Role of Artificial Intelligence in Novel Drug Delivery Systems

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Abstract - Artificial intelligence (AI) has emerged as a transformative force in pharmaceutical science, fundamentally altering the methods of drug discovery, formulation, and delivery to patients. The integration of AI with novel drug delivery systems (NDDS) signifies a groundbreaking advancement in contemporary medicine, presenting unparalleled prospects for addressing enduring obstacles in pharmacotherapy, including inadequate bioavailability, nonspecific toxicity, and patient noncompliance. This comprehensive review provides an in-depth examination of AI fundamentals, including machine learning, deep learning, and neural network architectures, followed by a systematic analysis of AI applications across the pharmaceutical industry. Special emphasis is placed on the transformative role of AI in the design, optimization, and clinical translation of novel drug delivery systems, including nanoparticle-based carriers, liposomes, polymeric micelles, hydrogels, transdermal systems, and stimuli-responsive platforms. This review also addresses the integration of AI with bioinformatics and systems biology for personalized medicine, discusses the regulatory landscape for AI-driven pharmaceutical products, and identifies key challenges and future directions. Evidence from over 200 published studies demonstrates that AI-powered approaches consistently reduce formulation development timelines by 40-60%, improve targeting efficiency, and enable real-time quality monitoring. We conclude that AI is not merely a computational tool but a paradigm-shifting technology that will define the future of drug delivery.

Keywords- Artificial Intelligence, Machine Learning, Deep Learning, Novel Drug Delivery Systems, Drug Design, Pharmaceutical Technology

I.INTRODUCTION

Artificial intelligence is a department of computer generation. Artificial intelligence (AI) focuses only on building machines that can perform tasks that would otherwise require human expertise and input. The rapidly evolving field of artificial intelligence (AI) is transforming several industries, including the healthcare sector. In recent years, artificial intelligence (AI) has shown promising results in the context of drug delivery systems. John McCarthy coined the word "A.I." for the number one time in 1956. AI may be used primarily to create new prescription drugs. Artificial intelligence plays a crucial role in method development. Many types of synthetic networks, such as deep or neural networks, have been employed in drug control. Targeting the proteins used in drug distribution is a crucial strategy to enhance and provide a higher success rate for drug management.[1]

Fundamentals of Artificial Intelligence

1. Core Concepts and Definitions:

Artificial intelligence is a broad term for any computer system that can perform tasks that usually require human intelligence, such as understanding language, learning, cognitive thinking, and perceiving things. [2] [3] This field is supported by several significant distinctions.

Narrow AI (or weak AI) refers to systems designed to execute certain well-defined tasks. All existing AI systems, including those used in pharmaceutical research, are narrow AI. Examples include image recognition systems, language models, and predictive-analytics platforms.

General AI (Strong AI) refers to hypothetical systems that can achieve human-level intelligence in any domain. However, no such system currently exists.

Machine learning (ML) is a subset of artificial intelligence in which systems learn patterns from data without explicit programming. ML includes supervised, unsupervised, semi-supervised, and reinforcement learning paradigms.

Deep Learning (DL): A branch of machine learning that models hierarchical data representations using multi-layered artificial neural networks. Most recent advances in AI have been driven by deep learning [4].

2. Machine Learning Algorithms:

Machine learning algorithms are broadly categorized based on the type of feedback they receive during training. Table 1 summarizes the major ML categories and their pharmaceutical significance. [5] [6]

Supervised learning algorithms are the most commonly used in pharmaceutical research. Support Vector Machines (SVMs) are widely used for molecular classification and QSAR development. Random forests and gradient boosting approaches (XGBoost and LightGBM) provide outstanding predictive performance with built-in feature importance ranking, which is useful for detecting critical formulation factors. [5] [6]

Artificial neural networks, ranging from simple multilayer perceptrons to complicated deep architectures, can approximate any function, making them useful for solving nonlinear, high-dimensional problems that arise in drug formulation and delivery. [5][7]

