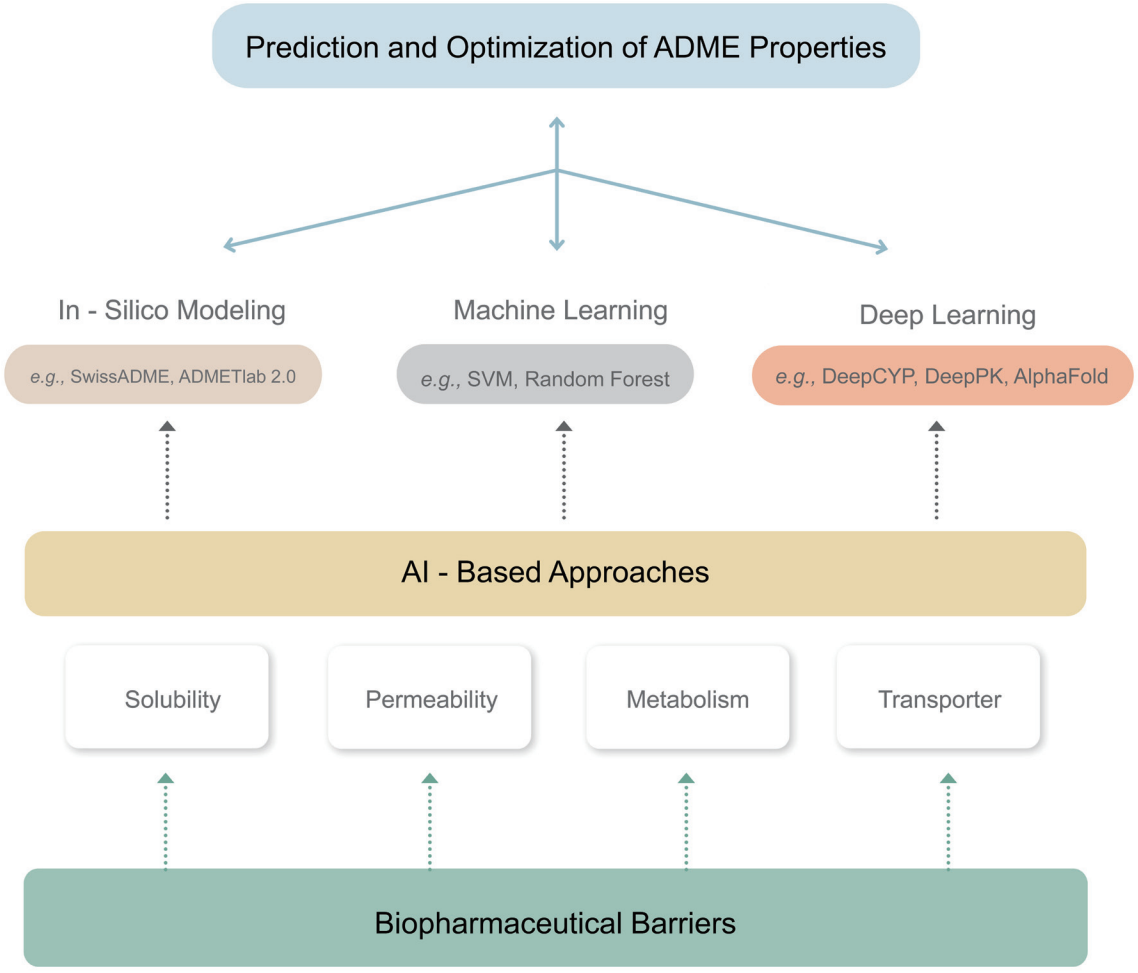


**Fig. 1. The role of AI in biopharmaceuticals utilizes in silico modeling, machine learning, and deep learning to enhance ADME properties and improve drug bioavailability and development success.** ADME, absorption, distribution, metabolism, and excretion; AI, artificial intelligence; SVM, support vector machine.

guide structural optimization, or classify drug candidates.[5,6] An advanced form of ML called deep learning can recognize patterns in large and complex datasets, detecting genetic information and molecular structures that would be difficult to identify manually. Natural language processing is also being used to analyze massive amounts of biomedical literature and clinical trial data to uncover connections that might otherwise be missed. Additionally, experts and generative models are being employed to design drugs and predict molecular behavior. These AI techniques are making pharmaceutical research faster, more accurate, and more efficient, as illustrated in Figure 1. The goal of this review is to provide a comprehensive overview of the major biopharmaceutic barriers to drug success, including poor solubility, limited permeability, transporter-mediated efflux, and extensive metabolism. It also discusses recent technological developments and computational innovations aimed at overcoming these challenges, as well as regulatory considerations and future directions for integrating these approaches into modern drug development.

