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AI -DRIVEN NANOMEDICINE FOR DRUG DELIVERY: INTERPLAY OF NANOCARRIER DESIGN, BIOLOGICALBARRIER AND THERAPEUTIC PERFORMANCE

Dipali Patil*

Ashokrao Mane College of Pharmacy, Peth Vadgaon, Kolhapur, Maharashtra, India.

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***Corresponding Author: Dipali Patil**
Ashokrao Mane College of Pharmacy, Peth Vadgaon, Kolhapur, Maharashtra, India.
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ABSRACT

By enabling individualised diagnostics and treatments, artificial intelligence (AI) is revolutionising the management of chronic illnesses. In this context, nanotechnology-based drug delivery systems support patient-specific interventions through precise and data-driven design.[21] Because of their small size and adjustable surface characteristics, nanocarriers provide better efficacy, stability, and decreased toxicity when compared to traditional drug formulations. For the delivery of drugs, numerous organic and inorganic nanocarriers have been created. Important characterisation techniques, translational difficulties, and the developing role of artificial intelligence in nanocarrier design and optimisation are highlighted in this review.[22] The rational design of programmable and stimuli-responsive drug delivery systems is made possible by the convergence of artificial intelligence and nano architectonics. This strategy moves nanomedicine from empirical formulation to intelligent, clinically transferable precision therapeutics by combining data-driven target identification, nanocarrier optimisation, and predictive modelling.[23] By enabling predictive, data-driven nanocarrier design, artificial intelligence and big data analytics are revolutionising drug delivery based on nanomaterials. AI enhances reproducibility, speeds up optimisation, and facilitates clinical translation by combining physicochemical, pharmacokinetic, and biological datasets. AI-assisted nanomedicine is now positioned as a major force behind precision and patient- centered treatments thanks to this convergence.[24] Improved cancer treatment is possible with targeted drug delivery using nanocarriers, but this approach is constrained by intricate tumour biology and nano-bio interactions. Artificial intelligence speeds up the creation of efficient, tumor-specific cancer treatments by enabling data-driven nanocarrier design and predictive optimisation.[25] The convergence of artificial intelligence and nanomedicine is transforming targeted drug delivery and personalised therapeutics by enabling predictive modelling, optimised pharmacokinetics, and reduced experimental burden. Despite challenges in data standardisation, transparency, and regulation, interdisciplinary collaboration is essential to fully realise the clinical potential of AI-enabled nanomedicine.[26] Drug delivery by nanoparticles promises targeted and controlled therapeutics, and is however hampered by difficult design issues. Artificial intelligence (AI) provides data-driven approaches to optimize NP properties, predict their biological interactions and speed up formulation development. This review showcases recent AI-based strategies and challenges along with prospect in smart nanomedicine.[27]

KEYWORDS: Artificial intelligence, Nanocarriers, Targeted drug delivery, Precision medicine.

INTRODUCTION

Nano medicinal artificial intelligence (nAI), as an approach that is designed to use AI to make a discovery and optimize of safer, more effective and targeted therapeutic nanomaterials, offers new prospects for the field of personalized medicine. With the favour of clinical and genetic data, AI becomes a dependable paradigm to perform outcome prediction, treatment optimization and personalized drug design although there are still questions on data integration, ethics and regulation. Such a review highlights the potential of interdisciplinary work to achieve AI-assisted nanomedicine for patient care.[28] Despite the potential of nanomedicine platforms, specific targeted drug delivery is still a big challenge in medicine. Nanoparticle optimization is impeded by the fact that this can be complex and highly multidimensional in regard to nanoparticle design, formulation, and selection. With the support of artificial intelligence and computational modeling, data capture analysis is allowing rational nanoparticle development as well as optimization of delivery performance.[29] Pharmaceutical nano-carriers have garnered a great deal of attention for their ability to improve the solubility, bioavailability, controlled release and site-specific delivery of drugs. However, their formulation consists of several materials and process parameters that have a significant impact on the quality and performance of the product. QbD outlines a consistent approach to characterizing CQA, MA and PP for the design of robust and reproducible nanocarriers. Integration of modern advances, such as d eep learning, with Q b D further enhances the understanding and optimization of the process.[30] Precision oncology relies on patient-specific tumor profiling, but tumor heterogeneity limits the effectiveness of nanoparticle-based drug delivery. Advances in liquid biopsies and nanodiagnostics enable real-time tumor monitoring, while artificial intelligence helps integrate complex data to optimize nanocarrier design and improve personalized cancer therapy.[31]

