Nanobiotechnology in Targeted Drug Delivery Systems

2

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Introduction

Nanobiotechnology has emerged as one of the most transformative interdisciplinary domains in contemporary biomedical and pharmaceutical sciences by integrating nanotechnology, molecular biology, biotechnology, materials science, and pharmaceutical engineering for the development of advanced therapeutic systems. The fundamental objective of nanobiotechnology in drug delivery is to improve the precision, efficacy, and safety of therapeutic interventions through nanoscale engineering of drug carriers capable of selective interaction with diseased tissues and cellular targets. Conventional dosage forms frequently exhibit limitations including poor aqueous solubility, rapid systemic clearance, nonspecific biodistribution, limited permeability across biological barriers, inadequate intracellular uptake, dose-dependent toxicity, and low therapeutic index. Nanobiotechnology addresses these limitations by developing nanoscale delivery systems capable of enhancing solubility, protecting labile molecules from degradation, improving pharmacokinetics, prolonging systemic circulation, and enabling controlled or stimuli-responsive release at target sites (1,2). The conceptual basis of targeted drug delivery is historically linked with Paul Ehrlich's "magic bullet" theory, which proposed that therapeutic agents should selectively destroy diseased cells while sparing healthy tissues. Although classical pharmaceutical systems could not fully achieve this principle, nanoscale delivery platforms have significantly advanced the realization of selective therapy. Nanocarriers including liposomes, polymeric nanoparticles, dendrimers, polymeric micelles, solid lipid nanoparticles, nanotubes,

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metallic nanoparticles, nanocrystals, quantum dots, and polymersomes possess tunable physicochemical characteristics that permit site-specific delivery and molecular-level interactions with pathological tissues (3). Biological systems naturally operate at the nanoscale level. Proteins, enzymes, DNA, RNA, receptors, viruses, ion channels, and intracellular vesicular systems possess dimensions within the nanometer range. Nanobiotechnology exploits this nanoscale compatibility to engineer delivery systems capable of mimicking natural biological interactions. Such nanosystems can cross physiological barriers, interact with cell membranes, enter intracellular compartments, and release therapeutic cargo in a controlled manner. The emergence of targeted nanomedicine has therefore profoundly altered therapeutic strategies in oncology, infectious diseases, neurological disorders, cardiovascular diseases, inflammatory disorders, regenerative medicine, gene therapy, and vaccine development (4).

Fundamental Principles of Targeted Nanodrug Delivery

The efficiency of nanoparticle-mediated drug delivery is primarily governed by particle size, morphology, surface charge, hydrophobicity, biodegradability, ligand conjugation, and colloidal stability. Nanoparticles generally range between 1 and 1000 nm, although most biomedical nanocarriers are designed within the 10–200 nm range to optimize tissue penetration and systemic circulation. Reduction in particle size substantially increases surface area-to-volume ratio, thereby enhancing dissolution kinetics and saturation solubility of poorly water-soluble compounds. The physicochemical basis of enhanced dissolution is described by the Noyes–Whitney equation:

$$\frac{dC}{dt} = \frac{DA(C_s - C)}{h}$$

Where dC/dtrepresents dissolution rate, Ddenotes diffusion coefficient, Aindicates surface area, $C_s$represents saturation solubility, Cdenotes bulk concentration, and $h$indicates diffusion layer thickness. Reduction in particle size therefore significantly accelerates dissolution and absorption of hydrophobic drugs (5).

The increase in saturation solubility with decreasing particle radius is further explained by the Kelvin equation:

$$\ln\left(\frac{S}{S_0}\right) = \frac{2\gamma V_m}{rRT}$$

Where Srepresents saturation solubility of nanoparticles, S_0denotes bulk solubility, γrepresents interfacial tension, $V_m$indicates molar volume, $r$is particle radius, $R$is the gas constant, and Trepresents temperature. These principles collectively explain the

improved dissolution and enhanced oral bioavailability observed with nanosized drug formulations (6). Targeted nanodrug delivery operates through passive targeting, active targeting, and stimuli-responsive mechanisms. Passive targeting relies primarily on physiological abnormalities associated with diseased tissues. In tumors, defective angiogenesis generates leaky vasculature with fenestrations ranging from 100 to 800 nm, while impaired lymphatic drainage leads to nanoparticle accumulation through the Enhanced Permeability and Retention (EPR) effect. Active targeting involves surface functionalization of nanocarriers with ligands such as antibodies, peptides, folate, aptamers, transferrin, or carbohydrates that specifically recognize overexpressed receptors on diseased cells (7). Surface engineering critically influences biological fate and biodistribution. Hydrophobic nanoparticles are rapidly opsonized by plasma proteins and cleared by the mononuclear phagocyte system. Polyethylene glycol coating, commonly referred to as PEGylation, creates steric stabilization that minimizes protein adsorption and prolongs circulation half-life. Shape also influences vascular dynamics and cellular uptake because spherical, rod-shaped, worm-like, and tubular nanostructures exhibit distinct margination, endocytosis, and tissue retention characteristics (8).

