



ARTIFICIAL INTELLIGENCE IN DRUG DELIVERY: REAL-TIME MONITORING, PERSONALIZED THERAPY, AND ADAPTIVE RELEASE

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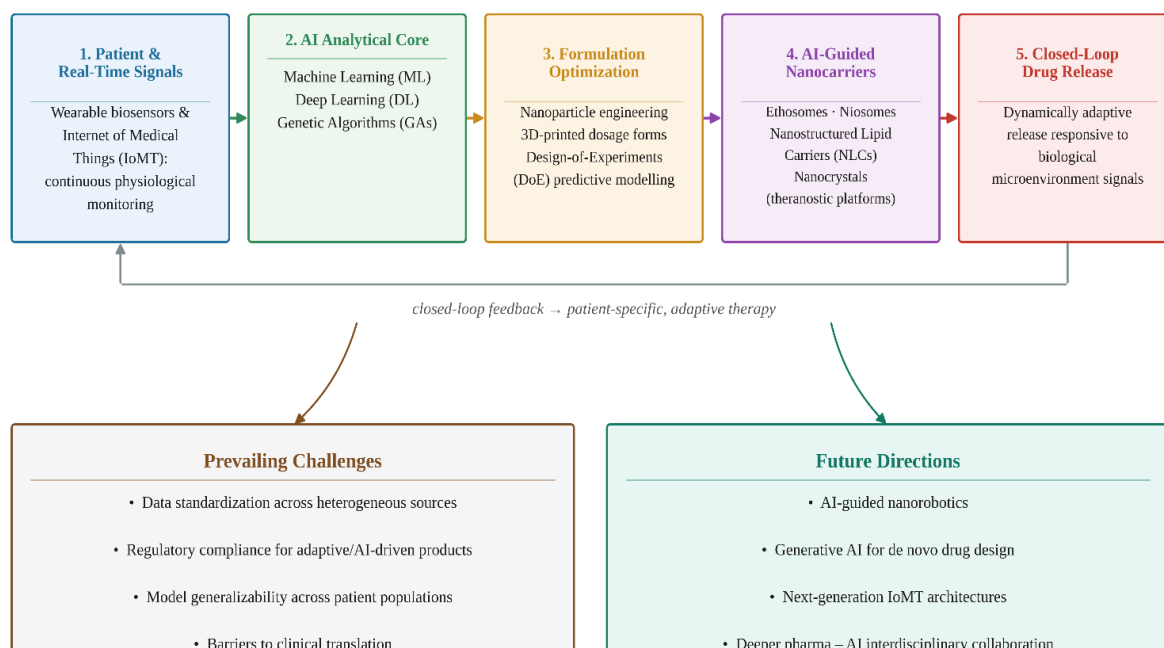
ABSTRACT

Artificial intelligence (AI) is transforming smart drug delivery systems (SDDS) by enabling real-time physiological monitoring, patient-specific formulation design, and dynamically adaptive drug release. Unlike earlier reviews that address AI in general healthcare, this review focuses specifically on AI's role across the pharmaceutical drug delivery continuum, from nanocarrier engineering to closed-loop therapeutic control. We examine how machine learning (ML), deep learning (DL), genetic algorithms (GAs), and the Internet of Medical Things (IoMT) together enable continuous health surveillance, early pathological detection, and timely intervention. The contribution of AI to formulation optimization, including nanoparticle engineering, 3D-printed dosage forms, and design-of-experiments-assisted predictive modelling, is discussed alongside adaptive release algorithms that respond to biological microenvironment signals. Particular attention is given to theranostic platforms and AI-guided nanocarrier systems such as ethosomes, niosomes, nanostructured lipid carriers (NLCs), and nanocrystals. Prevailing challenges, including data standardization, regulatory compliance, model generalizability, and clinical translation barriers, are critically assessed, and future directions such as AI-guided nanorobotics, generative AI for drug design, and next-generation IoMT architectures are outlined. This review underscores the need for sustained interdisciplinary collaboration between pharmaceutical scientists and AI developers to realize the translational potential of intelligent drug delivery.