Table 01: Major Machine Learning Categories and Pharmaceutical Applications

ML Category	Learning Paradigm	Key Algorithms	Pharmaceutical Application
Supervised Learning	Labelled data	Linear Regression, SVM, Random Forest, Boost, Neural Networks	QSAR modelling, toxicity prediction, bioavailability estimation
Unsupervised Learning	Unlabelled data	K-Means, DBSCAN, PCA, Autoencoders, GANs	Drug clustering, biomarker discovery, formulation space exploration
Semi-supervised Learning	Partially labelled	Label Propagation, Semi-supervised GANs	Drug repurposing with sparse data
Reinforcement Learning	Reward signals	Q- Learning, PPO, DDPG, Actor-Critic	Drug dosage optimization, treatment policy learning
Transfer Learning	Pre-trained models	BERT, GPT, ResNet fine-tuning	Drug- protein interaction prediction, literature mining
Federated Learning	Distributed data	FedAvg, FedProx	Multi-institutional clinical data analysis without data sharing

3. Deep Learning and Neural networks:

A class of machine learning techniques known as "deep learning" uses numerous layers of information processing stages in hierarchical structures for pattern recognition and unsupervised feature learning. It lies at the intersection of signal processing, neural networks, graphical modeling, optimization, and pattern recognition. The current popularity of deep learning can be attributed to two key factors: the dramatically reduced cost of computer gear and the greatly enhanced processing power of chips (such as GPU units). Deep learning has proven successful since 2006 in various applications, including computer vision, phonetic recognition, voice search, spontaneous speech recognition, speech and image feature coding, semantic utterance classification, handwriting recognition, audio processing, information retrieval, and robotics. [7][3]

Deep learning has traditionally relied on recurrent neural networks (RNNs) and convolutional neural networks (CNNs) for sequence modelling tasks such as language translation. Although RNNs are powerful, they suffer from sequential computation constraints that slow training and limit parallelization, whereas CNNs improve parallelism but struggle with long-range dependencies. The paper Attention Is All You Need introduced the Transformer, a neural network architecture that eliminates recurrence and convolution entirely, relying solely on attention mechanisms. At its core, the transformer uses self-attention and multi-head attention to capture

relationships between words regardless of their distance in a sequence, supported by feed-forward layers and positional encodings to preserve order. This design allows faster training, greater parallelization, and superior performance compared with previous models. The Transformer achieved state-of-the-art results in machine translation, surpassing RNN and CNN-based systems while requiring significantly lower computational costs. By reducing the path lengths between dependencies and enabling constant-time operations, self-attention has proven to be a more efficient and scalable foundation for deep learning in natural language processing. [8]

4. Natural Language Processing in Pharma:A Review

Natural language processing (NLP) enables computers to understand, interpret, and generate human languages. In pharmaceutical sciences, NLP has become an essential tool for mining exponentially growing biomedical literature [9]. Transformer-based models, such as BioBERT and PubMedBERT, pretrained on biomedical corpora, have set new benchmarks for biomedical NLP tasks and are increasingly used to automate knowledge graph construction for drug discovery and NDDS development [9] [10].

5. AI Infrastructure and Computing

Open-source software frameworks, such as TensorFlow, PyTorch, Keras, and Scikit-learn, alongside domain-specific cheminformatics toolkits (RDKit, Open Babel, and DeepChem), provide a computational ecosystem for AI-driven pharmaceutical research. The availability of curated databases such as ChEMBL, PubChem, DrugBank, the Protein Data Bank (PDB), and clinical trial registries provides the data foundation essential for model development and validation [11]

AI in Pharmaceutical Sciences: An Overview

1. Drug Discovery and Target Identification

Traditional drug discovery is costly and time-consuming, with only approximately 10% of clinical candidates achieving regulatory approval. AI and ML provide transformative solutions to these challenges by enhancing disease modeling and target identification. By leveraging diverse datasets, AI models can predict drug target properties, establish biological relationships, and streamline the drug discovery process. Techniques such as deep learning and graph neural networks are utilized in various phases, including target identification and lead optimization of drug candidates. The integration of multi-omics data with AI strategies has shown significant promise in the experimental validation of AI-identified targets. AI methods expedite molecular docking, drug repurposing, and high-throughput virtual screening, outpacing traditional approaches in terms of accuracy and efficiency. Key achievements showcase AI's potential of AI, such as DeepMind's AlphaFold for protein structure prediction. AI is also pivotal in drug repurposing and improving clinical trial modeling, leading to faster therapeutic development for diseases, including COVID-19. However, challenges in data accessibility, interpretability, and regulatory compliance persist, highlighting the necessity for standardized datasets and robust ethical frameworks to facilitate the clinical application of AI discoveries.[11][3]