## Biopharmaceutic barriers to drug success

Drug discovery and development is an extremely long and expensive process, taking up to 10 years and costing over one to two billion dollars. Despite these investments, more than 90% of drug candidates fail during clinical development. What makes this even more concerning is that this 90% failure rate only applies to drugs that actually make it into clinical trials. If preclinical failures were included, the odds of success would be even lower.[7,8] The main reasons behind these failures include lack of efficacy, which accounts for approximately 40–50% of cases, followed by safety-related issues such as toxicity (around 30%). In addition, poor drug-like properties, including low solubility, limited permeability, or extensive metabolism, contribute to about 10–15% of failures. Although significant progress has been made in optimizing drug-like properties, the overall clinical success rate has not improved considerably and still remains low, at around 10–15%.[7]

### *Solubility and permeability issues*

Although a drug can be pharmacologically effective *in vitro*, it must first dissolve in gastrointestinal fluids and traverse the intestinal epithelium to exert therapeutic effects when administered orally. Solubility is the first and most critical requirement for absorption, and its absence often results in limited or erratic bioavailability. Drugs must cross the gut wall to reach the bloodstream, which

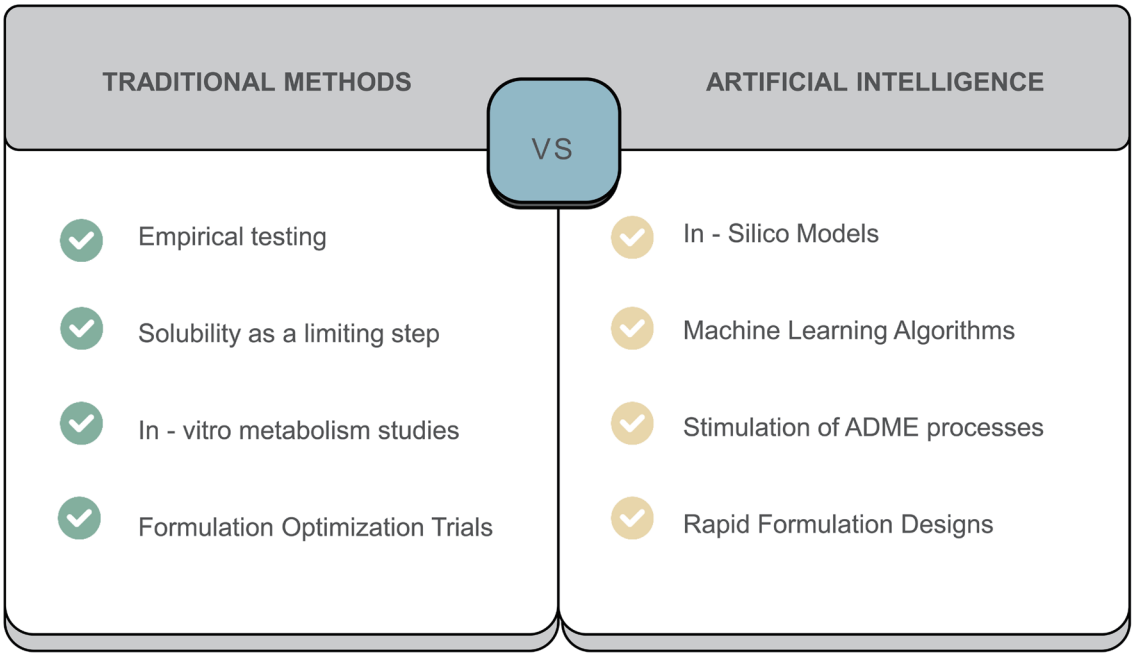


**Fig. 2. Comparison of traditional and AI-based drug development strategies shows that AI approaches utilize predictive models, while traditional methods depend on iterative laboratory testing.** ADME, absorption, distribution, metabolism, and excretion; AI, artificial intelligence.

