INTERNATIONAL JOURNAL OF PROGRESSIVE RESEARCH IN ENGINEERING MANAGEMENT AND SCIENCE (IJPREMS)
(Int Peer Reviewed Journal)
Vol. 05, Issue 12, December 2025, pp : 530-535
www.ijprems.com
editor@ijprems.com
e-ISSN : 2583-1062
Impact Factor : 7.001

THE FUNCTION OF NANOTECHNOLOGY IN PRECISE DRUG DELIVERY

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DOI: https://www.doi.org/10.58257/IJPREMS45415

ABSTRACT

Nanotechnology has revolutionized drug delivery through the engineering of nanoscale materials that facilitate precise, controlled, and targeted release of therapeutic agents. In the last ten years, notable progress in the design of nanocarriers—such as lipid nanoparticles, polymeric nanoparticles, dendrimers, metallic nanoparticles, and biomimetic systems—has broadened possibilities for clinical application. The effective use of lipid nanoparticle (LNP)-based mRNA COVID-19 vaccines showcased the scalability and practical effectiveness of nano-drug delivery systems, spurring global research and investment. Nevertheless, obstacles like toxicity issues, unclear regulatory pathways, inconsistent reproducibility, and variability in tumor targeting (such as inconsistencies in the EPR effect) continue to hinder widespread adoption. This review highlights advancements in science, progress in clinical settings, existing challenges, and the future potential of nanotechnology-based targeted drug delivery.

Keywords: Nanotechnology, Targeted Drug Delivery, Lipid Nanoparticles, Cancer Therapy, Stimuli-Responsive Systems.

1. INTRODUCTION

Conventional methods of drug delivery encounter significant challenges including non-specific distribution, low bioavailability, short circulation time, and toxicity related to dosage. Targeted drug delivery enhances therapeutic precision by directing medications to affected tissues while reducing systemic adverse effects (6). Nanotechnology significantly contributes to the enhancement of targeted therapies by employing carriers at the nanoscale, typically ranging from 10 to 200 nanometers, which can interact with cellular and molecular structures, traverse biological barriers, and facilitate controlled release mechanisms (7,8). Recent adva ncements in nanomedicine from 2015 to 2025 comprise innovations such as lipid-based mRNA delivery systems, peptides designed to penetrate tumors, biomimetic vesicles, and nanoplatforms that respond to stimuli (9,10).

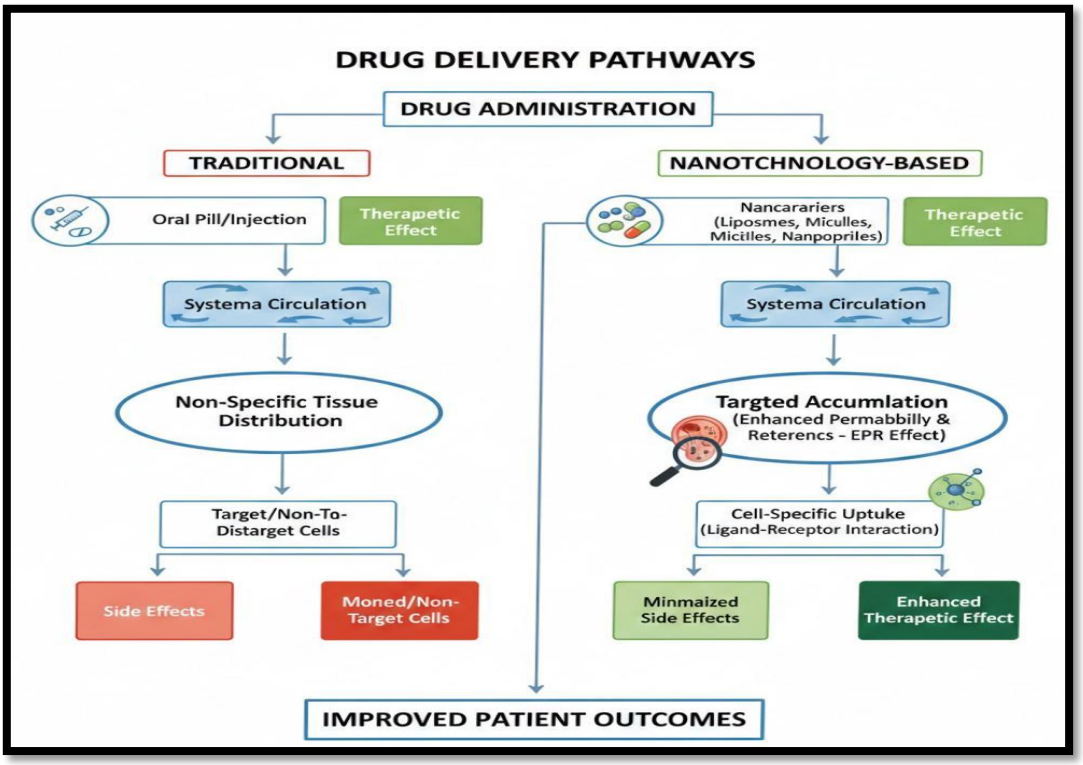

Figure 1: Overview of traditional vs. nanotechnology-based drug delivery pathways

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PRINCIPLES OF TARGETED DELIVERY USING NANOTECHNOLOGY

Size, Shape & Surface Chemistry

Particle size affects biodistribution, clearance, and cellular uptake. Nanocarriers between 50–150 nm demonstrate prolonged circulation and improved cellular entry (11). Surface charge influences interaction with biological membranes; PEGylation is used to improve circulation by avoiding immune recognition (12).