2. Computer-Aided Drug Design

Computer-aided drug design (CADD) encompasses both structure- and ligand-based approaches. Structure-based methods use the three-dimensional structure of a biological macromolecule to guide the design of complementary small molecules, with AI-enhanced scoring functions outperforming classical approaches. Generative models, such as variational autoencoders, generative adversarial networks, and transformer-based molecular generators, can propose novel chemical entities with desired multi-property profiles. [12]

3. High-Throughput Screening

Active learning frameworks, in which AI models iteratively suggest the most informative compounds to screen next, can reduce the number of experiments required to identify active hits by several orders of magnitude. Deep neural network-based virtual screening models trained on HTS data have demonstrated enrichment factors of 10-100-fold compared to random screening. [4]

4. Pharmacokinetics and Pharmacodynamics Modeling

Artificial intelligence models have been developed to predict absorption, distribution, metabolism, excretion, and toxicity (ADMET) based solely on chemical structure. Neural ordinary differential equations (Neural ODEs) offer a versatile framework for modeling drug kinetics by combining mechanistic structures with data-driven parameter estimation. [13]

5. Clinical Trials Optimization

NLP applied to electronic health records enables the rapid identification of eligible patients for trial enrolment, reducing recruitment timelines by 30-50% in reported case studies. [9] Federated learning approaches allow multi-institutional AI model training without centralizing sensitive patient data. [9][14]

6. Pharmacovigilance and Drug Safety

AI systems mining social media, electronic health records, scientific literature, and spontaneous report databases can detect safety signals with greater sensitivity and speed than traditional methods. Deep learning models trained on pharmacovigilance databases can predict the ADR profiles of new drugs based on their structural similarity to drugs with known safety liabilities. [10]

7. Regulatory Affairs

Regulatory agencies, including the FDA and EMA, have released guidance documents acknowledging AI's transformative potential of AI. In manufacturing, AI-enabled real-time release testing under the Process Analytical Technology (PAT) framework replaces time-consuming offline quality control with in-line measurements and predictive models. [15]

Table 02: Representative AI Applications in Pharmaceutical Sciences

Application Area	AI Approach	Key Achievement
Protein Structure Prediction	Deep Learning (AlphaFold2)	Near-experimental accuracy for >200M proteins
Virtual Screening	GNN, Transformer	10-100x enrichment vs random
ADMET Prediction	Multi-task DNN	>90% accuracy for key endpoints
Molecule Generation	VAE, GAN, Transformer	Novel, synthesizable candidates
Clinical Trial Recruitment	NLP on EHR	30-50% reduction in recruitment time
Pharmacovigilance	NLP, social media mining	Earlier signal detection
Drug Repurposing	Knowledge graph, GNN	COVID-19candidate identification

II. NOVEL DRUG DELIVERY SYSTEMS: CONCEPTUAL FRAMEWORK

Novel drug delivery systems represent an extraordinarily diverse class of pharmaceutical technologies developed to overcome these limitations [16][17]. Table 3 provides a comprehensive classification.

Table 03: Classification of Novel Drug Delivery Systems

Category	Subtypes	Size Range	Primary Applications
Lipid-based	Liposomes, SLNs, NLCs, LNPs, Nanoemulsions	20-500 nm	Cancer, gene therapy, vaccine delivery
Polymeric	PLGA NPs, Polymeric micelles, Dendrimers	10-500 nm	Sustained release, brain targeting, cancer
Inorganic Nanoparticles	Gold NPs, Iron oxide NPs, Silica NPs, Carbon nanotubes	1-200 nm	Theranostics, imaging, PTT
Protein/Peptide-based	Albumin NPs, Gelatin NPs, Ferritin cages	10-200 nm	Anticancer, protein delivery
Hydrogels	Thermoresponsive, pH-responsive, Injectable	Macro-nano	Wound healing, local drug release
Transdermal	Patches, Microneedle arrays, Transfersomes, Ethosomes	1 nm- 1 cm	Systemic & local skin delivery
Stimuli-Responsive	pH, thermo, redox, photo, magnetic-responsive	10-500 nm	Cancer, inflammation, diabetes
Nucleic Acid-based	Liposomal siRNA, LNP-mRNA, Polyplexes, Exosomes	50-300 nm	Gene therapy, vaccines, cancer
Aptamer/Antibody Conjugates	Immunoliposomes, ADCs, Aptamer-NPs	10-200 nm	Active tumor targeting

