

Artificial Intelligence in Pharmaceutical Formulation and Drug Delivery

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ABSTRACT

Pharmaceutical formulation development and drug delivery are among the most technically demanding and cost-intensive phases of the drug development pipeline. Traditional formulation strategies are largely dependent on iterative trial-and-error experimentation, which often results in extended development timelines, substantial resource consumption, and a high likelihood of late-stage formulation failure. In recent years, artificial intelligence (AI) and machine learning (ML) have gained significant attention as powerful computational tools capable of analysing complex, high-dimensional pharmaceutical datasets and generating data-driven predictions to guide formulation decisions. By enabling systematic optimisation, adaptive learning, and improved decision-making, these approaches offer a paradigm shift from empirical experimentation to predictive formulation design. This review critically examines the expanding role of AI and ML in pharmaceutical formulation development and advanced drug delivery systems, highlighting commonly employed algorithms, formulation-centric applications, modelling frameworks, regulatory considerations, and emerging research directions. Particular focus is placed on practical deployment, model interpretability, and the translational potential of AI-enabled methodologies within industrial pharmaceutical development.

KEYWORDS: Artificial intelligence, machine learning, pharmaceutical formulation, drug delivery systems, predictive modelling, deep learning

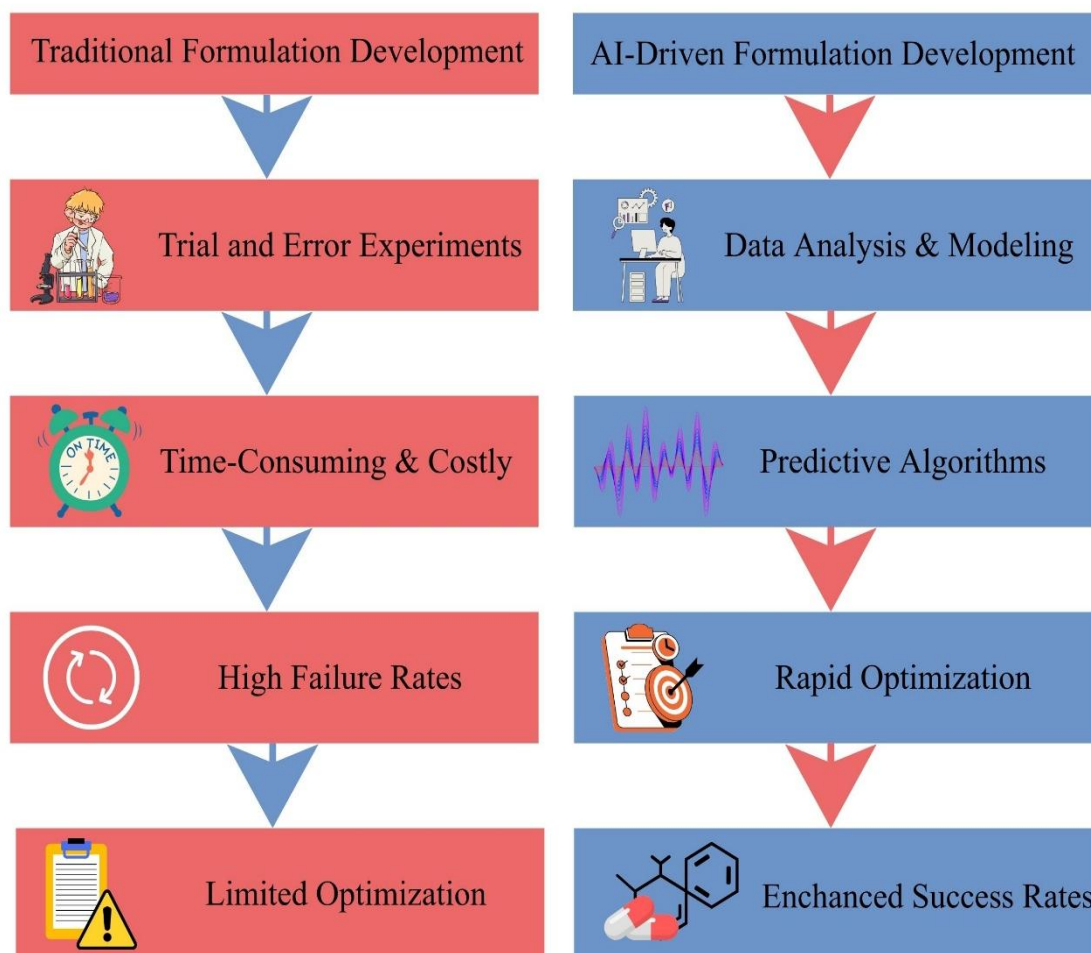
I. INTRODUCTION

Pharmaceutical formulation and drug delivery play a decisive role in converting pharmacologically active compounds into safe, effective, and reproducible therapeutic products. Despite major advances in medicinal chemistry and molecular pharmacology, a substantial number of

drug candidates fail to progress successfully through development due to formulation-related challenges, including limited aqueous solubility, chemical or physical instability, suboptimal bioavailability, and variability in manufacturing performance. Conventional formulation development has historically depended on experimental trial-and-error approaches, often supported by statistical methodologies such as Design of Experiments (DoE). Although these strategies have significantly contributed to pharmaceutical innovation, they become increasingly inadequate when applied to formulation systems characterised by multiple interdependent variables and complex interactions.