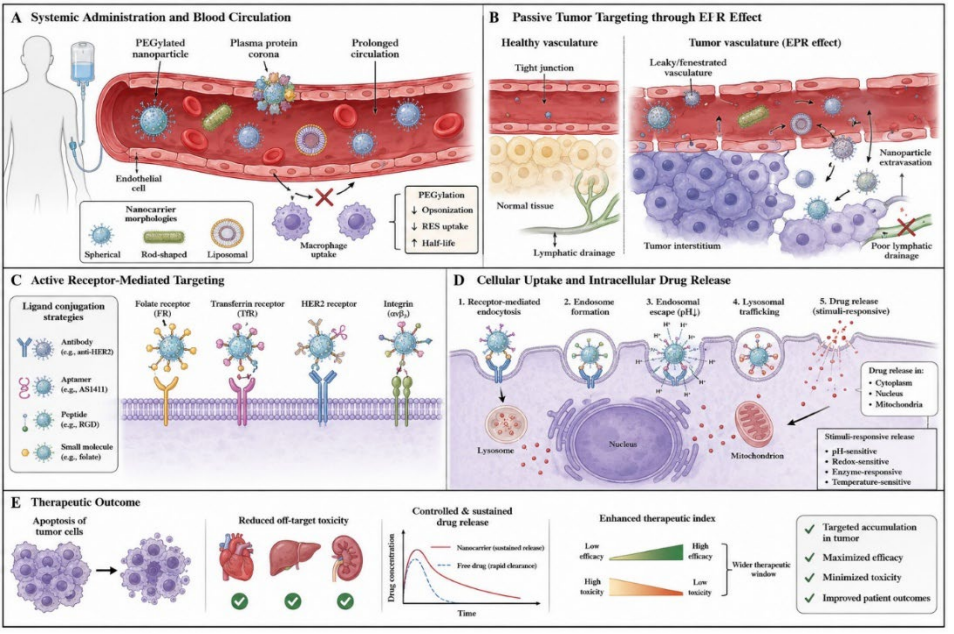


Figure-1: Mechanisms and Pathways of Targeted Nanodrug Delivery in Biological Systems

Nanoparticles as Pharmaceutical Delivery Platforms

Nanoparticles constitute one of the most versatile nanobiotechnological platforms in targeted drug delivery. These colloidal carriers can encapsulate hydrophilic drugs, hydrophobic molecules, peptides, proteins, vaccines, nucleic acids, and imaging agents. Their nanoscale dimensions permit efficient penetration across biological membranes and physiological barriers, including the blood-brain barrier. Nanoparticles improve therapeutic efficacy through sustained release, enhanced intracellular uptake, reduced systemic toxicity, and improved pharmacokinetic behavior (9).

Nanoparticles may be fabricated from biodegradable polymers, lipids, proteins, silica, metals, phospholipids, or hybrid biomaterials. The drug may be entrapped within the carrier matrix, adsorbed onto the surface, chemically conjugated, or dissolved within an internal cavity depending on carrier design. Their exceptionally high surface area enhances interaction with biological membranes and facilitates receptor-mediated uptake. Nanoparticles are particularly valuable for poorly soluble drugs including paclitaxel, amphotericin B, cyclosporine, tacrolimus, and camptothecin, whose clinical performance is often limited by low dissolution rates (10).