1. Nanoparticle- Based Systems

Nanoparticles are defined as particles within the size range of 1–1000 nm and are extensively utilized in modern drug delivery systems. They can be engineered from a wide variety of materials to encapsulate, adsorb and conjugate therapeutic agents. These systems offer significant advantages, including enhanced drug stability, improved bioavailability, and targeted delivery.[18]

The in vivo performance of nanoparticles is governed by several critical parameters, such as particle size and size distribution. Additionally, surface charge (zeta potential) plays a key role in stability and cellular interactions. Surface chemistry further influences biological compatibility and targeting efficiency of nanocarriers.

Other important factors include drug loading efficiency, encapsulation efficiency, and drug release kinetics, which determine the therapeutic effectiveness. These parameters are highly interdependent and strongly influenced by formulation variables. Consequently, nanoparticle formulation involves a complex and high-dimensional design space, making optimization challenging. Conventional approaches like one-variable-at-a-time (OVAT) are insufficient to address this complexity, necessitating the use of advanced optimization strategies.[18] [19]

2. Liposomal and Vesicular Systems

Liposomal and vesicular systems have emerged as highly versatile platforms in advanced drug delivery because of their ability to encapsulate both hydrophilic and hydrophobic therapeutic agents. Liposomes, composed of phospholipid bilayers, closely mimic biological membranes, enhancing their biocompatibility and reducing toxicity. Their structural flexibility allows for surface modification, such as PEGylation, which improves circulation time and minimizes rapid clearance by the reticuloendothelial system (RES). The success of PEGylated liposomal formulations, such as doxorubicin, marked a significant milestone in nanomedicine, demonstrating improved therapeutic efficacy with reduced side effects. [20]

3. Polymeric Systems

Polymeric systems are a cornerstone of nanotechnology-based drug delivery, offering precise control over drug release and enhanced stability of therapeutic agents. Among these, poly (lactic-co-glycolic acid) (PLGA) is the most extensively investigated polymer owing to its excellent biocompatibility and biodegradability. PLGA degrades into lactic and glycolic acids, which are naturally metabolized via the Krebs cycle, ensuring minimal toxicity. One of the major advantages of PLGA-based nanoparticles is their ability to provide controlled and sustained drug release profiles. Surface modification of PLGA systems further allows targeted delivery to specific tissues and cells. Owing to these advantages and its strong regulatory approval history, PLGA continues to be a preferred material in the design of advanced drug delivery systems.[21]

4. Hydrogels and Smart Materials

Hydrogels and smart materials represent an advanced class of drug delivery systems characterized by unique three-dimensional crosslinked polymeric networks. These systems possess a remarkable ability to absorb and retain large amounts of water without dissolution, thereby maintaining structural integrity and biocompatibility. Owing to their high watercontent and soft consistency, hydrogels closely resemble natural biological tissues, making them particularly suitable for biomedical applications.

Stimuli-responsive or “smart” hydrogels exhibit dynamic behavior by undergoing reversible physicochemical changes in response to external or internal triggers, such as pH, temperature, light, enzymes, or ionic strength. These responses can lead to controlled swelling, deswelling, sol–gel transitions, and modulation of drug diffusion rates. These properties enable precise spatial and temporal control over drug release, enhancing therapeutic efficacy while minimizing side effects. Additionally, smart hydrogels can be engineered for site-specific delivery, particularly in targeted cancer therapies and tissue engineering. Their tunable mechanical strength, biodegradability, and responsiveness make them promising candidates for next-generation intelligent drug delivery systems. [22]

5. Transdermal Delivery Systems

Transdermal drug delivery systems have gained significant attention as effective alternatives to conventional routes of administration. The skin provides a large and accessible surface area, making it an attractive route for systemic drug delivery. One of the major advantages of transdermal delivery is the avoidance of first-pass hepatic metabolism, which enhances the bioavailability of the drug. Additionally, this route is noninvasive, improves patient compliance, and allows sustained and controlled drug release over extended periods.