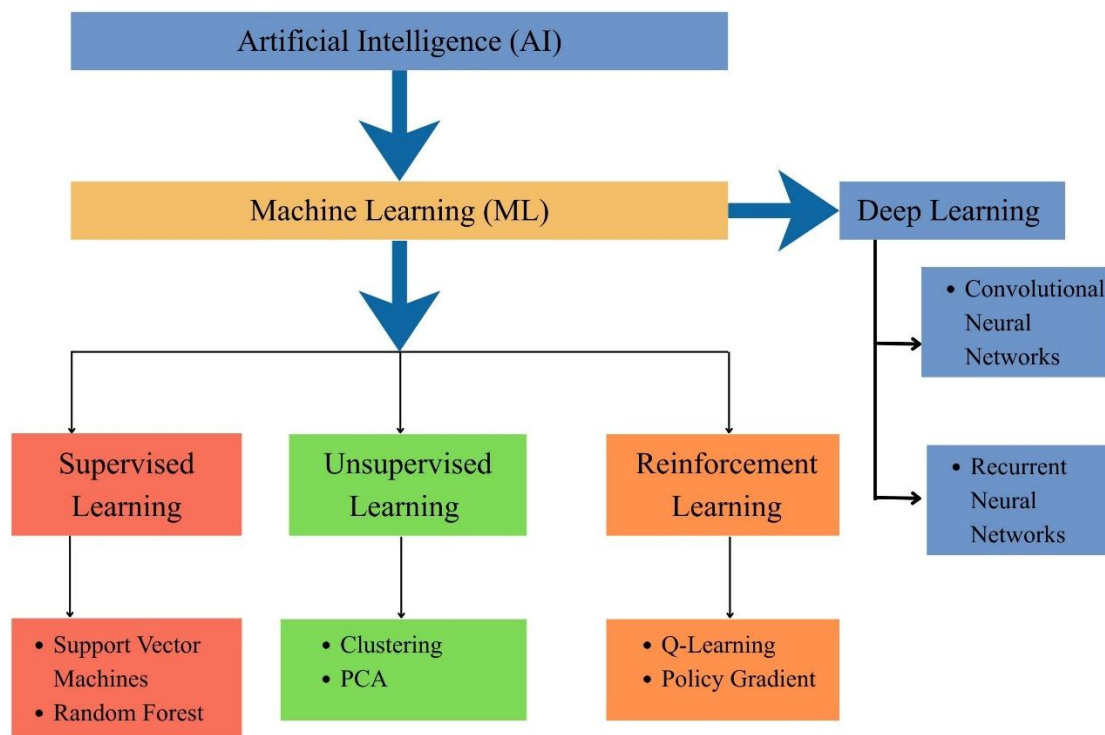
The growing dominance of poorly water-soluble compounds, biologics, nanomedicines, and personalised therapeutic platforms has further intensified formulation complexity. Such systems frequently display nonlinear and dynamic relationships between formulation constituents, processing conditions, and critical quality attributes that are difficult to model using traditional statistical techniques. In this context, artificial intelligence (AI) and machine learning (ML) introduce a transformative, data-centric framework for formulation development. By learning from large and diverse historical datasets, AI-driven models can uncover hidden patterns, predict formulation performance, and guide optimisation strategies that extend beyond the capabilities of conventional methods. This shift from purely empirical experimentation toward predictive and adaptive formulation design has the potential to substantially reduce development timelines, enhance product robustness, and improve overall formulation success rates.

Fig.1. Comparison between conventional trial-and-error-based pharmaceutical formulation development and AI-driven formulation strategies, highlighting differences in efficiency, cost, and optimisation capability.



OVERVIEW OF ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING

Fig.2. Classification of Artificial Intelligence, Machine Learning, and Deep Learning.



Artificial intelligence encompasses a broad range of computational methodologies developed to replicate selected cognitive functions of human intelligence, such as learning from experience, logical reasoning, and informed decision-making. Within pharmaceutical sciences, AI does not replace domain expertise but instead serves as a sophisticated analytical framework that supports scientists in interpreting complex datasets and guiding experimental decisions. Machine learning (ML), a core subset of AI, is distinguished by its ability to generate predictive models that evolve through exposure to data rather than reliance on predefined, rule-based programming. This characteristic is particularly valuable in pharmaceutical formulation research, where formulation performance is governed by multiple interacting variables and non-linear dependencies.