Polymeric Nanoparticles

Polymeric nanoparticles are among the most extensively investigated nanosystems for targeted drug delivery due to their biodegradability, tunable release kinetics, and structural versatility. These nanoparticles are prepared using synthetic polymers such as poly(lactic acid) (PLA), poly(glycolic acid) (PGA), poly(lactic-co-glycolic acid) (PLGA), polycaprolactone, and polycyanoacrylate, as well as natural polymers including chitosan, gelatin, dextran, albumin, and alginate (11). Polymeric nanoparticles exist either as nanospheres or nanocapsules. In nanospheres, therapeutic molecules are dispersed throughout the polymer matrix, whereas nanocapsules possess a core-shell architecture where the drug is confined within an internal cavity surrounded by a polymeric membrane. Such systems provide controlled degradation, sustained release, improved drug stability, and enhanced site-specific delivery. PLGA nanoparticles loaded with paclitaxel, doxorubicin, and docetaxel have demonstrated enhanced tumor accumulation and reduced systemic toxicity in several experimental cancer models (12).

Lipid-Based Nanocarriers

Lipid-based nanocarriers have gained remarkable importance because of their biocompatibility and membrane-mimicking properties. Liposomes are vesicular systems composed of phospholipid bilayers surrounding an aqueous core. Their amphiphilic

structure allows simultaneous encapsulation of hydrophilic and hydrophobic therapeutic agents. Liposomes protect drugs from enzymatic degradation and reduce systemic toxicity while permitting controlled release (13). PEGylated liposomes, commonly referred to as stealth liposomes, exhibit prolonged circulation times due to reduced recognition by the reticuloendothelial system. Clinically approved liposomal formulations such as Doxil and Daunosome have demonstrated substantial success in cancer chemotherapy by improving therapeutic efficacy while reducing cardiotoxicity associated with conventional anthracycline therapy (14). Solid lipid nanoparticles (SLNs) were developed to combine the advantages of liposomes and polymeric nanoparticles while minimizing solvent-associated toxicity. SLNs consist of solid physiological lipids stabilized by surfactants and exhibit excellent biocompatibility, controlled release behavior, and enhanced stability. Their lipidic nature facilitates interaction with biological membranes and improves penetration across physiological barriers including the blood-brain barrier (15).

Polymeric Micelles, Polymersomes, and Dendrimers

Polymeric micelles are self-assembled nanostructures formed from amphiphilic block copolymers possessing hydrophobic cores and hydrophilic coronas. Their hydrophobic interior efficiently solubilizes poorly water-soluble drugs, whereas the hydrophilic shell enhances systemic stability and prolongs circulation time. Polymeric micelles are especially valuable for delivering hydrophobic anticancer agents such as paclitaxel and docetaxel (16). Polymersomes resemble liposomes structurally but are composed of amphiphilic block copolymers rather than phospholipids. Their thicker polymeric membranes confer greater mechanical stability, tunable permeability, and prolonged circulation. These systems are highly promising for controlled release, protein delivery, theranostics, and gene therapy applications (17). Dendrimers are highly branched nanoscale macromolecules possessing multiple surface functional groups and internal cavities capable of high drug loading. Therapeutic agents may be encapsulated within internal cavities or covalently linked to terminal groups. Their precise molecular architecture permits extensive surface modification for receptor-mediated targeting, making dendrimers highly suitable for gene delivery and anticancer therapy (18).

Nanobiotechnology in Brain Targeted Drug Delivery

The blood-brain barrier (BBB) represents one of the greatest obstacles in neuropharmacology because tightly joined endothelial cells restrict penetration of most therapeutic molecules into the central nervous system. Nanobiotechnology has enabled development of nanosystems capable of crossing the BBB through receptor-mediated