becomes difficult if they are too hydrophilic or too large.[9] In fact, it is estimated that approximately 40% of approved drugs and nearly 90% of drug candidates in development are poorly water-soluble, a condition that severely affects their clinical success and market translation.[10–12] The Biopharmaceutics Classification System (BCS) was developed to conceptualize the relationship between solubility and permeability. According to this system, compounds are classified into four classes based on their solubility in water and their permeability across the gut wall.[13,14] For example, Class I medications, such as propranolol, are highly soluble and highly permeable, and therefore typically do not encounter significant absorption problems. Class II drugs, like carbamazepine, have good permeability but poor solubility, so formulation strategies such as solid dispersions, amorphous forms, or lipid-based delivery systems must be employed.[15] In contrast, BCS Class III drugs, such as alendronate and acyclovir, dissolve readily but are poorly absorbed due to limited membrane permeability, necessitating bioenhancers or advanced delivery systems such as microparticles and liposomes.[16] BCS Class IV compounds, which lack both solubility and permeability, pose substantial formulation challenges and often exclude oral administration unless innovative technologies are used.[15] To overcome absorption limitations in these classes, lipid-based nanocarriers, solid dispersions, and 3D-printed microstructures are actively being investigated. Computational tools, including quantitative structure-activity relationship models, ML, and AI, now allow molecular libraries to be screened for solubility and permeability characteristics at high throughput, streamlining formulation design and candidate selection.[17] This integrated approach reduces development costs and late-stage attrition caused by unfavorable biopharmaceutical properties. Unlike traditional solubility screening methods, which are labor-intensive and require empirical formulation development, AI-based tools such as ADMETlab 2.0 and SwissADME can predict solubility profiles, BCS classes, and permeability in real time with high accuracy.[18,19] Compared with standard *in vitro* screens, these platforms provide better insights for formulation decisions at an earlier stage of compound triaging, as illustrated in Figure 2.

### *Transporters like P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP)*

Even if a drug dissolves efficiently and demonstrates good permeability, it still faces another obstacle: efflux transporters. Proteins such as P-gp and BCRP are present in the intestinal lining and can significantly affect drug absorption. These transporters, often referred to as "cellular bouncers",[20] actively export drugs back into the intestinal lumen, thereby reducing both absorption and overall bioavailability.[21] Drugs such as digoxin, paclitaxel, and topotecan are classic examples affected by P-gp and BCRP.[22–24] These transporters not only influence intestinal absorption but also play crucial roles in drug distribution and elimination. P-gp and BCRP are expressed in multiple tissues, including the liver, kidney, placenta, and blood-brain barrier. Their physiological function is to protect tissues from xenobiotics; however, this protective mechanism can severely limit the accessibility of therapeutic agents to target sites. Additionally, genetic polymorphisms in transporter genes such as ABCB1 and ABCG2 can alter transporter expression, affecting the pharmacokinetics and therapeutic response of substrates.[25,26] In cancer therapy, overexpression of P-gp in tumor cells can lead to multidrug resistance, where cancer cells become resistant to chemotherapy despite high drug doses.[27] To study efflux-mediated transport, the Caco-2 cell line is widely used due to its similarity to human enterocytes. However, differentiation and formation of tight junctions take 21–24 days, making it less suitable for high-throughput screening.[28] AI-based tools such as quantitative structure–property relationship modeling have emerged as efficient alternatives, capable of predicting permeability and efflux interactions in silico. Platforms like DeepTox and other ML-based transporter prediction models can screen large compound libraries for P-gp and BCRP affinity, ena-