Machine learning methodologies are commonly classified according to their learning mechanisms and the nature of the data utilised. Supervised learning approaches rely on labelled

datasets in which experimental inputs are directly associated with known outputs, such as drug release profiles, tablet mechanical strength, or stability parameters, making them highly applicable to formulation performance prediction. In contrast, unsupervised learning techniques operate on unlabeled datasets to reveal intrinsic patterns, groupings, or correlations, supporting applications such as excipient clustering, trend identification, and dimensionality reduction. Deep learning methods, based on multi-layered neural network architectures, extend these capabilities by capturing highly complex and nonlinear relationships, thereby enabling advanced modelling in areas such as nanocarrier design and image-driven quality assessment. Reinforcement learning introduces an adaptive, goal-oriented learning paradigm in which models iteratively refine decision-making strategies through interaction with a defined environment, offering emerging potential for dynamic formulation optimisation and sequential process control.

Table 1. Comparison of Machine Learning Algorithms Used in Pharmaceutical Research

Algorithm	Learning Type	Typical Applications in Pharmaceutics	Strengths	Limitations
Artificial Neural Networks (ANN)	Supervised	Solubility prediction, dissolution modeling, formulation optimization	Handles non-linearity, high accuracy	Requires large datasets, low interpretability
Support Vector Machines (SVM)	Supervised	Classification of formulations, stability prediction	Effective in high-dimensional space	Sensitive to kernel choice
Random Forest (RF)	Supervised	Excipient selection, QbD modeling	Robust, reduces overfitting	Less effective for extrapolation
k-Nearest Neighbor (k-NN)	Supervised	Similarity-based formulation prediction	Simple and intuitive	Poor scalability
Deep Learning (CNN, RNN)	Supervised/Unsupervised	Image-based defect detection, complex pattern recognition	High predictive power	Computationally intensive

PRE-FORMULATION STUDIES

Preformulation investigations provide the fundamental scientific basis for rational dosage form design by systematically evaluating the physicochemical characteristics of active pharmaceutical ingredients. Inadequate assessment at this early stage can have downstream consequences, often resulting in formulation instability, suboptimal performance, or late-stage development failure associated with significant time and resource loss. To address these challenges, artificial intelligence-based methodologies are increasingly being incorporated into preformulation workflows to improve predictive reliability and minimize reliance on extensive experimental screening.

Among the various preformulation applications, the use of AI for solubility prediction

has demonstrated particularly high impact. Insufficient aqueous solubility remains one of the primary contributors to poor oral absorption and unsuccessful formulation development. Machine learning models leveraging molecular descriptors—including lipophilicity, ionization behavior, hydrogen-bonding potential, and molecular size—have shown strong capability in forecasting solubility profiles across diverse solvent systems and pH environments. Early access to such predictive insights allows formulation scientists to anticipate solubility-related limitations and strategically select appropriate interventions, such as salt selection, amorphous solid dispersions, or nanoscale delivery platforms, thereby improving development efficiency and formulation success.

Table.2. AI Applications in Preformulation Studies

Preformulation Parameter	AI Technique Used	Input Variables	Predicted Output	Advantage
Solubility	ANN, RF	Molecular descriptors, pKa, logP	Solubility class	Reduces experimental screening
Stability	SVM	Temperature, humidity, excipient data	Shelf-life	Early degradation prediction
Polymorphism	Deep Learning	XRPD/DSC data	Stable polymorph	Prevents late-stage failures
Hygroscopicity	ANN	Environmental parameters	Moisture uptake	Packaging optimization

Beyond solubility assessment, artificial intelligence has been increasingly applied to the