KEYWORDS: Artificial intelligence; smart drug delivery systems; machine learning; real-time monitoring; adaptive drug release; nanocarriers; Internet of Medical Things; theranostics; formulation optimization; clinical translation.

Artificial Intelligence in Smart Drug Delivery Systems

From Nanocarrier Engineering to Closed-Loop Therapeutic Control



1. INTRODUCTION

Conventional drug therapy has long relied on a population-average paradigm: fixed doses delivered to physiologically heterogeneous patients through formulations that are indifferent to individual variability. This approach carries well-documented limitations, including narrow therapeutic windows, substantial inter-individual variability in drug metabolism, and adverse drug reactions that remain a leading cause of preventable morbidity.

These limitations have driven the emergence of smart drug delivery systems (SDDS), engineered platforms designed to release therapeutic agents in a controlled, targeted, and often stimulus-responsive manner. Early SDDS relied on physicochemical stimuli such as pH gradients, temperature changes, and redox environments. While conceptually significant, their responsiveness remained passive, governed by preformulated parameters rather than real-time patient status. The next frontier is the integration of active intelligence: systems capable of sensing, processing, and autonomously responding to dynamic biological signals.^[1]

Artificial intelligence has emerged as the enabling technology for this transition. The convergence of large biomedical datasets, computational power, and advanced algorithmic architectures has positioned AI to augment every stage of the drug delivery continuum, from formulation design to real-time dose adjustment. Existing reviews largely address AI in general healthcare or specific drug classes^[2-5]; a focused synthesis of AI's role across the full smart drug delivery pipeline remains

lacking. This review addresses that gap, emphasizing data-driven, replicable AI applications relevant to pharmaceutical formulation and delivery science.

Smart drug delivery systems are engineered therapeutic platforms capable of delivering drugs to specific target tissues or cell populations in a controlled and responsive manner, with the dual aim of enhancing therapeutic effect and minimizing systemic adverse reactions. Their "smartness" lies in the capacity to respond to endogenous stimuli (pH, enzyme activity, redox potential, temperature, hypoxia) or exogenous triggers (light, ultrasound, magnetic fields, electric current), modifying release kinetics accordingly.

Artificial intelligence in healthcare encompasses supervised and unsupervised machine learning, deep neural network architectures, reinforcement learning, natural language processing, and evolutionary algorithms applied to diagnosis, outcome prediction, and treatment optimization. In drug delivery, AI specifically supports formulation optimization, pharmacokinetic modelling, patient stratification, release-kinetics prediction, and real-time therapeutic adjustment.

Personalized medicine refers to the tailoring of therapeutic interventions to the genetic, epigenetic, proteomic, metabolomic, and environmental characteristics of individual patients. Theranostics, a portmanteau of therapeutics and diagnostics, represents its most integrated expression: platforms that simultaneously deliver therapy and generate diagnostic

readouts, enabling closed-loop feedback between administration and monitoring.

2. Fundamental AI Technologies in Drug Delivery

2.1 Machine Learning

Machine learning is the computational foundation of AI-driven drug delivery, involving algorithms that learn patterns from data and generalize them to unseen inputs. Supervised learning trains models on labelled datasets linking formulation variables to known outcomes, such as drug release rates, while unsupervised learning identifies latent structure in unlabelled data, supporting patient clustering and phenotyping.

Supervised algorithms, including random forests, support vector machines, gradient boosting ensembles, and artificial neural networks (ANNs), have been widely applied to predict drug release kinetics, nanocarrier stability, and bioavailability. Random forests provide robust, interpretable predictions; gradient boosting methods such as XGBoost and LightGBM offer superior accuracy in high-dimensional pharmaceutical datasets.^[9,10]; and ANNs, as universal function approximators, capture nonlinear input–output relationships that traditional response surface methods cannot. Unsupervised approaches such as k-means clustering, hierarchical clustering, and dimensionality reduction (PCA, t-SNE) help identify patient subgroups with distinct pharmacodynamic profiles. Online learning, in which models are continuously updated as new data arrive, allows delivery algorithms to adapt over time without full retraining.