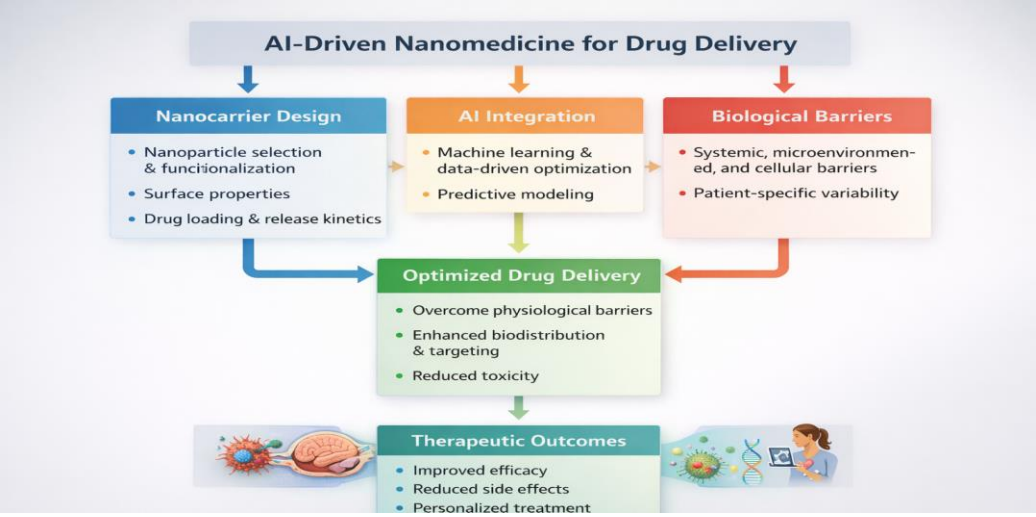


Diagram 1: Ai driven nanomedicine for drug delivery.

The growing burden of neurological disorders has increased the need for effective brain drug development models. While animal models can mimic some aspects of blood-brain barrier (BBB) complexity, they are expensive, take a lot of time, and often do not predict human outcomes well. As a result, in vitro BBB and BBB-on-chip models have emerged as good alternatives for studying BBB function, disease mechanisms, and drug transport. Still, completely replicating the structural and functional complexity of the human BBB is a major challenge.[32] Conventional treatments like chemotherapy and radiation are constrained by systemic toxicity and inadequate efficacy, and cancer continues to be a major cause of death worldwide. A promising substitute is immunotherapy, especially mRNA-based vaccines that

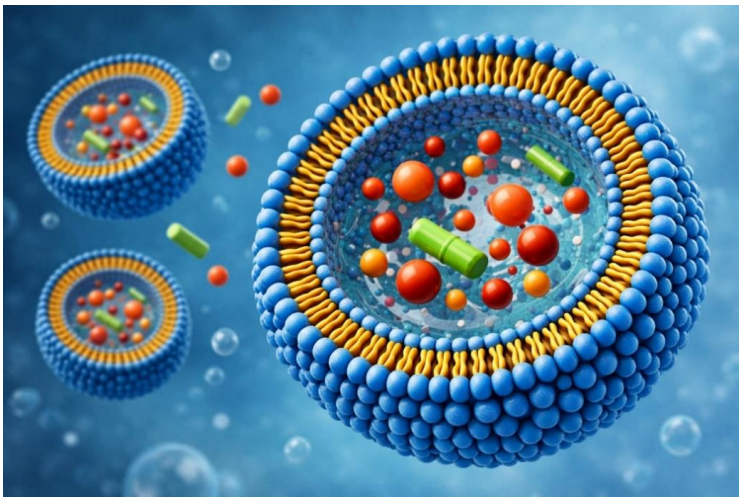
elicit strong antitumor immune responses. However, poor cellular uptake and enzymatic degradation make effective mRNA delivery difficult. As evidenced by COVID-19 vaccines, lipid nanoparticles (LNPs) have overcome these constraints by facilitating safe and effective mRNA delivery, and they are currently being investigated for cancer immunotherapy.[33]