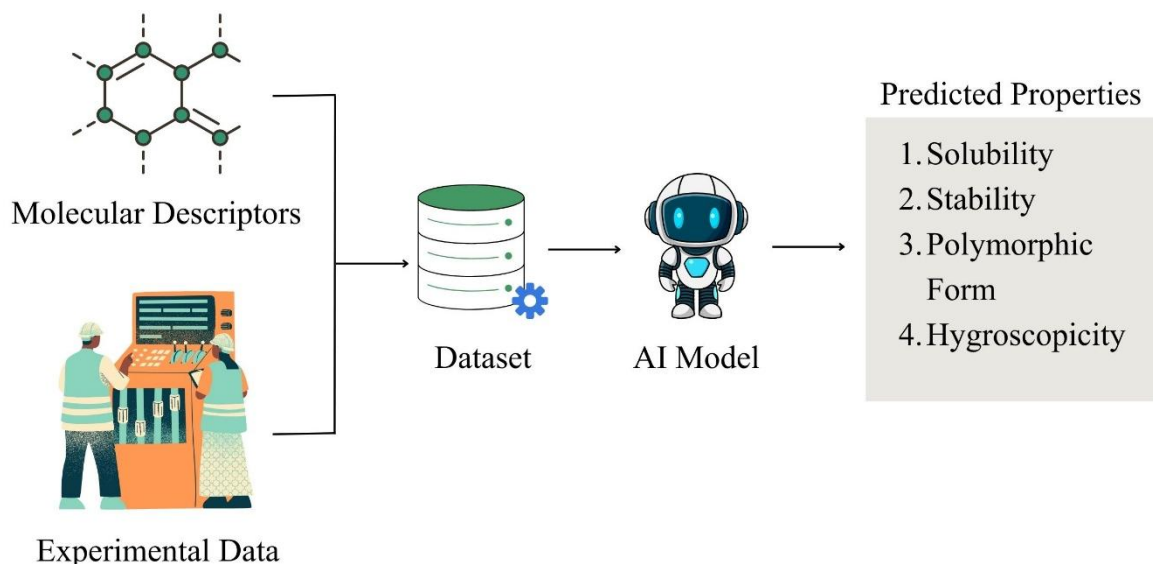
evaluation of both chemical and physical stability during preformulation development. By integrating

datasets that capture the influence of environmental stress factors—such as temperature fluctuations, humidity levels, light exposure, and interactions with formulation excipients—machine learning models can identify degradation trends and stability-limiting conditions. These data-driven insights enable early prediction of product shelf life, support the rational selection of stabilizing excipients, and facilitate the identification of potential incompatibilities before extensive experimental testing is undertaken.

In addition to stability prediction, AI-based approaches have demonstrated significant utility in

modeling solid-state attributes that directly influence manufacturability and product performance. Parameters such as polymorphic form, degree of crystallinity, and moisture sensitivity play a decisive role in the processing behavior and long-term stability of solid dosage forms. Machine learning models trained on thermal, spectroscopic, and structural data can assist in anticipating these solid-state characteristics, thereby reducing the risk of unexpected phase transformations and stability issues during scale-up and storage.

Fig.3. AI-based preformulation workflow illustrating data acquisition, model training, validation, and prediction of physicochemical properties.



AI-DRIVEN PHARMACEUTICAL FORMULATION DESIGN

Table.3. Traditional DoE v/s AI-based Formulation Design

Parameter	Traditional DoE	AI-based Approach
Experimental Runs	High	Low
Handling Non-linearity	Limited	Excellent
Adaptability	Static	Dynamic
Prediction Accuracy	Moderate	High
Time Requirement	Long	Short

Pharmaceutical formulation design represents a complex, multi-criteria optimization challenge in which multiple, often competing objectives must be addressed simultaneously. These include ensuring physicochemical and

microbiological stability, achieving adequate bioavailability, maintaining manufacturability at scale, enhancing patient acceptability, and meeting regulatory expectations. As formulation complexity increases, particularly with the inclusion of multiple

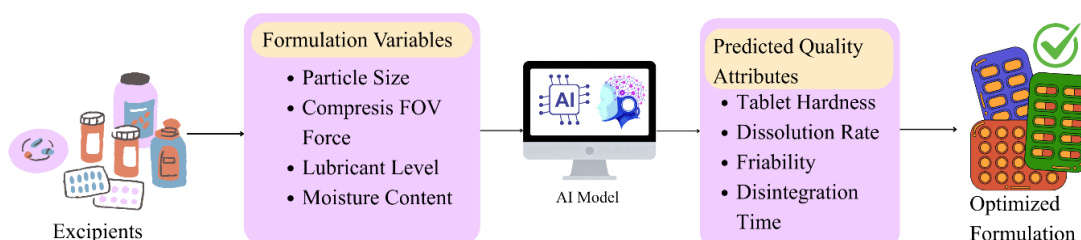
excipients and processing variables, conventional experimental strategies become progressively inefficient and resource-intensive. AI-driven formulation design overcomes these limitations by capturing and modeling nonlinear, multidimensional relationships between formulation variables and product performance attributes that are difficult to resolve using traditional approaches.

Machine learning techniques enable a more systematic and knowledge-based approach to excipient selection by assessing functional roles, compatibility profiles, and concentration-dependent effects within a formulation matrix. Through analysis of historical formulation datasets, AI models can detect synergistic and antagonistic interactions between active pharmaceutical ingredients and excipients, thereby guiding the identification of optimal composition windows. This data-driven narrowing of formulation space substantially reduces the need for exhaustive

experimental screening. In contrast to classical Design of Experiments methodologies, AI-based frameworks efficiently manage high-dimensional variable spaces and can continuously refine predictions as additional data are generated.