2.2 Deep Learning Architectures

Deep learning uses multi-layered neural networks for hierarchical feature extraction. Convolutional neural networks (CNNs), originally developed for image recognition, are used for nanoparticle morphology classification, drug crystal identification, and spectral analysis. Recurrent neural networks (RNNs) and their variants, including long short-term memory (LSTM) networks and gated recurrent units (GRUs), suit sequential, time-series data from continuous monitoring, modelling pharmacokinetic trajectories and anticipating physiological deterioration before clinical manifestation. Transformer architectures, adapted from natural language processing, integrate heterogeneous data streams such as genomic sequences, sensor time-series, and clinical records, while graph neural networks (GNNs) extend deep learning to molecular and biological network data, aiding prediction of drug–target interactions and nanocarrier–membrane binding.

2.3 Genetic Algorithms

Genetic algorithms (GAs) are evolutionary optimization methods well suited to high-dimensional, multimodal problems that resist analytical solutions. In formulation science, GAs simultaneously optimize variables such as polymer concentration, surfactant type, and drug-to-excipient ratio against competing objectives, such as

maximizing encapsulation efficiency while minimizing particle size. Through iterative selection, crossover, and mutation, GAs identify global optima in formulation landscapes with multiple local optima^[21,22], and, combined with ANN surrogate models, accelerate rational formulation development. Together, ML, DL, and GA form the core computational toolkit for AI-driven drug delivery, with IoMT providing the real-world data infrastructure that activates them clinically.

2.4 IoT and IoMT Integration

The Internet of Things has evolved into the Internet of Medical Things (IoMT), encompassing wearable physiological monitors, implantable delivery devices, smart dispensers, and remote diagnostic tools networked to healthcare data infrastructure. IoMT closes the feedback loop between patient physiology and therapeutic intervention^[16,17]: physiological data streams continuously to AI inference engines, which trigger dynamically adjusted drug release, replacing infrequent, population-based dosing with continuously adaptive, individualized therapy. The fusion of IoT infrastructure with AI analytics, sometimes termed AIoT, converts raw sensor signals into clinically actionable insight, while edge computing, performing inference locally on the device, enhances responsiveness and privacy.

3. Real-Time Monitoring Systems

3.1 Wearable Sensors and Telemetry

Wearable sensors form the sensory interface of AI-integrated drug delivery. Contemporary devices include electrochemical sensors for continuous glucose and lactate monitoring, optical sensors for heart-rate variability and oxygen saturation, piezoelectric sensors for respiratory rate and activity, and bioimpedance sensors for body composition and fluid status. Advances in miniaturization, flexible substrates, and low-power wireless protocols (Bluetooth Low Energy, Zigbee, NFC) have enabled comfortable, continuous data acquisition. Integrating diverse sensor modalities into unified, AI-analyzed data streams allows physiological signals to feed directly into drug release decisions, for example triggering insulin infusion adjustment on detection of rising glucose.

3.2 Inference Models for Predictive Monitoring

Inference models are ML algorithms trained on historical physiological data to identify patterns and anomalies indicative of impending health events. They perform signal processing and artifact rejection, pattern recognition of sub- or supratherapeutic states, and predictive inference of future physiological trajectories. Effective inference models require large, well-annotated datasets, a historically scarce resource that transfer learning partially addresses by fine-tuning models pretrained on related domains. Clinical inference models must also be well calibrated, and Bayesian and ensemble methods provide the uncertainty quantification needed to preserve clinician judgement in ambiguous cases.

3.3 Remote Patient Monitoring

Remote patient monitoring (RPM) platforms transmit continuous wearable sensor data to healthcare providers for AI-driven analysis and automated or clinician-mediated intervention. RPM programs have demonstrated reductions in 30-day hospital readmission rates of 15–40%^[16] across cardiovascular, respiratory, and diabetic populations. In drug delivery, AI-driven RPM learns individual physiological baselines and flags deviations, for example declining anticoagulant effectiveness or emerging chemotherapy toxicity, triggering dose adjustment and creating a closed feedback loop that is continuous and predictive rather than reactive and episodic.