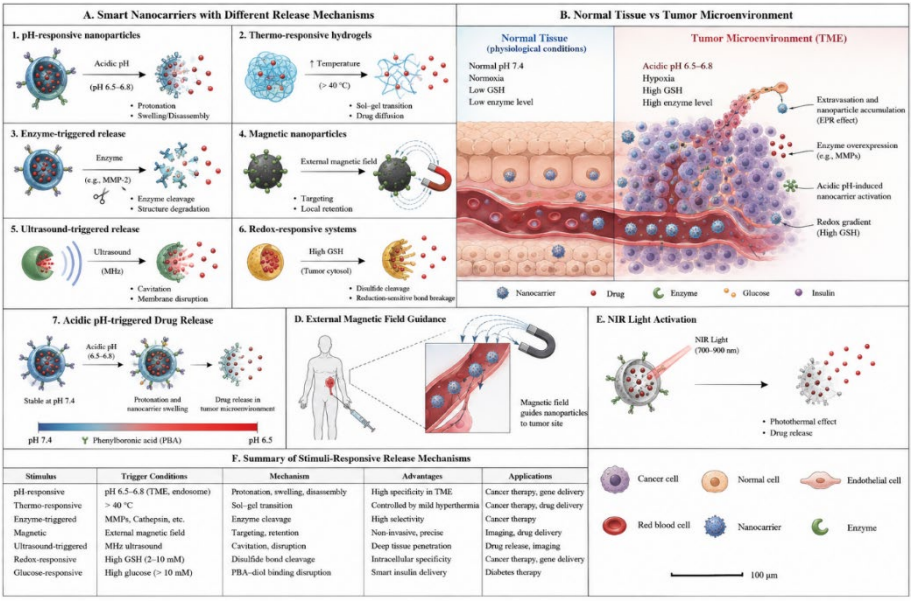
transcytosis, adsorptive-mediated transport, or carrier-mediated mechanisms (19). Nanoparticles coated with transferrin, lactoferrin, polysorbate-80, glutathione, or Angiopep exhibit enhanced BBB penetration and selective brain accumulation. PEGylated nanoparticles loaded with paclitaxel, methotrexate, and doxorubicin have shown promising results in glioblastoma therapy by increasing intracerebral drug concentration while minimizing systemic toxicity. Angiopep-functionalized nanoparticles demonstrate high transcytosis efficiency through interaction with low-density lipoprotein receptor-related protein-1 (LRP-1) expressed on brain endothelial cells (20).

Nanobiotechnology in Gene and Vaccine Delivery

Gene therapy requires carriers capable of protecting nucleic acids from enzymatic degradation while enabling intracellular delivery and endosomal escape. Viral vectors, although efficient, present risks related to immunogenicity and mutagenesis. Nanobiotechnology has therefore accelerated development of non-viral vectors based on polymeric nanoparticles, dendrimers, cationic liposomes, and solid lipid nanoparticles (21). Cationic nanocarriers electrostatically interact with negatively charged DNA, RNA, siRNA, or mRNA molecules to form compact nanocomplexes facilitating cellular uptake through endocytosis. Lipid nanoparticles have become especially important in mRNA vaccine technology because they protect nucleic acids from degradation and enhance intracellular delivery. Nanoparticle-based vaccines also improve antigen presentation and stimulate stronger immune responses by targeting dendritic cells and antigen-presenting cells (22).

Stimuli-Responsive and Smart Nanocarriers

Recent advances in nanobiotechnology have resulted in development of intelligent drug delivery systems capable of responding to environmental or external stimuli including pH, temperature, enzymes, redox potential, magnetic fields, ultrasound, glucose concentration, and light exposure. Such systems permit site-specific release and reduce premature leakage of therapeutic agents (23). Tumor tissues often exhibit acidic microenvironments and elevated enzyme expression. pH-sensitive polymeric nanoparticles therefore remain stable under physiological conditions but rapidly release drugs under acidic conditions within tumors or intracellular lysosomes. Smart hydrogels and molecularly imprinted polymers represent advanced biomimetic systems capable of auto-regulated therapeutic release, including glucose-responsive insulin delivery systems for diabetes management (24).



Stimulus	Trigger Conditions	Mechanism	Advantages	Applications
pH-responsive	pH 6.5–6.8 (TME, endosome)	Protonation, swelling, disassembly	High specificity in TME	Cancer therapy, gene delivery
Thermo-responsive	> 40 °C	Sol–gel transition	Controlled by mild hyperthermia	Cancer therapy, drug delivery
Enzyme-triggered	MMPs, Cathepsin, etc.	Enzyme cleavage	High selectivity	Cancer therapy
Magnetic	External magnetic field	Targeting, retention	Non-invasive, precise	Imaging, drug delivery
Ultrasound-triggered	MHz ultrasound	Cavitation, disruption	Deep tissue penetration	Drug release, imaging
Redox-responsive	High GSH (2–10 mM)	Disulfide bond cleavage	Intracellular specificity	Cancer therapy, gene delivery
Glucose-responsive	High glucose (> 10 mM)	PBA–diol binding disruption	Smart insulin delivery	Diabetes therapy

Figure-2: Smart and Stimuli-Responsive Nanocarriers for Precision Drug Delivery

Nanotoxicology and Safety Concerns

Despite enormous therapeutic potential, nanoparticle safety remains a critical challenge in clinical translation. Nanoparticles possess high surface reactivity and may interact unpredictably with proteins, membranes, and intracellular components. Potential adverse effects include oxidative stress, inflammation, genotoxicity, immunotoxicity, pulmonary toxicity, and neurotoxicity (25). Carbon nanotubes, metallic nanoparticles, and poorly biodegradable nanomaterials may persist within tissues such as lungs, liver, spleen, kidneys, and brain following chronic exposure. Oxidative stress induced through reactive oxygen species generation represents one of the major mechanisms of nanoparticle-mediated toxicity. Comprehensive toxicological evaluation, biodistribution studies, biodegradation assessment, and long-term safety monitoring are therefore essential before clinical implementation of nanomedicines (26).