In the context of solid dosage forms, AI models have demonstrated strong capability in predicting critical quality attributes such as tablet hardness, friability, disintegration behavior, and dissolution performance using input variables including compression pressure, particle size distribution, lubricant levels, and moisture content. Similarly, for liquid and semi-solid dosage forms, machine learning approaches support the prediction of key performance parameters such as viscosity, emulsion stability, phase separation tendencies, and drug release kinetics. Collectively, these predictive capabilities contribute to shorter development timelines, enhanced formulation robustness, and improved batch-to-batch reproducibility.

Fig.4. AI-Guided Formulation Optimisation Workflow



AI IN ADVANCED DRUG DELIVERY SYSTEMS

Advanced drug delivery platforms—including nanoparticles, liposomes, polymeric micelles, and stimuli-responsive carrier systems—introduce a high level of formulation complexity arising from the interplay of numerous formulation and processing variables. In such systems, even minor adjustments in formulation composition or

manufacturing conditions can lead to substantial changes in critical attributes, such as particle size distribution, drug encapsulation efficiency, surface characteristics, and release profiles. Managing this degree of variability through conventional experimental approaches is both time-consuming and inefficient, prompting increasing reliance on AI-driven modelling strategies to guide formulation development.

Table.4. AI Applications in Advanced Drug Delivery Systems

DDS Type	AI Application	Predicted Parameter	Outcome
Nanoparticles	ANN, RF	Particle size, EE	Optimized delivery
Liposomes	ML models	Stability, release	Improved shelf-life
Hydrogels	Deep Learning	Swelling behavior	Controlled release
Micelles	ANN	CMC, drug loading	Enhanced solubility

Machine learning models trained on comprehensive datasets derived from nanoscale formulation studies have demonstrated strong predictive capability for key performance parameters, including particle size, polydispersity index, surface charge, drug loading efficiency, and release kinetics. By enabling accurate prediction of these attributes, AI-based tools significantly reduce experimental trial requirements and accelerate the identification of optimal formulation conditions. In addition, AI methodologies facilitate the rational

engineering of targeted and stimuli-responsive delivery systems by modelling carrier behaviour in response to physiological cues such as pH variations, enzymatic activity, temperature changes, or redox gradients. These data-driven design strategies support enhanced site-specific drug delivery, improved therapeutic outcomes, and reduced off-target toxicity, thereby strengthening the translational potential of advanced drug delivery technologies.

Fig.5. AI-Assisted Nanoparticle Design

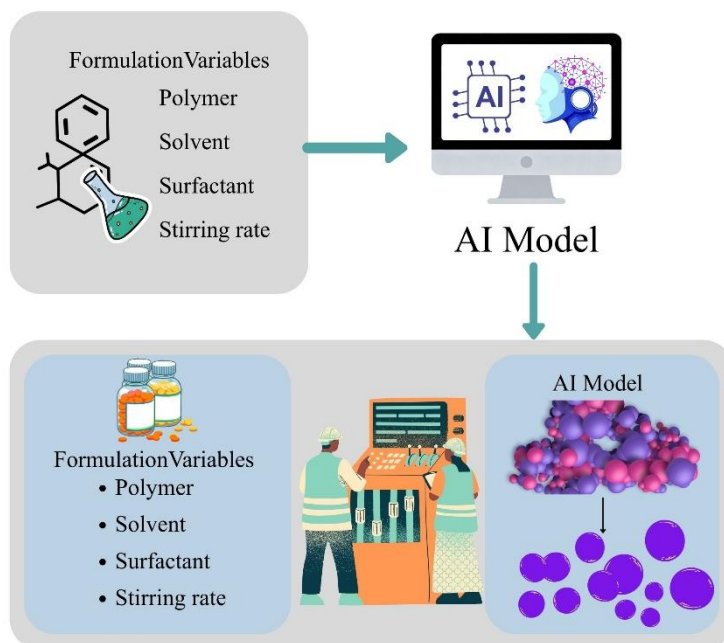
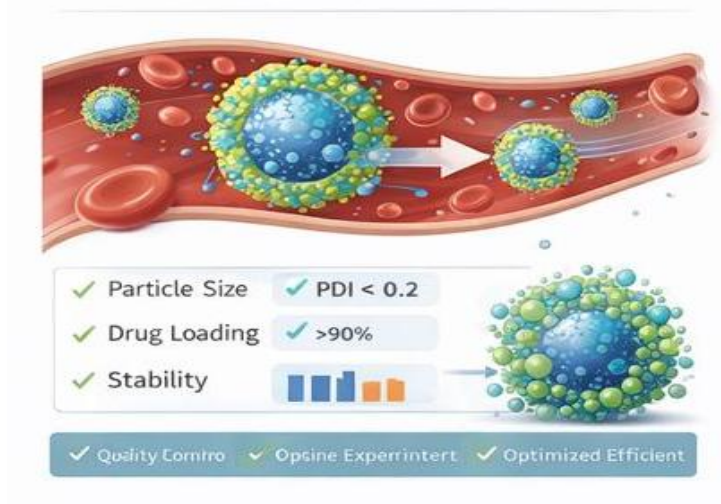