3. Nanocarrier Design: Principles and Parameters

3.1. Types of nanocarrier

3.1.1. Liposomes

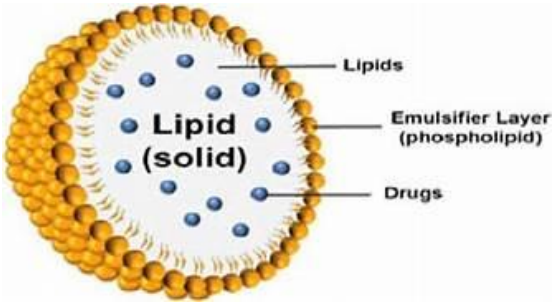
Both hydrophilic and lipophilic medications can be encapsulated in liposomes, which are amphiphilic phospholipid vesicles that spontaneously form bilayer structures in aqueous environments. Membrane composition, size, surface charge, and structural organization all affect how effective they are. Multilamellar vesicles offer sustained release because of multiple bilayers, while unilamellar vesicles offer faster drug release. Cholesterol decreases permeability and increases membrane stability. Polyethylene glycol (PEG) surface modification reduces immune recognition, extending circulation time. The pharmacokinetics and therapeutic efficacy of liposomal drug delivery systems are greatly enhanced by these structural modifications.[41] Liposomes are divided into unilamellar (SUV, LUV), multilamellar (MLV), and multivesicular vesicles (MVV) based on their size and lamellarity. Multilamellar vesicles have several concentric layers, whereas unilamellar vesicles only have one bilayer. For hydrophilic medications, encapsulation efficiency rises with vesicle size but falls with more bilayers. Because of their advantageous circulation characteristics, vesicles between 50 and 150 nm are typically chosen for drug delivery. Size, surface charge, composition, and targeting ligands all affect liposome–cell interactions, which take place through endocytosis, fusion, or phagocytosis.[42] The enhanced permeability and retention (EPR) effect, which permits nanoparticles to flow through leaky tumour vasculature, is the main mechanism underlying liposome accumulation in tumours. However, their circulation time is limited by the mononuclear phagocyte system's quick clearance. Polyethylene glycol (PEG) surface modification prolongs systemic circulation and decreases immune recognition. Tumour selectivity and therapeutic efficacy are further improved by active targeting with receptor-specific ligands.[43]



3.1.2. Solid lipid nanoparticle

Solid lipids scattered in an aqueous phase and stabilised by surfactants form the spherical carriers known as solid lipid nanoparticles (SLNs), which range in size from 40 to 1000 nm. Both hydrophilic and hydrophobic medications can be encapsulated in them, and stability and release behaviour are influenced by the lipid composition. Benefits of SLNs

include cost-effectiveness, solvent-free preparation, scalability, and biocompatibility. However, issues like limited drug loading, particle growth, and lipid crystallisation may limit their effectiveness.[44]



Particle size, lipid crystallinity, and drug–lipid interactions all affect drug release from SLNs. While homogeneous drug dispersion within the solid matrix encourages sustained release, smaller particles increase release because of their larger surface area. Drug diffusion is accelerated by increased drug mobility and lipid crystallisation. The release profile is ultimately determined by the drug incorporation model, which is impacted by formulation and preparation techniques.[45] Solid physiological lipids distributed in an aqueous surfactant system make up solid lipid nanoparticles (SLNs), which are lipid-based nanocarriers. Their internal structure can be homogeneous, drug-enriched core, or drug-enriched shell models, depending on the formulation and preparation technique. Therapeutic agents can be delivered in a controlled and targeted manner thanks to these structural variations that control drug distribution and release behaviour.[46]

3.1.3. Hybrid nanocarrier

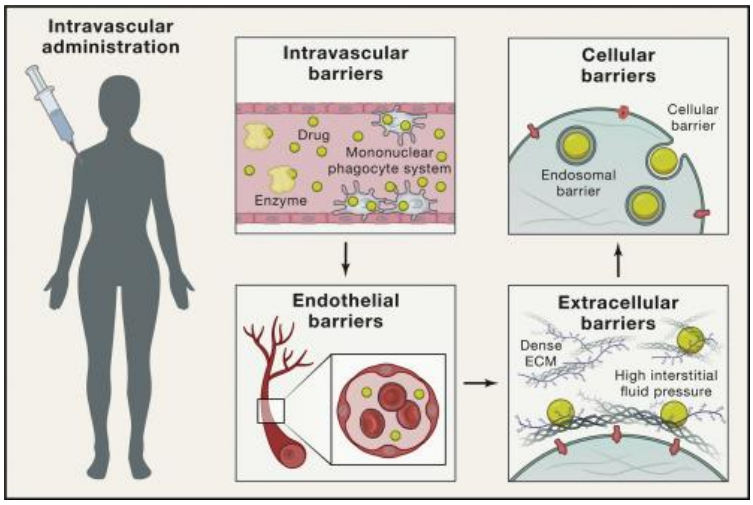
Gemcitabine HCl, acetaminophen, and other analytical-grade reagents were purchased from reputable commercial vendors. Tripolyphosphate (TPP), chitosan, and BSA were utilised exactly as supplied. RPMI and F12K media supplemented with 10% foetal bovine serum and antibiotics were used to cultivate human lung adenocarcinoma cell lines (H460 and A549) as monolayers at 37°C in a 5% CO2 atmosphere. Every cell culture consumable and reagent was obtained from reputable commercial suppliers.[47] Phosphatidylcholine, cholesterol, sodium cholate, and Pluronic® P123 were used in the thin-film hydration method to create functional bilosomes. Stable nanosized vesicles were obtained by sonicating the lipid film after it had been hydrated with an aqueous phase. For dual-drug loading, methylene blue (hydrophilic) and curcumin (lipophilic) were added.[48] Free-radical graft polymerisation of acrylamide onto silica sol using cerium (IV) ammonium nitrate under argon at 20 °C produced hydrophilic SiO_2-g-PAAm hybrids (Hyb1 and Hyb2). Light scattering, elemental analysis, thermogravimetric analysis, and viscometry were used to characterise the hybrids with different graft numbers and molecular weights that were produced by applying different initiator ratios.[49] delivery of numerous medications. Specifically, biodegradable polymeric nanoparticles improve therapeutic efficacy while reducing adverse effects by enabling targeted drug delivery and safely breaking down into non-toxic monomers.[50]