Table-1: Major Nanocarrier Systems Used in Targeted Drug Delivery

Nanocarrier System	Principal Composition	Typical Size Range	Major Therapeutic Applications	Key Technical Advantages

Polymeric nanoparticles	PLA, PLGA, chitosan, gelatin	10–1000 nm	Cancer therapy and vaccine delivery	Controlled release and biodegradability
Liposomes	Phospholipid bilayers	50–500 nm	Anticancer and antifungal therapy	Biocompatibility and dual drug loading
PEGylated liposomes	PEG-coated phospholipid vesicles	80–200 nm	Tumor targeting	Prolonged circulation time
Solid lipid nanoparticles	Physiological lipids and surfactants	50–1000 nm	Dermal and parenteral delivery	High stability and controlled release
Polymeric micelles	Amphiphilic block copolymers	10–100 nm	Hydrophobic anticancer drugs	Solubilization enhancement
Polymersomes	Diblock copolymer vesicles	50–500 nm	Gene and protein delivery	Mechanical robustness
Dendrimers	Branched polymeric macromolecules	1–20 nm	Gene delivery and imaging	High drug loading capacity
Chitosan nanoparticles	Cationic polysaccharide	50–500 nm	Mucoadhesive delivery	Permeation enhancement
Gold nanoparticles	Metallic gold	5–100 nm	Photothermal therapy	Optical and plasmonic properties
Iron oxide nanoparticles	Iron oxide	10–100 nm	MRI and magnetic targeting	Superparamagnetism
Quantum dots	Semiconductor nanocrystals	2–10 nm	Imaging and theranostics	Fluorescence stability
Nanocrystals	Pure drug crystals	50–500 nm	Poorly soluble drugs	Enhanced dissolution kinetics

Source references: (5,10–18).

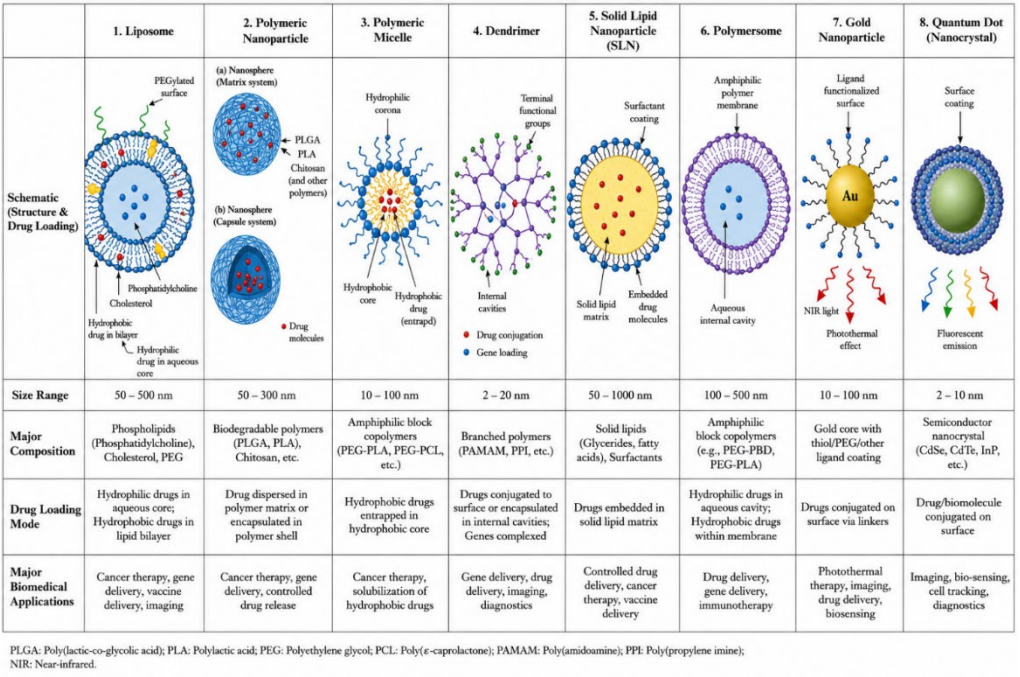


Figure-3: Classification and Structural Architecture of Major Nanocarrier Systems Used in Targeted Drug Delivery