3.4 Real-Time Data Integration

Clinical utility depends on the quality, completeness, and timeliness of data feeding inference algorithms. Healthcare data exists in heterogeneous silos, including electronic health records, imaging systems, laboratory systems, and wearable platforms, each with distinct standards. HL7 FHIR has emerged as the leading interoperability standard, enabling structured data sharing across systems. AI-powered data-quality algorithms flag or impute corrupted segments arising from motion artifact, electrode displacement, or battery depletion, preserving inference performance under imperfect acquisition conditions.

3.5 Case Studies in AI-Integrated Monitoring

Closed-loop insulin delivery, or artificial pancreas systems, continuously measure interstitial glucose and use ML-augmented control algorithms to adjust insulin infusion, demonstrating superior time-in-range and reduced nocturnal hypoglycaemia compared with sensor-augmented pump therapy.^[11–13] In cardiovascular medicine, AI analysis of continuous ECG data detects atrial fibrillation with sensitivity and specificity exceeding 95%^[14,15], enabling earlier anticoagulation. In oncology, RPM platforms monitoring chemotherapy patients detect early signs of neutropenic fever, dehydration, and cardiac toxicity, enabling proactive supportive care before complications require hospitalization.

4. Personalized Medicine Approaches

4.1 Patient-Specific Drug Delivery

Individuals differ profoundly in the physiological, genetic, and environmental determinants of pharmacokinetics and pharmacodynamics. Genetic polymorphisms in cytochrome P450 enzymes can produce ten-fold or greater differences in drug exposure at identical doses, while hepatic impairment, renal dysfunction, and inflammatory states further complicate dose–response relationships. AI integrates these determinants into individualized pharmacokinetic–pharmacodynamic models, adapting the delivery vehicle, such as nanocarrier surface chemistry, release kinetics, and targeting ligands, rather than the drug itself.

4.2 AI-Driven Formulation Optimization

Formulation optimization has historically relied on design-of-experiments (DoE) methodologies. Response surface methodology (RSM), including Box–Behnken design (BBD), central composite design, and D-optimal designs, maps formulation variables to product-quality responses through polynomial regression, but is limited in capturing highly nonlinear relationships. ANNs extend this capability as universal function approximators: ANN models trained on BBD-generated data have consistently outperformed polynomial RSM models in predicting release kinetics, particle size, zeta potential, and encapsulation efficiency.^[6–8] The recommended workflow uses BBD to generate a statistically efficient dataset and then trains an ANN on that data for superior predictive accuracy, an approach that amplifies rather than replaces DoE. Such performance claims should nonetheless be interpreted cautiously, as accuracy is dataset- and context-specific and requires independent validation.

Nanoparticle-based carriers, including polymeric nanoparticles, solid lipid nanoparticles, NLCs, polymersomes, dendrimers, and lipid–polymer hybrids, represent a particularly active area for AI-driven optimization, given the high dimensionality of variables such as polymer molecular weight, lipid composition, and processing parameters that determine particle size, charge, and release profile. Three-dimensional printing (3DP) technologies, including fused deposition modelling, selective laser sintering, stereolithography, and binder jetting, further enable dosage forms tailored to target release profiles. AI plays a prescriptive role here, using inverse design to back-calculate printing parameters from a desired pharmacokinetic profile^[18–20], a capability especially valuable for age-appropriate paediatric and geriatric dosage forms.

4.3 Theranostics Integration

Theranostic platforms simultaneously deliver therapy and generate diagnostic information, enabling closed-loop feedback between administration and disease monitoring. AI guides the rational design of multi-functional nanocarriers, analyzes diagnostic signals to assess therapeutic response, and adjusts release rates based on imaging or biosensor feedback. In oncology, iron oxide nanoparticles loaded with chemotherapeutics provide simultaneous MRI contrast and cytotoxic delivery, with AI-analyzed signal evolution informing adaptive dosing.^[23,24] gold nanoparticle theranostics similarly combine photothermal therapy with AI-mapped drug distribution. Integrating genetic predisposition data, including polygenic risk scores and pharmacogenomic profiles, with real-time biomarker monitoring further enables precision-guided cardiovascular therapy.