Fig.6. AI in Stimuli-Responsive Drug Delivery

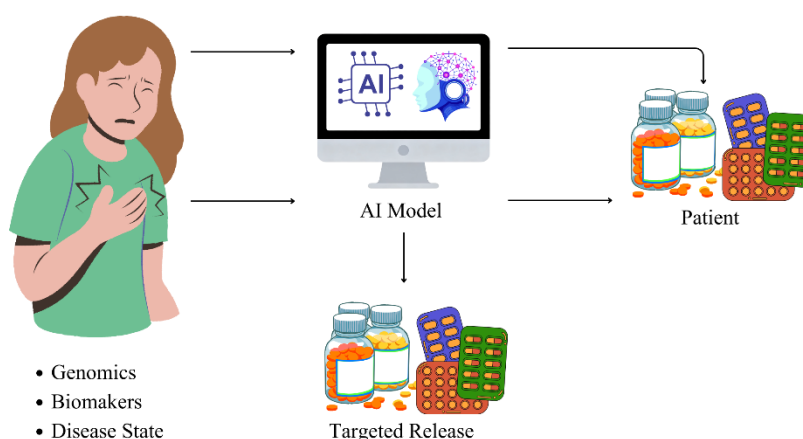


PERSONALIZED DRUG DELIVERY AND PRECISION MEDICINE

Traditional pharmaceutical dosage forms are typically developed with the assumption of a representative or “average” patient population, despite extensive evidence demonstrating significant variability among individuals in terms of genetic makeup, physiological characteristics, disease state,

and therapeutic response. This generalized approach frequently results in reduced treatment effectiveness or an increased risk of adverse drug reactions in specific patient subgroups. AI-enabled personalized drug delivery strategies seek to overcome these limitations by incorporating patient-specific information into formulation design and dosing optimization.

Fig.7. AI-Driven Personalised Drug Delivery Framework



Machine learning frameworks are capable of integrating diverse data streams, including genomic profiles, disease-associated biomarkers, pharmacokinetic and pharmacodynamic parameters, and real-world clinical data, to support individualised drug delivery solutions. Such models

facilitate tailored dose selection, dynamic control of drug release behaviour, and the development of delivery systems optimised for individual patient needs. The clinical relevance of personalised drug delivery is particularly pronounced in therapeutic areas such as oncology, neurological disorders, and

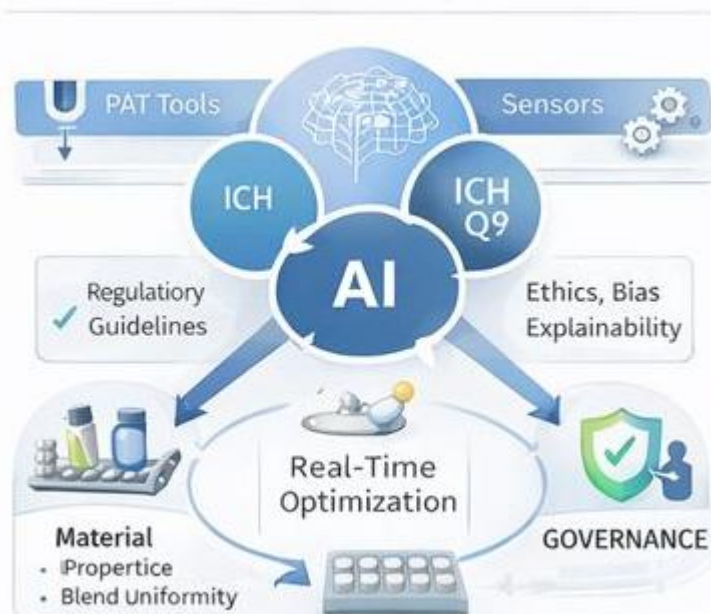
chronic disease management, where narrow therapeutic indices and substantial interpatient variability necessitate highly precise and adaptive treatment strategies.

AI IN PHARMACEUTICAL MANUFACTURING AND QUALITY CONTROL

Pharmaceutical manufacturing comprises a series of interrelated unit operations in which minor fluctuations in processing conditions can propagate into substantial variations in final product quality. Gaining comprehensive process understanding and

maintaining consistent control across these operations remains a major challenge in industrial pharmaceuticals. In this context, artificial intelligence has gained increasing prominence as an enabling technology for process optimisation, predictive control, and data-driven decision support. Machine learning models are capable of extracting actionable insights from large volumes of manufacturing data generated during operations such as granulation, blending, drying, coating, and tablet compression, allowing prediction of critical process parameters and associated quality outcomes.