bling early detection of liabilities and reducing the need for extensive *in vitro* testing.[29] In addition to P-gp and BCRP, organic cation transporters and organic anion transporters (OATs) play important clinical roles. They are primarily expressed in the kidney and liver, where they regulate systemic availability and clearance of many therapeutics.[21,30] For example, organic cation transporter 2 mediates the renal uptake of metformin[31] and cisplatin[32]; its inhibition or genetic variation can alter drug efficacy and toxicity.[33] Similarly, OAT1 and OAT3 facilitate the uptake and elimination of penicillin, methotrexate, and NSAIDs, making them critical determinants of drug half-life and renal clearance.[34] Understanding whether a drug is a substrate or inhibitor of these transporters is now considered a critical component of preclinical evaluation. Regulatory agencies, including the U.S. Food and Drug Administration (FDA) and the European Medicines Agency, increasingly require comprehensive *in vitro* and *in vivo* data on transporter interactions.[35] This is essential for predicting and managing drug-drug interactions, which may result in enhanced toxicity or therapeutic failure. Advanced in silico models and AI-based prediction platforms are also used to detect transporter-related liabilities early in development.[36,37] By identifying transporter interactions early and integrating this data with pharmacokinetic modeling, developers can optimize dosing strategies, anticipate population variability, and improve the safety and efficacy profile of novel therapeutics.[38]

### *Metabolism and CYP450 enzymes*

Another critical barrier to drug bioavailability is metabolism. Even if a drug is absorbed, it can be extensively metabolized by liver enzymes before reaching systemic circulation, diminishing its therapeutic efficacy. This phenomenon, known as first-pass metabolism, is primarily carried out by the cytochrome P450 family, especially CYP3A4, CYP2D6, and CYP2C9, which together metabolize approximately 80% of commonly used drugs.[39] A classic example is propranolol, which has only about 25% bioavailability due to significant hepatic metabolism.[40] Similarly, midazolam is almost entirely metabolized by CYP3A4.[41] One of the most significant challenges posed by CYP-mediated metabolism is its high interindividual variability, largely due to genetic polymorphisms. These variations can drastically influence drug exposure and patient response, classifying individuals as "poor metabolizers" or "ultra-rapid metabolizers," which increases the risk of side effects or therapeutic failure.[42] Co-administered drugs or foods can also inhibit or induce CYP enzymes, leading to dangerous drug-drug interactions. A notable example is grapefruit juice, which contains furanocoumarins that inhibit intestinal CYP3A4, resulting in elevated plasma levels of simvastatin and potentially causing myopathy and hepatotoxicity.[43] Modern drug development increasingly integrates computational approaches to address these challenges. AI-enabled tools such as SMARTCyp, DeepCYP, and MetaSite utilize molecular characteristics and structure-activity relationships to predict vulnerable sites of metabolism, assisting medicinal chemists in designing metabolically stable drug candidates.[44–46] Integrating predictive metabolism modeling during early-stage development enhances candidate selection, minimizes late-stage failures, and supports rational dose design,[39] particularly in pharmacogenetically diverse populations.[47]

## AI & computational modeling in biopharmaceutics

### *ADME & in silico models*

The optimization of drug therapy depends on the precise prediction of how a medication is ADME within the body. Biopharmaceutics integrates knowledge from pharmacology, chemistry, and physiology to optimize drug discovery and development. At its core, biopharmaceutics studies how a drug's formulation influences its ADME, ultimately impacting efficacy and safety.[48,49] Unfavorable ADME properties are a major cause of late-stage drug candidate failure, resulting in significant financial losses and time expenditure in research and development.[17] To address this challenge, in silico modeling was introduced, with its earliest models dating back to the 1970s–1980s. These models primarily employed quantitative structure-activity relationships to predict drug-receptor interactions based on molecular properties.[50] In silico models use computational techniques to develop pharmacological models that predict biological and chemical processes, thereby aiding drug discovery and development. Increasing computational power has expanded the scope of in silico modeling, reducing costs and improving efficiency in the drug discovery process.[17,51]

#### ADME screening methods

ADME screening is used to identify and optimize new chemical entities, the primary focus of drug discovery. Traditional ADME screening methods relied on low-throughput *in vitro* and *in vivo* assays, which were manual and inefficient.[52] Around the year 2000, high-throughput *in vitro* ADME (HT-ADME) methods were introduced. While still relying on biological assays, HT-ADME operates on an industrial scale using robotics, advanced analytical techniques such as LC/MS/MS, liquid handlers, and miniaturized assay plates, making the process more efficient and cost-effective than low-throughput methods. However, HT-ADME is still limited compared with in silico models, as it relies on physical experiments, expensive equipment, consumables, and considerable time to generate data.[53,54]