3.2. Biological Barrier in Drug Delivary

3.2.1. Tissue-Specific barrier

The oral mucosa hosts a very diverse microbiome and serves as a crucial barrier that strikes a balance between immune tolerance and defence. Commensal microbes aid in the regulation of local immunity, with innate defences (such as saliva components and antimicrobial peptides) and IL-17-mediated responses being crucial in the management of

pathogens such as Candida albicans. Furthermore, when dysregulated, oral microbial interactions can affect systemic and local immunity, which can lead to inflammatory diseases.[51] Before entering target tissues, intravascularly administered medications must pass through a series of biological barriers. These include the mononuclear phagocyte system's sequestration of nanoparticles, renal clearance, and enzymatic degradation. Afterward, drugs must cross the endothelial barrier, penetrate the extracellular matrix, and overcome tumor-related obstacles like dense ECM and high interstitial pressure. Lastly, in order to reach therapeutic targets, intracellular delivery necessitates membrane transport and escape from endosomal degradation.[52]



3.2.2. systemic Biological barriers

The therapeutic efficacy of nanomedicines for a variety of illnesses, such as cancer and inflammatory conditions, is severely constrained by biological barriers. Nanoparticles must overcome a number of physiological obstacles, including hydrodynamic shear forces, protein corona formation, and quick systemic clearance, in order to accomplish efficient biodistribution and target-site accumulation. Conventional uniform delivery strategies are insufficient because these barriers vary significantly among patients and are frequently altered under pathological conditions. Systemic, tissue microenvironmental, and cellular barrier heterogeneity complicates their identification and logical characterisation. Therefore, the logical design of engineered nanocarriers requires a thorough understanding of both common and patient-specific biological barriers. Precise site-specific drug delivery will continue to be challenging until nanocarrier architectures are optimised to address these complex obstacles. However, ongoing developments in delivery system engineering and nanomedicine present encouraging prospects for creating next-generation nanotherapeutics that can get around these biological limitations.[11] The nature and stage of the disease, as well as the mode of administration, determine the biological challenges that nanoparticles face. Local delivery methods can get around a number of systemic distribution barriers, but they frequently call for intrusive procedures or technically challenging interventions that come with extra restrictions. Furthermore, diseases that are limited to clearly defined and accessible locations, like solid tumours or traumatic lesions, are best suited for localised administration. As a result, the most popular method for delivering drugs using nanoparticles is still systemic administration.[12] The physicochemical characteristics of nanomedicines control their biodistribution and clearance, and they are engineered to interact with particular tissues. Therefore, maximising therapeutic efficacy and reducing off-target effects depend heavily on pharmacokinetic behaviour.[13] There is mounting evidence that tumour heterogeneity, such as aberrant vasculature,

dense extracellular matrix, hypoxia, acidic pH, redox imbalance, and immune suppression resulting from interactions between the cancer and the tumour microenvironment, significantly restricts nanocarrier-based drug delivery.[14,15]

Therefore, to direct future developments in drug delivery techniques, a succinct summary of this dynamic tumour landscape is crucial.