Table-2: Biomedical Applications of Nanobiotechnology-Based Drug Delivery

Disease/Condition	Nanocarrier Used	Therapeutic Agent	Clinical Advantage
Breast cancer	Liposomes	Doxorubicin	Reduced cardiotoxicity
Glioblastoma	PEGylated nanoparticles	Paclitaxel	Enhanced BBB penetration
Tuberculosis	Solid lipid nanoparticles	Rifampicin	Improved bioavailability
Visceral leishmaniasis	Liposomal carriers	Amphotericin B	Macrophage targeting
Parkinson's disease	Polymeric nanoparticles	Dopamine precursors	Sustained CNS delivery
Alzheimer's disease	Ligand-coated nanoparticles	Neuroprotective agents	BBB transport

Rheumatoid arthritis	Dendrimers	Anti-inflammatory drugs	Target specificity
Ocular infections	Chitosan nanoparticles	Antibiotics	Prolonged ocular retention
HIV infection	Polymeric nanoparticles	Antiretroviral drugs	Improved adherence
Gene therapy	Cationic liposomes	DNA/siRNA	Enhanced transfection
Fungal infections	Liposomal amphotericin B	Amphotericin B	Reduced nephrotoxicity
Diabetes mellitus	Smart hydrogels	Insulin	Glucose-responsive release
Brain tumors	Angiopep nanoparticles	Paclitaxel	Receptor-mediated transport
Cardiovascular imaging	Iron oxide nanoparticles	MRI contrast agents	Enhanced imaging precision
Theranostics	Quantum dots	Imaging-drug conjugates	Simultaneous diagnosis and therapy

Source references: (13–24).

Future Perspectives

The future of nanobiotechnology in targeted drug delivery is closely associated with advances in precision medicine, artificial intelligence, molecular diagnostics, biomimetic engineering, and smart biomaterials. Future nanocarriers are expected to evolve beyond passive drug encapsulation toward multifunctional systems capable of simultaneous diagnosis, targeted delivery, controlled release, and therapeutic monitoring. Such theranostic systems may permit real-time assessment of disease progression and treatment response while enabling individualized therapeutic adjustment (27). Biomimetic nanoparticles inspired by exosomes, viral envelopes, and cell membranes are likely to dominate next-generation nanomedicine because of their superior immune compatibility and biological communication capabilities. Integration of biosensors, microelectronics, and nanofabrication technologies may also result in autonomous drug delivery systems capable of physiological sensing and feedback-controlled release. Clinical translation will nevertheless require scalable manufacturing,

reproducible characterization, rigorous toxicological assessment, and harmonized regulatory frameworks to ensure long-term safety and therapeutic reliability (28).

Conclusion

Nanobiotechnology has transformed targeted drug delivery from a conceptual pharmaceutical aspiration into a highly sophisticated biomedical reality. Through nanoscale engineering of therapeutic carriers, it has become possible to improve drug solubility, protect unstable molecules, prolong systemic circulation, enhance intracellular uptake, cross biological barriers, and selectively deliver therapeutic agents to pathological tissues. Nanoparticles, liposomes, polymeric systems, dendrimers, solid lipid nanoparticles, polymeric micelles, quantum dots, and smart biomaterials collectively represent the foundation of next-generation pharmaceutical biotechnology. Their applications in cancer therapy, brain targeting, infectious diseases, vaccine delivery, gene therapy, and theranostics demonstrate the immense translational potential of nanobiotechnology in precision medicine. Despite remarkable scientific progress, challenges related to nanoparticle toxicity, biodegradability, manufacturing reproducibility, regulatory approval, and long-term safety remain substantial barriers to broader clinical implementation. Continued advances in biomaterials engineering, molecular targeting, stimuli-responsive systems, biosensing technologies, and artificial intelligence are expected to reshape the future of nanomedicine into a more intelligent, personalized, and clinically integrated therapeutic platform. Nanobiotechnology is therefore poised to remain a cornerstone of future pharmaceutical innovation and targeted therapeutics.

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