However, the primary challenge in transdermal delivery is the highly protective nature of the stratum corneum, which acts as a formidable barrier to drug permeation into the skin. To overcome this limitation, several advanced strategies have been developed. Microneedle arrays create microscopic channels in the skin, enabling painless and efficient drug transport. Chemical penetration enhancers temporarily disrupt the lipid structure of the stratum corneum to increase its permeability. Furthermore, nanocarrier-based systems, such as transfersomes and ethosomes, enhance drug penetration by improving skin diffusion and targeting deeper layers. These innovations have significantly expanded the scope of transdermal systems, making them promising platforms for local and systemic drug delivery. [23]

III.ROLE OF AI IN DESIGN AND OPTIMIZATION OF NOVEL DRUG DELIVERY SYSTEMS

1.AI-Driven Formulation Design

The formulation of novel drug delivery systems is an inherently complex multi-objective optimization problem [24]. Bayesian optimization frameworks treat the formulation problem as a global optimization under uncertainty, using Gaussian process regression to maintain a probabilistic model of the response surface and selecting each new experiment at the point of maximum expected improvement [25]. Reported applications in nanoparticle formulation have achieved optimized formulations in 10-30 experiments compared to 50-200 for conventional factorial designs.[26]

Machine learning models trained on curated formulation databases enable the predictive formulation design of new drug molecules. ANN-based models for liposome and lipid nanoparticle formulations have demonstrated predictive accuracy exceeding $R2 = 0.90$ for key quality attributes. These models allow formulation scientists to computationally screen thousands of formulation compositions before committing to laboratory syntheses. [24] [25]

2.AI for Targeted and Active Drug Delivery

The selection and optimization of targeting ligands for NDDS represent a multidimensional problem involving receptor specificity, binding affinity, stability, immunogenicity, and manufacturing complexity, all of which can be addressed using AI tools. AI-driven aptamer discovery allows the prediction of high-affinity aptamer sequences without exhaustive experimental SELEX cycles, dramatically accelerating the discovery of targeting ligands for cancer cells, tumor vasculature, and blood-brain barrier (BBB) transporters. [27]

3.Stimuli-Responsive Drug Delivery Systems

Molecular dynamics simulations augmented by machine learning force fields enable the rapid computational evaluation of stimulus-responsive polymer conformational changes and drug-release kinetics. Reinforcement learning algorithms have been applied to optimize the architecture of multilayered, multi-stimulus-responsive coatings on nanoparticles, with AI agents learning release policies that maximize therapeutic index through simulated tumor microenvironment models.[28]

4.AI in Oral Drug Delivery Optimization

Physiologically based pharmacokinetic (PBPK) models for oral drug absorption, which mechanistically simulate gastrointestinal physiology, are increasingly coupled with machine learning components to address parameter uncertainty. ANN-based optimization of SEDDS formulations has identified optimal oil-surfactant-cosurfactant combinations for solubilization of BCS Class II drugs.[29]

5.AI in Pulmonary Drug Delivery

Computational fluid dynamics (CFD) simulations of airway particle deposition, augmented by machine learning surrogate models, enable the rational design of inhaler devices and particle engineering strategies to maximize regional lung deposition. Neural network models for prediction of mucus diffusion coefficients from nanoparticle surface properties are enabling rational design of mucus-penetrating particles for improved lung targeting.[30]

6.AI in Ocular Drug Delivery

AI has been applied to optimize nanoparticle formulations for ocular delivery and predict corneal permeability from molecular descriptors using random forest models trained on ex vivo bovine cornea datasets. AI models for personalized intravitreal dosing regimens in age-related macular degeneration, trained on longitudinal OCT and visual acuity data, are being developed to predict when individual patients require retreatment.[31]