Due to poor tumour accumulation, cell membrane-based nanocarriers exhibit limited clinical translation despite notable advancements. The sequential biological barriers from systemic circulation to intracellular delivery cannot be overcome by membrane coating alone, even though it enhances circulation time, biocompatibility, and partial targeting. After being administered intravenously, nanoparticles are opsonised and cleared by the mononuclear phagocyte system, have limited tumour penetration because of high interstitial pressure, and are further constrained by drug efflux and lysosomal degradation.[16] The administration method and disease characteristics determine the biological barriers that nanoparticles must overcome. Local delivery is restricted to accessible, localised conditions and frequently necessitates invasive procedures, even though it can get around some systemic obstacles. As a result, the most popular method for delivering drugs using nanoparticles is still systemic administration.[17] Because biological barriers change depending on the disease state, traditional one-size-fits-all approaches are frequently ineffective. Precise site-specific drug delivery will continue to be difficult until these obstacles are overcome by sensible nanocarrier design. However, it is anticipated that overcoming these challenges will propel the creation of next-generation nanotherapeutics with enhanced clinical efficacy.[18,19]

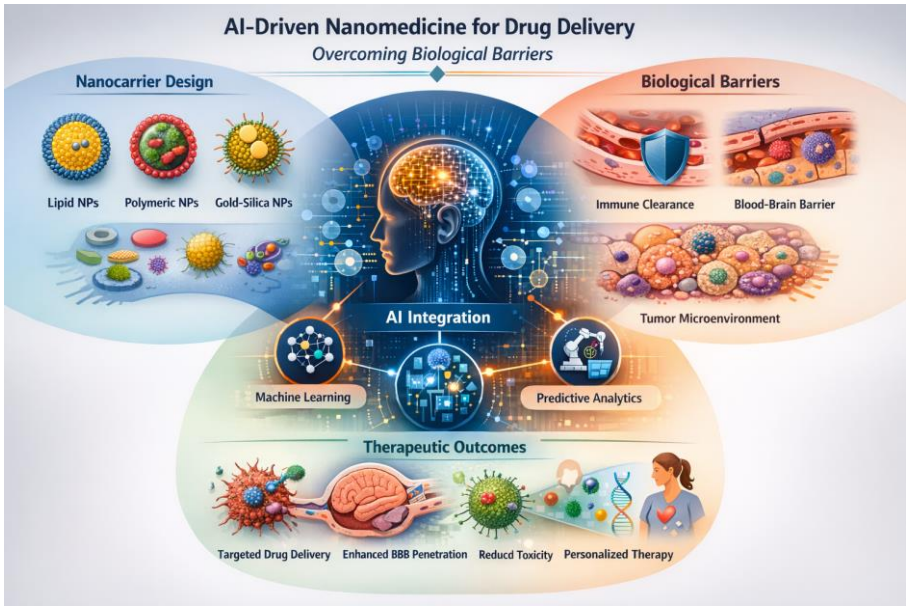
3.3. Role of Artificial Intelligence in Nanomedicine

3.3.1. AI Technique in drug delivery

Because of their easy synthesis and affordable production, small molecules are still crucial to the pharmaceutical industry. Higher specificity is provided by biomolecules, but they present difficult pharmacokinetic and stability issues.

While AI improves drug discovery and formulation development, human expertise is still needed to interpret results and make trustworthy decisions.[53] Both real-world and virtual applications of artificial intelligence in medicine improve surgical accuracy, diagnostic precision, and customised treatment plans. AI speeds up drug discovery and enhances clinical decision-making by evaluating enormous medical and molecular datasets, which eventually results in more effective and patient-centered healthcare.[54] The lengthy and complex process of drug discovery includes target identification, hit selection, lead optimisation, and clinical validation. Artificial intelligence accelerates this process through molecular design, virtual screening, and predictive modelling, boosting output while reducing costs and time.[55] Because of their high surface-to-volume ratio, improved stability, targeted biodistribution, and capacity to get past biological barriers, nanoparticles (NPs) provide a number of advantages in drug delivery. However, physiological variability, patient heterogeneity, and gaps between animal and human studies continue to limit clinical translation, underscoring the necessity of precision-driven nanomedicine approaches.[57] The use of AI in targeted drug delivery signifies a change from empirical approaches to closed-loop, intelligent design frameworks. This data-driven strategy speeds up therapeutic development by enabling ongoing optimisation through iterative feedback. In this context, there are three levels of adaptability: system-level adaptability, which allows real-time personalisation using patient-specific physiological inputs; computational adaptability, which involves AI models that improve predictions as new data emerges; and material adaptability, where nanocarriers respond to stimuli like pH or enzymes. These layers work together to support intelligent, flexible, and customised drug delivery methods.[20] The ability of machines to mimic

human cognitive processes is known as artificial intelligence (AI). Automated data analysis, high-precision forecasts, ongoing learning, and early disease detection and monitoring via sophisticated data interpretation are some of its main benefits.[34] The use of computational algorithms, such as machine learning (ML) and natural language processing (NLP), to evaluate medical data and assist clinical decision-making is referred to as artificial intelligence (AI) in the medical field. By identifying patterns in vast amounts of healthcare data, AI improves patient monitoring, drug discovery, treatment planning, and diagnostic accuracy. Medical imaging, virtual health assistants, electronic health records, and personalised medicine are just a few of its uses. AI has developed through advances in machine learning and deep learning since its beginnings in early expert systems like MYCIN, and it is now a key component of precision and data-driven healthcare.[35]