Fig.8. AI-Integrated Pharmaceutical Manufacturing Line



Within a Quality by Design (QbD) framework, AI-based tools contribute to more robust design space development and facilitate continuous, real-time process monitoring through integration with Process Analytical Technology (PAT) systems. In addition, deep-learning-based machine vision platforms have demonstrated superior performance in the detection of visual defects in solid dosage forms and

packaging components compared with conventional manual inspection methods. Predictive quality control strategies powered by AI enable the early identification of process deviations, thereby minimising batch rejection, reducing waste, and enhancing overall manufacturing efficiency and product reliability.

Table 5. AI Applications in Pharmaceutical Manufacturing

Manufacturing Stage	AI Role	Monitored Parameters	Benefit
Granulation	Process optimization	Moisture, torque	Batch consistency
Compression	Defect detection	Hardness, weight	Reduced rejection
Coating	Thickness prediction	Spray rate	Uniform coating
Inspection	Vision-based AI	Surface defects	Automated QC

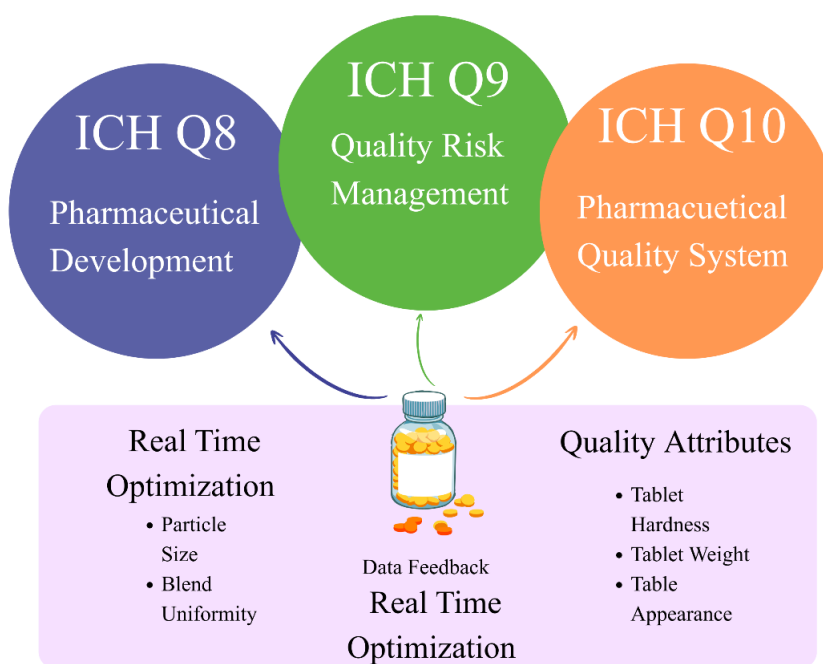
REGULATORY CONSIDERATIONS AND CHALLENGES

Although artificial intelligence offers substantial technical benefits, its widespread adoption within regulated pharmaceutical environments continues to face significant regulatory hurdles. Regulatory authorities place strong emphasis on transparency, reproducibility, and scientifically defensible decision-making throughout formulation development and manufacturing processes. A major concern arises from the use of complex AI models—particularly deep learning architectures—that often function as opaque systems, making it challenging to clearly interpret the rationale behind their predictions or recommendations.

Established regulatory guidelines, including ICH Q8 (Pharmaceutical Development),

ICH Q9 (Quality Risk Management), and ICH Q10 (Pharmaceutical Quality System), prioritise thorough process understanding and risk-based control strategies. Aligning AI-driven methodologies with these frameworks requires careful integration into existing quality systems. To achieve regulatory acceptance, AI models must undergo rigorous validation, be supported by comprehensive documentation, and demonstrate consistent performance across defined operating conditions. In this context, explainable artificial intelligence has gained increasing importance, as it provides interpretable insights into model behaviour and helps bridge the gap between advanced computational approaches and regulatory expectations.

Fig.9. Alignment of AI with ICH Q8–Q10 Framework



LIMITATIONS AND ETHICAL CONSIDERATIONS

Despite the significant advantages offered by artificial intelligence, its application in pharmaceutical sciences is accompanied by important technical and ethical limitations that must be carefully considered. The performance of machine learning models is intrinsically linked to the quality and representativeness of the data used

for training; datasets that are biased, incomplete, or inconsistently generated can compromise model reliability and lead to misleading predictions. In addition, overfitting remains a persistent challenge, particularly when models are developed using limited or poorly curated datasets, reducing their robustness and predictive validity. Another critical limitation relates to model transferability, as algorithms optimised for specific formulations or

delivery platforms may exhibit reduced performance when applied to novel chemical entities or alternative delivery systems.