Table 04: Summary of AI Applications in Major NDDS Categories

NDDS Type TNDDS n	AI Approach Used	Optimized Parameters	Outcome
PLGA Nanoparticles	ANN, Random Forest	Size, EE, Release Rate	R2>0.90, 5x less experiments
Liposomes/LNPs	Bayesian Optimization	Lipid ratio, mRNA-LNP efficacy	Enhanced transfection efficiency
Polymeric Micelles	Genetic Algorithm + ANN	CMC, Drug loading	Improved thermodynamic stability
Hydrogels	Support Vector Regression	Gelation temp, drug release kinetics	Precise thermoresponsive tuning
SEDDS (Oral)	D-Optimal DoE + ANN	Emulsification time, globule size	BCS II bioavailability enhanced
Transdermal Patches	RF, GBM models	Skin permeability, flux prediction	Candidate screening enabled
Stimuli-Responsive NPs	RL, MD + ML force fields	Release trigger, kinetics	pH-selective tumor release
Inhalation Formulations	CFD + ML Surrogate	Fine particle fraction, deposition	Patient-specific dosing
Ocular NPs	Random Forest	Corneal permeability from structure	Predictive screening tool

IV.AI IN MANUFACTURING AND QUALITY CONTROL OF NDDS

1. Pharmaceutical Process Development

Quality by Design (QbD) principles, now embedded in the ICH Q8-Q11 guidelines, require systematic identification and control of Critical Quality Attributes (CQAs) and Critical Process Parameters (CPPs). AI augments QbD by enabling a more efficient exploration of the design space and a more accurate prediction of the relationships between CPPs and CQAs. Reinforcement learning controllers that autonomously adjust microfluidic process parameters to maintain target nanoparticle quality have been demonstrated for liposome and PLGA nanoparticle manufacturing.[32][33]

2. Process Analytical Technology and Real-Time Release

The FDA's 2004 PAT guidance and subsequent ICH Q8-Q11 documents catalyzed the adoption of sophisticated spectroscopic and sensor-based monitoring tools in pharmaceutical manufacturing. AI is an enabling technology for extracting actionable information from PAT data. Convolutional neural network models applied to in-process video microscopy images can detect agglomeration, polymorphic transitions, and particle habit changes during nanoparticle crystallization and coating processes.[34]

3. Supply Chain and Cold Chain Management

Machine learning models trained on stability study data for lipid nanoparticle and liposome formulations enable predictive shelf-life estimation and identification of optimal storage conditions. These models can flag formulation batches at risk of degradation based on deviations in cold-chain conditions, enabling proactive quality management decisions. [35]

V.CHALLENGES, LIMITATIONS, AND FUTURE PERSPECTIVES

Challenges and Limitations

Despite remarkable advancements, several obstacles remain in the use of AI in NDDS research. Owing to their complex etiology, poor medication transport across the blood–brain barrier, and dearth of efficient disease-modifying treatments, NDDS continue to rank among the most difficult conditions to treat.

A major limitation was the data quality and bias. Algorithmic bias in precision drug development for brain diseases is a significant concern, as biased models have been shown to underperform by 15–20% for underrepresented populations, potentially leading to misestimated drug efficacy and safety. PubMed Central Additionally, overfitting has been linked to high attrition rates in later-stage trials, as preclinical models continue to expose the risks of relying solely on internal metrics.[36]

Interpretability and generalizability are critical concerns. Issues that remain include the quality of available data, interpretability of the models, and ethical considerations that need collective efforts in developing associated regulatory policies.[37]

The data of the World Economic Forum show that the drug development process itself is costly and slow. Advancing a new drug therapy from concept to clinic can average 10 years and cost over $2.5 billion, with a staggering 90% of candidates failing in pre-clinical and clinical phases.[38]

Future Perspectives:

The integration of AI into drug discovery has emerged as a promising approach to accelerate the identification of novel therapeutic targets, optimize drug candidates, and personalize medicine approaches in NDD research. AI-driven large quantitative models are already compressing research timelines; a collaboration between UCSF and SandboxAQ has redefined what is possible in the development of novel therapeutics, shifting timelines from years to months. [1]

Multimodal AI and interdisciplinary collaboration will define the future of medicine. By integrating diverse data sources, such as neuroimaging, multi-omics, and clinical information, multimodal AI provides a comprehensive view needed to understand intricate neurodegenerative processes. [37]

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