In order to find patterns and produce predictive insights for the diagnosis and treatment of diseases, artificial intelligence (AI) algorithms examine complicated datasets. While deep learning (DL) uses multilayer neural networks to process big and complicated datasets, machine learning (ML), a subset of artificial intelligence, allows systems to learn from data without explicit programming. By utilising digital clinical and omics data, AI-driven ML and DL models in oncology have revolutionised prognosis and treatment planning. Supervised learning, which uses labelled data to predict outcomes, unsupervised learning, which finds hidden molecular patterns, and semi-supervised learning, which combines both for increased accuracy, are examples of machine learning techniques. In medical imaging, deep neural networks—convolutional neural networks in particular—are frequently used to analyse CT, MRI, and histopathological images.[36] Inspired by biological neural systems, artificial neural networks (ANNs) are effective tools for simulating intricate, nonlinear relationships in pharmaceutical development. Early research showed that they were superior to conventional response surface techniques for both establishing in vitro–in vivo correlations and predicting drug release from controlled-release formulations. Comparative studies revealed that feedforward and generalised regression neural networks linked pharmacokinetic behaviour to dissolution profiles with high accuracy. By fusing interpretable "if-then" rules with robust predictive performance, hybrid neurofuzzy models further improved formulation modelling. All things considered, ANN-based methods offer reliable, data-driven assistance for knowledge extraction, process control, and formulation optimisation in drug development.[37]

Table 1: Small Molecules vs Biomolecules vs AI in Drug Development.

	Small Molecules	Biomolecules	AI Approach
Size	Small (<1 kDa)	Large & complex	Computational
Stability	High	Sensitive	Data-dependent
Cost	Low	High	Reduces R&D cost
Administration	Mostly oral	Mostly injectable	Not applicable
Key Advantage	Easy synthesis	High specificity	Fast prediction & optimization

A. Machine learning

Using techniques like supervised and unsupervised learning, machine learning (ML), a branch of artificial intelligence, allows models to identify patterns in data and make predictions without the need for explicit programming. In order to analyse complex and sequential data, deep learning (DL), an advanced version of machine learning, uses neural network architectures such as feedforward networks, recurrent neural networks (RNNs), and transformers.[56]

Machine learning (ML), which is a component of artificial intelligence (AI), allows data-driven prediction of intricate, high-dimensional relationships that are challenging to understand with conventional linear models. By effectively modelling multi-parameter interactions and optimising structure-function relationships beyond traditional trial-and-error methods, AI/ML helps drug delivery overcome the "curse of dimensionality."[58] By locating binding sites and calculating binding affinity using sequence and structural data, sophisticated machine learning and deep learning models are being used more and more to forecast protein–peptide interactions. This ability is demonstrated by tools like PepBind, CAMP, and InterPep, though their efficacy is frequently limited by reliance on comprehensive structural data and pre-existing template information.[61]

B. Deep learning

Deep learning (DL) has great potential in medical imaging and bioinformatics because it makes it possible to model complex, high-dimensional biomedical data effectively using flexible multilayer neural networks. However, the creation of reliable, comprehensible, and flexible DL models is required due to issues like scarce labelled data, biological sample variability, distribution shifts, and ethical restrictions.[56]

C. Futuristic AI in Drug Design

Lipinski's Rule of Five-guided traditional small molecules have given way to novel approaches in modern drug discovery that target intricate and previously "undruggable" biological systems. Target identification, virtual screening, ADME/T prediction, and hit-to-lead optimisation are now improved by artificial intelligence (AI) and deep learning (DL), allowing for more effective and logical drug design.[59] Scientific and technological developments quickly impact drug discovery, where better early-stage design lowers expensive late-stage failures. By evaluating large datasets, finding the best targets and ligands, and facilitating the quicker, more effective creation of safe, efficient, and possibly patient-tailored treatments, artificial intelligence (AI) speeds up this process.[60]

3.3.2 AI -Guidelines strategies to overcome biological barrier

A total of 36 articles—19 guidelines, 14 consensus statements, and 3 standards—published between 2019 and 2022 were examined. Twenty publications came from China and Australia, and sixteen came from Europe and the US. Clinical applications included radiology practice, reporting guidelines for AI interventions, and disease screening, diagnosis, and treatment—most frequently in retinal disease, colorectal tumours, pulmonary nodules, and glaucoma.