#### Advantages of AI models in ADME prediction

AI models in in silico screening provide significant advantages, particularly in predictive accuracy and efficiency. Using computational methods such as ML, these models can analyze large datasets to identify complex patterns related to pharmacokinetic properties. By simplifying relationships between physicochemical parameters and ADME endpoints, AI enables rapid identification of promising candidates without extensive wet lab experiments.[51] These models enhance new chemical entity design by simultaneously optimizing multiple ADME parameters alongside bioactivity.[55,56]

One such model is SwissADME, a free web tool with a user-friendly interface that provides access to robust predictive models for pharmacokinetics, physicochemical properties, drug-likeness, and medicinal chemistry friendliness. SwissADME stands out for its advanced prediction algorithms, including the BOILED-Egg model, bioavailability radar, and Lipinski's Rule of Five. These algorithms serve diverse purposes, from evaluating drug-likeness to predicting gastrointestinal absorption and blood-brain barrier permeability.[18,57]

Another recent model, Deep-Pk, uses graph neural networks and graph-based signatures to deliver strong predictive performance across multiple endpoints. Deep-Pk predicts ADMET (absorption, distribution, metabolism, excretion, and toxicity) across 73 endpoints, achieving an external validation mean Matthews correlation coefficient of 0.58 and receiver operating characteristic – area under the curve (ROC-AUC) scores exceeding 0.80 for most classification tasks.[58] However, like many deep learning models, Deep-Pk may struggle with interpretability and could exhibit bias when applied to chemical spaces differing from its

training set. kMoL, an open-source ML library, has demonstrated strong performance on benchmark datasets, achieving ROC-AUC scores above 0.75 in ADME and toxicity tasks, both in centralized and federated settings.[59] By using graph convolutional networks to model molecular structures as graphs, kMoL outperforms traditional methods.[59,60] Despite its flexibility and focus on privacy preservation, performance can vary depending on dataset size and quality, making careful hyperparameter tuning essential. While uncertainties remain in in silico predictions, particularly in drug discovery, methods to quantify these uncertainties can enhance interpretability and improve confidence in model predictions.[61]

### *ML applications in formulation design*

ML, a branch of AI, creates predictive models trained on previous datasets, which can be derived from both *in vivo* and *in vitro* experiments. ML-based approaches are increasingly common, providing significant predictive power and screening capabilities that help identify the most suitable drug candidates, thereby enhancing accuracy and efficiency.[62] The most commonly used ML techniques for screening are support vector machines (SVMs) and random forests (RFs). SVMs excel in high-dimensional spaces by identifying hyperplanes that maximize class separation, but they require careful tuning and are less efficient with large datasets. In contrast, RFs use multiple decision trees to handle large or noisy datasets with minimal tuning, offering resistance to overfitting. Although RFs may lack some interpretability compared to SVMs, they are better suited for diverse real-world data. SVMs work best with structured data, while RFs are preferred for scalability.[63,64]

Both techniques are widely employed in drug formulation design, particularly for classification and regression tasks. SVMs are highly effective for binary classification and high-dimensional datasets, making them suitable for predicting ADME properties such as solubility. ML-based models also analyze diverse genomic, proteomic, and clinical datasets to identify potential drug targets and prioritize candidates based on criteria such as drug-likeness and therapeutic relevance.[62,65] The AlphaFold program, developed by DeepMind, has transformed AI-driven drug discovery by predicting 3D protein structures with unmatched accuracy through deep learning. AlphaFold aids structure-based drug design by identifying protein-ligand interaction sites, supporting target validation and virtual screening. With over 200 million structures available in the AlphaFold Protein Structure Database, it has become an essential resource in rational drug design.[66,67] As target structure prediction improves, efficient screening of vast compound libraries becomes increasingly important in identifying optimal candidates.

Modern drug discovery heavily relies on compound libraries containing millions of molecules. For example, the ZINC22 library houses 4.1 billion molecules. The growing size of these libraries necessitates faster and more efficient screening methods.[68] Early ML models using RFs focused on computational prioritization but lacked scalability.[69] The sheer volume of data from genomics, proteomics, metabolomics, imaging, and electronic health records requires AI to discern meaningful patterns, process large datasets efficiently, and analyze longitudinal patient data. This capability enables understanding of individual patient trajectories, which is essential for predicting how a drug is absorbed and metabolized over time.[70]