4.4 Precision Medicine Applications

Precision medicine seeks to match the right drug, dose, and delivery system to the right patient at the right time. AI integrates genomic, transcriptomic, proteomic,

metabolomic, microbiome, and clinical data into individualized therapeutic recommendations. AI-guided surface functionalization of nanocarriers with targeting ligands, informed by quantitative structure–activity relationship (QSAR) modelling, improves selectivity of drug accumulation at pathological tissues, translating to enhanced efficacy at lower doses. AI-optimized nanocarrier formulations have demonstrated 5- to 20-fold improvements in oral bioavailability for poorly water-soluble BCS Class II compounds in preclinical models, a category comprising an estimated 40% of marketed drugs.

4.5 Clinical Research Implications

Translating AI-personalized delivery from preclinical promise to clinical reality requires trial designs suited to patient-specific effect sizes. Adaptive designs, including N-of-1 trials, platform trials, and Bayesian adaptive randomization, are better suited to precision medicine evaluation than traditional population-powered randomized trials, and AI tools enable real-time analysis of accruing trial data to inform adaptive modifications while maintaining statistical rigour.

5. Adaptive Release Mechanisms

5.1 Smart Release Systems

Adaptive release is the operational expression of AI-integrated drug delivery. Passive stimulus-responsive systems rely on prebuilt physicochemical triggers, such as pH-sensitive polymers, with predetermined responses that cannot be modified after manufacture. AI-controlled adaptive release instead operates through an active loop: sensing, AI interpretation, decision, release adjustment, and feedback, distinguishing it from conventional controlled release. Pathological tissues differ from healthy tissue in pH, redox potential, enzyme activity, and hypoxia, providing multiple stimulus dimensions that AI models can combine to trigger context-specific release. Closed-loop systems using model predictive control, particularly when augmented with Bayesian filtering to continuously update the underlying pharmacokinetic model, represent the most sophisticated implementation of adaptive, personalized therapy.

5.2 AI-Powered Formulation Design

Predicting drug release from complex delivery systems, involving diffusion, swelling, degradation, and drug–polymer interaction, is a substantial computational challenge. Physics-informed machine learning, which embeds mechanistic pharmaceutical principles as structural constraints, offers predictive accuracy alongside the interpretability needed for regulatory submission. ANN models trained on BBD-generated data for lipid-based nanoformulations have shown root-mean-square errors 40–60% lower than corresponding RSM models, with SHAP and permutation-importance analysis helping identify influential formulation variables without sacrificing accuracy.

5.3 Nanocarrier-Integrated AI Approaches

AI-assisted modelling of nano-bio interactions, including protein corona formation, cellular uptake, and intracellular trafficking, guides rational nanocarrier design, with molecular dynamics simulations augmented by ML-derived force fields informing surface modifications that prolong circulation half-life. High-throughput robotic formulation platforms, combined with automated characterization and AI predictive modelling, compress development cycles from years to months, an acceleration particularly consequential for rapidly evolving contexts such as pandemic response and rare cancer subtypes.

5.4 Electronically Controlled Systems

Implantable microchip-based delivery systems, using electrochemically degradable membranes over drug reservoirs, achieve precise, wirelessly programmable release triggered by AI control algorithms. Integration with indwelling microdialysis or electrochemical biosensors enables genuine closed-loop pharmacokinetic control, with predictive AI models anticipating therapeutic needs proactively, an advantage particularly valuable for narrow-therapeutic-window drugs such as immunosuppressants, anticoagulants, and antiepileptics.