Personalised medicine, biomedical dataset construction, and AI data collection and annotation across imaging modalities were covered in other articles. AI ethics and governance were the subject of five publications.[38] Codes of ethics and professional guidelines institutionalise journalistic norms and values, such as objectivity, impartiality, and transparency, which form the ethical basis of journalism. Guidelines shape what is considered "good" journalistic practice by translating moral principles into practical routines, while norms offer moral guidance. Journalism is viewed as a field shaped by normative, coercive, and mimetic pressures that propel standardisation and legitimacy-seeking behaviours across news organisations, according to Institutional Theory. Through negotiated and changing professional frameworks, these institutional dynamics explain both the continuation of journalistic practices and the gradual integration of innovations, including cutting-edge technologies like artificial intelligence.[39] Large-scale efforts to standardise and exchange healthcare data are motivated by the scarcity of high-quality medical datasets. Large-scale AI-driven analyses in fields like cancer, nephrology, and transplantation are made possible by the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM), which harmonises heterogeneous clinical data across institutions. Multimodal AI model development is improved by extensions like the Radiology CDM, which further integrate imaging and tabular data. Predictive modelling, patient stratification, and personalised treatment research are all supported by standardised CDMs; however, clinical translation is still hampered by inadequate reporting of AI-based clinical studies. In order to guarantee transparency, reproducibility, and the ethical application of clinical AI, reporting guidelines and FAIR (Findable, Accessible, Interoperable, Reusable) data principles have been promoted. This review highlights the significance of current AI reporting guidelines for enhancing the calibre and dependability of biomedical AI research.[40] Due to poor tumour accumulation and numerous biological barriers, cell membrane-based nanocarriers continue to be clinically limited despite their improved biocompatibility and circulation time. Nanoparticles encounter opsonisation, immune clearance, restricted tumour penetration, lysosomal degradation, and drug efflux following intravenous administration, all of which diminish therapeutic efficacy.[62]

Table 2: Biological Barrier Challenges AI-driven Strategy Key Outcome.

Blood circulation / MPS clearance	Rapid opsonization and liver/spleen uptake	ML models optimize nanoparticle size, shape, and surface chemistry (e.g., PEG density)	Prolonged circulation time
Protein corona formation	Altered targeting and loss of functionality	AI predicts protein corona composition using physicochemical datasets	Improved targeting stability
Tumor vasculature (EPR variability)	Heterogeneous permeability	ML-based patient stratification and EPR prediction	Enhanced tumor accumulation
Tumor extracellular matrix (ECM)	Dense ECM restricts penetration	AI-optimized particle size, stiffness, and enzyme-responsive coatings	Improved intratumoral penetration
Cell membrane	Low cellular uptake	AI-guided ligand selection for receptor-mediated endocytosis	Increased cellular internalization
Endosomal/lysosomal barrier	Drug degradation	DL models design pH/redox-responsive nanocarriers	Efficient endosomal escape
Blood–Brain Barrier (BBB)	Tight junctions limit drug entry	AI-assisted prediction of BBB-permeable nanomaterials	Enhanced CNS drug delivery
Mucus barrier	Trapping of nanoparticles	AI-optimized surface charge and hydrophilicity	Improved mucus penetration
Drug efflux pumps (e.g., P-gp)	Reduced intracellular drug levels	AI identifies efflux-inhibiting formulations	Increased drug retention
Immune recognition	Inflammatory clearance	AI-designed biomimetic or cell membrane-coated NPs	Reduced immunogenicity

3.4. Case studies and recent advice of al in drug delivery

3.4.1. Merging Advanced Technologies with Drug Delivery

By simulating structure-function relationships, optimising formulation parameters, and forecasting release kinetics for better therapeutic performance, artificial intelligence (AI) improves drug delivery. Although there are still issues with data quality, interpretability, and biological integration, future integration with smart devices, sensors, microchips, and robotic systems may allow for adaptive drug release and real-time monitoring.[63]

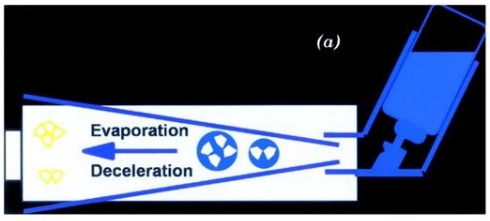
3.4.1.1. IMPROVING DRUG DELIVERY EFFICIENCY TO THE LUNG