### *How does AI predict and personalize drug absorption?*

AI has become increasingly important in screening compounds with favorable ADME properties. One recent advancement is RosettaVS, an AI-driven platform that uses physics-based protocols to dock billion-molecule libraries in days, achieving a 44% hit rate for Nav1.7 in just seven days.[71] AI and ML also play a crucial role in understanding the complex relationship between an individual's genetic makeup and drug response. In pharmacogenomics, genetic variations strongly influence drug metabolism and transport, directly affecting absorption. AI can analyze an individual's genetic profile to identify genes responsible for drug absorption and metabolism, predict likely drug responses, and enable selection of the safest and most effective treatment. AI-powered pharmacogenomics has the potential to revolutionize personalized medicine, providing innovative solutions and improved predictive accuracy to benefit patient care.[72,73] However, AI tools must undergo thorough evaluation to ensure they are applied safely and fairly, just as with any new therapeutic intervention.[74]

## Biopharmaceutics

### *3D-printed pharmaceuticals for personalized bioavailability*

Drug discovery has seen remarkable progress, yet scientific innovation continues to emerge rapidly across multiple fields. One such innovation is 3DP, a process that creates a three-dimensional object from a digital design. Unlike traditional subtractive manufacturing, which removes material, 3DP builds objects layer by layer,[75] 3DP enables customization of drug delivery systems, providing personalized treatment options. It allows the creation of complex dosage forms, such as multi-compartmental capsules, which can combine multiple drugs in a single dosage form and be adjusted according to combination therapy needs.[76,77] While 3DP shows great potential for improving drug bioavailability and facilitating personalized therapies, most current data comes from *in vitro* experiments or animal studies. Large-scale clinical trials validating these methods are limited, and regulatory approval pathways are still evolving.[78,79] 3DP also offers advantages for formulating drugs with poor water solubility.[80] Mesoporous materials can enhance the dissolution rate and bioavailability of such drugs using techniques such as fused deposition modeling or semi-solid extrusion (SSE). For example, drug-loaded mesoporous magnesium carbonate formulations have achieved high drug loading of 15.3% w/w.[81]

Techniques such as fused deposition modeling, stereolithography, selective laser sintering, binder jetting, SSE, and hot-melt extrusion offer diverse possibilities in pharmaceuticals.[82] For instance, SSE can produce tablets and suppositories with enhanced dissolution kinetics, increasing bioavailability by extruding a non-aqueous paste containing drug-loaded mesoporous materials.[83] Despite its potential, 3DP faces limitations, including material selection, biocompatibility concerns, potential toxicity from degradation products such as those from polylactic acid, regulatory hurdles, scalability issues, and cost-effectiveness. Customization of dosages also raises ethical concerns, as it relies on sensitive patient data that must be protected.[84] Nevertheless, the future of 3DP remains promising, especially when integrated with AI and ML to further expand its applications.[85]

### *Biodegradable nanocarriers for targeted drug delivery*

Nanocarriers are another promising avenue in drug discovery. These nanoscale delivery systems encapsulate and transport therapeutic agents, fine-tuning drug ADME profiles.[86] Biodegradable nanomaterials used in nanocarrier technology hold particular promise, as they safely degrade in the body into natural elements over time, reducing systemic toxicity. Nanocarriers are typically

composed of polymers, both natural and synthetic. Natural polymers include polysaccharides and proteins such as chitosan, alginates, albumin, and cellulose derivatives. Synthetic polymers, such as polylactic acid, are popular for their high biodegradability.[87] Nanocarriers provide targeted drug delivery through passive and active mechanisms. Passive targeting relies on inherent nanocarrier properties to accumulate in specific areas, such as tumor sites. Active targeting involves techniques such as ligand-mediated targeting or molecularly imprinted nanocarriers, facilitating site-specific drug delivery.[88] Despite these advances, concerns remain regarding long-term biocompatibility, potential toxicity from accumulation or immune responses, and challenges in large-scale manufacturing, limiting clinical translation.[89,90] For example, poly(lactic-co-glycolic acid)–polyethylene glycol (PLGA-PEG) nanoparticles co-encapsulating gemcitabine and botulinic acid have demonstrated improved anti-tumor efficacy in pancreatic cancer cell lines.[91]