5.5 Specific Nanotechnology Applications

Ethosomes, phospholipid vesicles enriched with ethanol, achieve enhanced skin permeation, and AI models integrating drug physicochemical properties, formulation composition, and skin characteristics enable personalized transdermal optimization. Niosomes offer chemical stability and manufacturing scalability advantages over liposomes, with ML models mapping formulation variables to vesicle size and release kinetics. Nanostructured lipid carriers show improved drug loading and reduced expulsion relative to first-generation lipid nanoparticles, while nanocrystals, combined with advanced imaging analysis, enable rapid bioavailability enhancement for poorly soluble drugs.

6. Integration with Pharmaceutical Formulation Expertise

6.1 AI and Traditional Formulation Methods

AI is most productively conceived as enhancing, rather than replacing, established formulation methodologies. Box–Behnken design provides an efficient experimental scaffold for AI model training, and characterization data such as FTIR spectra, dynamic light scattering measurements, and thermal analysis are directly amenable to AI-based analysis, for example CNN- or PLS-based spectral analysis for drug–polymer interaction quantification, creating a continuously enriching knowledge base linking formulation variables to physicochemical outcomes.

6.2 Phytochemical and AI Applications

AI has transformed the pharmaceutical development of plant-derived bioactives, where traditional screening is labour-intensive and poorly scaled to botanical chemical

diversity. AI-assisted virtual screening prioritizes natural product chemical space for evaluation, while ML models predicting the encapsulation efficiency and stability of multi-component phytochemical nanoformulations enable model-guided, rather than empirical, optimization, supported by AI-enhanced FTIR and NMR spectral characterization.

6.3 Drug Content and Release Kinetics Prediction

Traditional release-kinetics models, including zero-order, first-order, Higuchi, Korsmeyer–Peppas, and Weibull, provide useful but limited descriptions of complex, multi-mechanism release. ML models, particularly ANNs and gradient boosting regressors, trained on experimentally measured release profiles, capture the collective influence of formulation variables, including interaction effects invisible to traditional kinetic models, and similarly support stability prediction for accelerated shelf-life determination.

7. Current Challenges and Limitations

7.1 Technical Challenges

Data quality and standardization remain the most pervasive technical challenge: pharmaceutical and biomedical data are often affected by measurement variability, missing values, and inconsistent reporting, limiting the volume of data available for model training and calling for harmonized reporting standards. Model generalizability across patient populations is a related concern, since models trained on data from specific cohorts, often from high-income countries, may perform poorly under distributional shift when deployed in underrepresented populations. Integration with legacy hospital information systems, electronic health records, and pharmacy management systems further presents significant technical barriers to deployment.

7.2 Regulatory and Compliance Issues

Regulatory frameworks for AI-integrated drug delivery devices are still evolving. The FDA's Predetermined Change Control Plan provides a mechanism for pre-authorizing defined categories of AI model updates without requiring full resubmission for each iteration.^[25,26] Data privacy concerns are acute given continuous physiological monitoring, and frameworks such as GDPR and HIPAA impose stringent requirements on collection, storage, and processing of health data; federated learning, which trains models across distributed datasets without centralizing patient data, offers a privacy-preserving alternative^[27] that may facilitate compliance.

7.3 Clinical Implementation Barriers

The cost of AI infrastructure, including wearable platforms, IoMT connectivity, computing resources, and software licensing, presents a substantial barrier, particularly in resource-limited settings, and health-economic evidence of cost-effectiveness remains limited. Clinicians and pharmacists require sufficient AI literacy to evaluate AI-generated recommendations and

recognize failure modes, while patient acceptance is shaped by concerns about privacy, comfort, and the perceived depersonalization of AI-guided therapy.

7.4 Research Gaps

The field lacks large, publicly accessible, well-annotated datasets linking formulation variables to biological performance; most published studies rely on modest proprietary datasets, limiting reproducibility. Curated public repositories, analogous to the Cambridge Structural Database, would accelerate collaborative development and external validation. Longitudinal clinical studies with sufficient follow-up, and standardized benchmarking protocols across platforms, are similarly needed to establish long-term efficacy and enable meaningful comparison between systems.