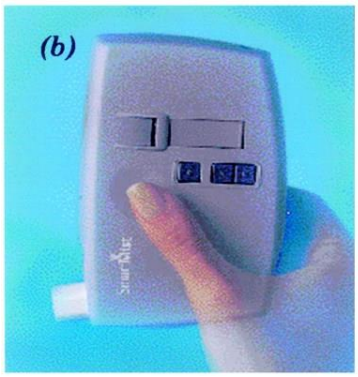
1. NEBULIZER

Patient breathing patterns and device design have a significant impact on lung deposition efficiency in nebulizer-based pulmonary drug delivery. Because of ongoing aerosol generation and drug loss during exhalation, conventional jet nebulisers usually only deliver 8–14% of the loaded dose to the lungs. By coordinating aerosol release with inspiration, recent developments like breath-actuated and computer-controlled nebulisers have increased dose-to-lung efficiency. For the best therapeutic results, the right device and operating conditions are crucial.[64]

2. Pressurized MDIs and Accessories

Because of their portability, precise dose metering, and ability to protect formulations using HFA propellants, metered-dose inhalers (MDIs) continue to be the gold standard for pulmonary drug delivery. However, adequate coordination between inhalation and actuation is crucial for effective lung deposition (DTL), with substantial drug loss taking place in the mouthpiece and oropharynx. Although spacers and reservoirs can enhance delivery and lessen throat deposition, incorrect use or design flaws can drastically reduce overall dosing efficiency.[64]





4. Challenges and limitation

Although AI-assisted robotic surgery improves cancer care precision, there are several obstacles to overcome, such as high costs, the requirement for specialised training, technical issues, and the absence of haptic feedback. Widespread adoption is further hampered by worries about algorithmic bias, data privacy, limited transparency, and ambiguous legal accountability. For safe and equitable clinical implementation, these problems must be addressed through

improved regulations, cybersecurity, explainable AI, and system integration.[65] Mammography, ultrasound, MRI, and biopsy are used to diagnose breast cancer. Although mammography is the gold standard, it frequently needs additional imaging due to its decreased sensitivity in dense breast tissue. While MRI offers high sensitivity but is more expensive and less accessible, ultrasound enhances detection but requires operator expertise. The invasive nature of biopsy highlights the need for safer, more affordable, and noninvasive alternatives for early detection, even though it is still the gold standard for diagnosis.[67]

4.1. Challenges Ahead with ML and AI in Nanotoxicology Modeling

A number of significant obstacles have surfaced as the combination of AI and ML advances nanomedicine research. Although these methods have expedited the design of lipid nanoparticles (LNPs) and uncovered intricate structure–activity relationships, their complete application is hampered by poor data quality, a lack of standardisation, inadequate model validation, and translational obstacles. To fully realise the potential of AI/ML in nanomedicine, these problems must be resolved through reliable datasets, uniform procedures, and interdisciplinary cooperation.[66] To guarantee responsible and secure applications, especially in nanotoxicology, ethical standards for AI and ML in nanomedicine are crucial. Advanced nanomaterial design and customised cancer treatments are made possible by ML-based tools like I-TASSER, but their full potential is still constrained by difficulties with computational prediction and intricate physiological modelling.[68]

5. Future Perspectives

The creation of highly effective and low-toxicity nanomedicines that can precisely target tumours while reducing systemic side effects is essential for the future of nanoparticle-based cancer immunotherapy. It will be crucial to gain a better understanding of the interactions between nanoparticles and the immune system, as well as to find trustworthy predictive biomarkers and tailored combination strategies. To successfully convert promising laboratory results into useful clinical applications, it is also crucial to establish clinically relevant preclinical models and enhance scalable and repeatable manufacturing processes.[69] By creating multifunctional nanoscale diagnostic and therapeutic platforms, nanotechnology is quickly revolutionising vascular imaging and targeted drug delivery. However, rational design of "smart" nanocarriers based on a thorough understanding of physicochemical properties, biological interactions, and disease-specific microenvironments is necessary to realise its full in vivo potential. In order to guarantee safe, effective, and clinically applicable nanomedicine applications in the future, it will be essential to address toxicity concerns and bolster basic research.[70]

6. CONCLUSION

By cleverly combining nanocarrier design, biological barrier navigation, and therapeutic performance, AI-driven nanomedicine is revolutionising drug delivery. Precision, efficacy, and safety can be increased by rationally optimising particle size, surface chemistry, targeting ligands, and drug release profiles using sophisticated machine learning models.

AI speeds up the creation of customised and effective nanotherapeutics by deciphering intricate nano–bio interactions and getting past physiological obstacles like the mononuclear phagocyte system, tumour microenvironment, and cellular membranes. In the end, the combination of nanotechnology and artificial intelligence has enormous potential to transform precision medicine and next-generation drug delivery.

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