Beyond technical constraints, the deployment of AI raises ethical concerns that are particularly relevant in healthcare-related applications. The use of patient-specific data for personalised drug delivery necessitates strict safeguards to protect data privacy and ensure compliance with ethical and legal standards. Furthermore, issues of algorithmic bias, accountability, and responsibility must be addressed, as erroneous AI-driven recommendations can have serious clinical implications. For these reasons, AI systems should be positioned as advanced decision-support tools that augment human expertise, rather than as autonomous decision-makers, ensuring that scientific judgment and regulatory responsibility remain under human control.

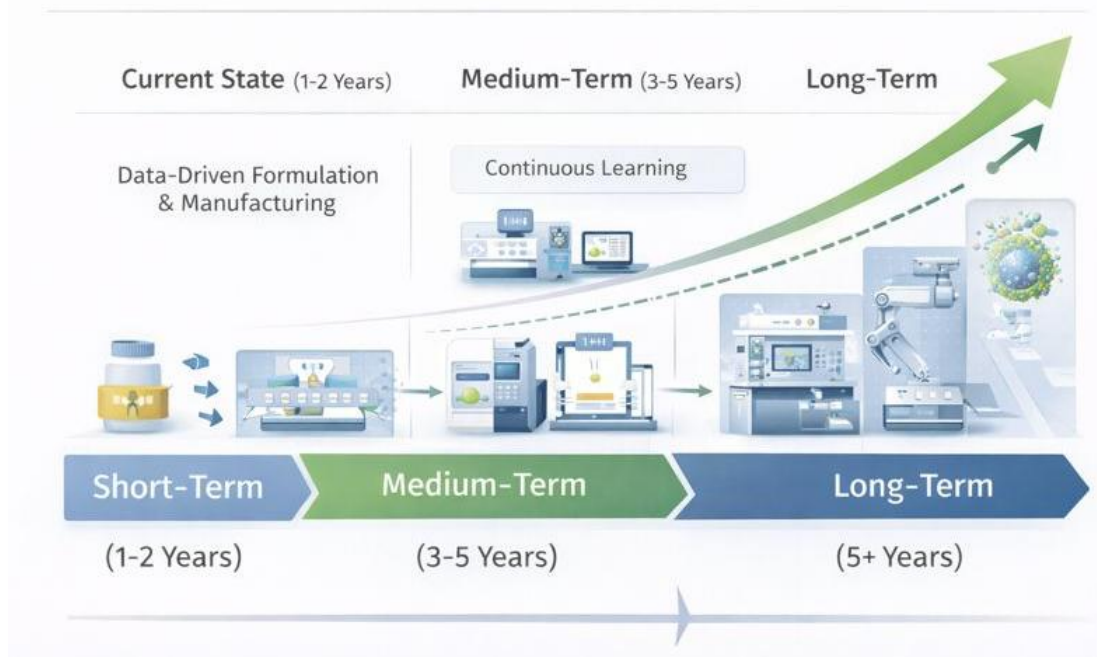
FUTURE PERSPECTIVES

The continued evolution of artificial intelligence in pharmaceutical formulation and drug delivery is closely linked to its convergence with emerging enabling technologies, including digital twin platforms, autonomous laboratory systems, and

three-dimensional pharmaceutical printing. The integration of AI with these technologies is expected to support real-time simulation, adaptive formulation design, and on-demand manufacturing, thereby transforming conventional development workflows. In parallel, the advancement of explainable artificial intelligence will be critical for enhancing model transparency, fostering scientific confidence, and facilitating regulatory acceptance by providing clear, interpretable insights into algorithmic decision-making.

As pharmaceutical data ecosystems become more standardized, interoperable, and comprehensive, and as collaboration between pharmaceutical scientists, data scientists, and regulatory experts strengthens, AI-based methodologies are likely to become increasingly embedded throughout the pharmaceutical product lifecycle. From early-stage preformulation assessment and formulation optimization to manufacturing control and post-marketing performance monitoring, AI is poised to transition from a supportive analytical tool to a foundational component of next-generation pharmaceutical development and drug delivery strategies.

Fig.11. Roadmap for AI Integration in Pharmaceutical Sciences



II. CONCLUSION

Artificial intelligence and machine learning are redefining pharmaceutical formulation and drug

delivery by shifting development strategies away from predominantly empirical experimentation toward data-driven, predictive, and patient-focused

approaches. Through advanced data analysis, modeling of complex formulation systems, and informed optimization, these technologies offer the potential to shorten development timelines while enhancing product performance and clinical effectiveness. Despite persistent challenges related to data integrity, model interpretability, and regulatory alignment, the careful and scientifically rigorous integration of AI within pharmaceutical research and development frameworks is expected to establish these tools as essential components of future formulation science and drug delivery innovation.

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