8. Future Directions

8.1 Emerging Technologies

AI-guided nanorobotics, autonomous nanoscale devices capable of navigation and on-demand delivery, represents a visionary application domain, with proof-of-concept DNA-based nanorobots already demonstrated in animal models^[29,30]; targeted delivery across the blood–brain barrier is a priority application given the severe inadequacy of current CNS-targeted approaches. Generative AI, including large language models, generative adversarial networks, and variational autoencoders, can generate candidate drug molecules or novel formulation compositions in previously unexplored chemical space.^[28] Next-generation IoMT architectures, incorporating implantable biosensor arrays and AI-integrated organ-on-chip systems, will expand physiological monitoring while reducing reliance on animal testing.

8.2 Research Priorities

Establishing standardized public datasets for AI drug delivery research, encompassing nanoparticle characterization, in vitro release profiles, and linked in vivo pharmacokinetic data, is the field's highest infrastructure priority, supporting development of in vitro–in vivo correlation models. Consortia modelled on the Minimum Information for Nanomaterial Characterization initiative should enforce standardized reporting, while longitudinal clinical efficacy studies incorporating patient-reported outcomes and health-economic analyses, alongside cross-platform algorithm standardization, would strengthen the evidence base for adoption.

8.3 Clinical Translation Pathways

Regulatory framework development must proceed alongside technological innovation, with mechanisms such as the FDA's Breakthrough Device Designation and the EMA's Innovation Office enabling early resolution of regulatory questions. Healthcare provider education, incorporating foundational AI literacy into medical and pharmacy curricula, and patient-centred design incorporating end-user perspectives from early

development stages, will support both clinical adoption and practical acceptability.

8.4 Integration with Medical Coding and Documentation

AI-assisted clinical documentation creates opportunities for automated, accurate capture of therapeutic interventions and outcomes. AI-assisted ICD-10-CM and CPT coding systems can extract and encode relevant clinical information from records and monitoring data, reducing administrative burden and improving accuracy. For AI-integrated delivery programs, automated coding of monitoring encounters, dosage adjustments, and adverse events would enable systematic outcome tracking, and healthcare informatics professionals with clinical coding expertise, including Certified Coding Specialists (CCS), play a critical role in ensuring that encounter coding accurately reflects the complexity of AI-guided interventions.

9. CONCLUSION

The integration of artificial intelligence into smart drug delivery systems represents one of the most consequential convergences in contemporary biomedical science, fusing computational power with pharmaceutical innovation to transform therapeutic outcomes. This review has examined that integration through three complementary lenses: real-time monitoring, personalized medicine, and adaptive release. In real-time monitoring, AI-powered wearable networks and inference models move drug delivery from episodic, clinic-based adjustment toward continuous, home-based optimization. In personalized medicine, AI-driven formulation optimization, encompassing nanocarrier design, 3D printing, and theranostic integration, tailors delivery systems to individual patients with a precision exceeding empirical formulation science alone. In adaptive release, machine learning algorithms that continuously process physiological data and adjust drug liberation create a paradigm in which patient physiology actively guides therapy rather than passively receiving a predetermined dose.

Bridging pharmaceutical formulation science with AI technologies requires sustained interdisciplinary collaboration: the pharmaceutical scientist's domain knowledge and the AI scientist's computational expertise are each necessary but insufficient alone. The path to clinical realization passes through clearly identified but tractable challenges, including data standardization, model generalizability, regulatory development, and healthcare system integration, the resolution of which promises more effective therapies, fewer adverse drug reactions, and more equitable access to precision medicine.

The future of drug delivery is intelligent, adaptive, and personalized. The approaches discussed throughout this review are positioned toward replicable, data-driven applications, validated prospectively and designed with

sufficient transparency for regulatory and scientific scrutiny. Claims about model performance and clinical translation should be interpreted conservatively, as most evidence remains preclinical or early-phase; independent validation at scale is necessary before these technologies can be considered established clinical tools. The convergence of AI with smart drug delivery is an emerging reality that demands the collaborative engagement of pharmaceutical scientists, AI developers, clinicians, regulators, and patients to realize its translational potential responsibly.

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