### *Regulatory challenges in biopharmaceutical innovation*

Although addressing biopharmaceutical needs by employing AI and other technologies shows promise, significant regulatory challenges remain. AI and ML heavily depend on representative data, but pharmaceutical datasets are complex and often uncertain, which can introduce bias in AI training and lead to inaccurate outcomes, potentially exacerbating health disparities. Ensuring data quality, reproducibility, and reliability is therefore critical.[92] Regulatory agencies, such as the FDA and the European Medicines Agency, are developing frameworks to govern AI use, incorporating real-world and open-source data along with robust quality standards to ensure fair and ethical implementation in drug discovery.[93] Innovations such as 3DP and biodegradable nanocarriers also face lengthy approval processes. Preclinical and clinical data are required to demonstrate safety and efficacy, imposing significant cost burdens. For 3DP, consistent quality, scalable production, and material safety, including inks used in printing, must be ensured. For nanocarriers, challenges include characterizing nanomaterials' size, shape, and surface properties, minimizing off-target accumulation, and ensuring biocompatibility and safety.

### *Implementation strategies for overcoming regulatory challenges in novel drug formulations*

To overcome these challenges, active communication with regulatory authorities is essential during development. The FDA's Emerging Technology Program, for example, provides developers with real-time guidance on novel manufacturing practices, aligning preclinical and clinical protocols with regulatory expectations and reducing issues in later stages.[94] Adopting quality by design principles allows manufacturers to build quality into the product from the outset, simplifying critical quality attributes and critical process parameters to ensure consistency and reproducibility.[95] Regulatory agencies, following ICH Q8–Q11 guidelines, endorse quality by design principles to streamline approvals for innovative products. By adopting these strategies, cutting-edge therapies can reach patients without compromising safety or efficacy.[96,97]

## Limitations and future prospects

The incorporation of AI, advanced predictive tools, and innovative drug formulation methods can help address the complex challenges associated with drug development. Future research should focus on validating AI-based prediction tools for drug ADME using extensive real-world patient datasets, enhancing regulatory acceptance of these algorithms.[98,99] Additionally, integrating AI with 3DP and designing nanocarriers creates new opportunities for personalized medicine, enabling drug delivery tailored to individual patient profiles. At the same time, it is essential to use data ethically, minimize biases in AI programs, and ensure transparency in AI-driven decisions throughout the drug development process.

Several limitations of this review should also be acknowledged. Given the rapid evolution of this field, some of the latest developments may not be fully covered, and the review aims to provide an overview of key biopharmaceutical barriers and emerging AI-driven strategies. While case studies and tool-specific examples are presented, many applications remain in preclinical or experimental stages and have not yet been tested in large populations. Furthermore, this review provides limited coverage of health equity implications, global regulatory harmonization, and the economic feasibility of adopting AI and advanced formulation technologies. These areas warrant further investigation in the near future.

## Conclusions

Biopharmaceutic challenges, including poor solubility, limited permeability, active drug efflux, and extensive metabolism, remain major reasons why many promising drug candidates fail to reach the market. While traditional formulation approaches aim to improve biopharmaceutical properties, they often overlook modern, multi-targeted, and chemically complex molecules. Addressing these obstacles in contemporary research requires integrating advanced technologies. In early stages of drug development, AI is increasingly applied to predict absorption and metabolism profiles using tools like SwissADME and DeepCYP, while generative models assist in synthesizing drug-like molecules with improved target characteristics. In silico simulations of transporter interactions also support risk evaluations prior to clinical trials. In drug formulation, 3DP enables the creation of multi-compartmental and layered tablets tailored to specific absorption windows and desired release kinetics. Meanwhile, lipid-based and PLGA-PEG nanoparticles serve as biodegradable carriers, improving the delivery of poorly soluble and unstable drugs in oncology and central nervous system therapies that require advanced delivery systems. These examples demonstrate that the application of these innovations is no longer a distant potential; they are already making meaningful impacts. As integration continues, it will be essential to align these tools with regulatory frameworks, ensure data transparency, and focus on clinically relevant endpoints to ensure their long-term impact on successful drug development.

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## Author contributions

Conceptualization (HBA, MBK), literature search, writing – origi-

nal draft (HBA), data interpretation, supervision, critical revision of the manuscript (MBK), writing – reviewing and editing (HBA, MBK). Both authors have approved the final version and publication of the manuscript.

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