Passive Targeting and EPR Effect

Passive targeting uses features of dysfunctional vasculature seen in tumors, enabling nanoparticle accumulation via the Enhanced Permeability and Retention (EPR) effect (13). However, research between 2019–2024 suggests EPR response varies between patients and tumor types, challenging earlier assumptions (14).

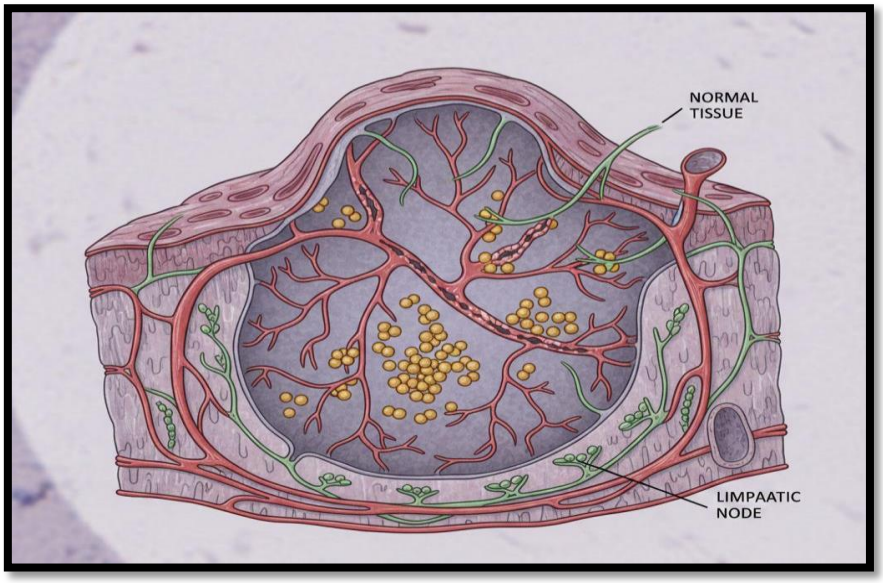

Figure 2: Mechanism of EPR effect in solid tumors

Active Targeting

Active targeting includes surface modification with ligands such as antibodies, aptamers, folate, or transferrin, enabling receptor-mediated uptake (15,16).

Smart and Stimuli-Responsive Systems

Stimuli-responsive nanocarriers can release drugs in response to pH, enzymes, redox environment, ultrasound, light, or temperature (17,18).

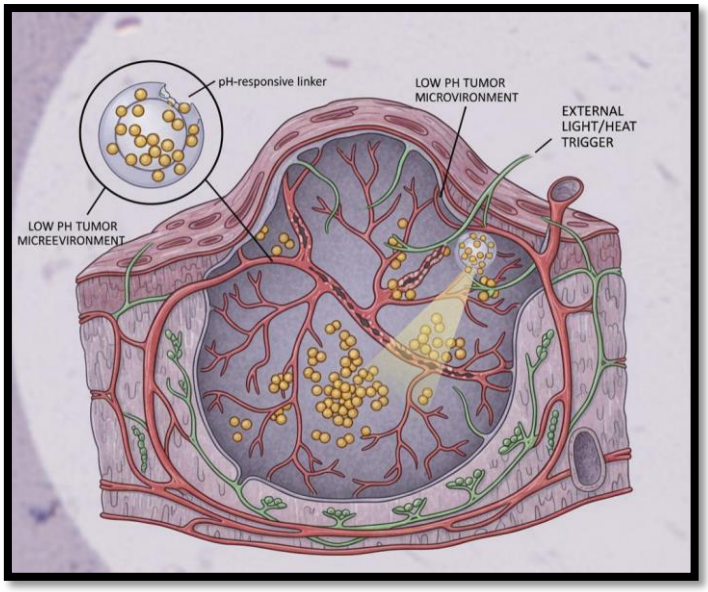

Figure 3: Mechanism of internal (pH) and external (light/heat) responsive nanocarriers

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TYPES OF NANOCARRIERS IN TARGETED DRUG DELIVERY

1. Lipid Nanoparticles (LNPs
2. Polymeric Nanoparticles
3. Dendrimers
4. Metallic Nanoparticles
5. Carbon-Based Nanostructures
6. Biomimetic Nanocarriers

Lipid Nanoparticles (LNPs)

LNPs became a milestone following success in mRNA vaccines. Ionizable lipid chemistry enables improved endosomal escape and reduced toxicity (19,20).

Polymeric Nanoparticles

Biodegradable polymers such as PLGA, chitosan, and PEG enable controlled release and reduced toxicity (21).

Dendrimers

These highly branched carriers allow multivalent conjugation and are used in cancer and gene delivery applications (22).

Metallic Nanoparticles

Gold, silver, and iron oxide nanoparticles are used in diagnostics, imaging, gene delivery, and photothermal therapy (23,24).

Carbon-Based Nanostructures

Carbon nanotubes and graphene possess high drug-loading capabilities but require toxicity modification strategies (25).

Biomimetic Nanocarriers

Recent research focuses on exosomes and cell-membrane-coated nanoparticles to evade immune clearance (26,27).

Table 1: Comparison of major nanocarrier types, advantages, and clinical status

Sr. No.	Nanocarrier Type	Structure/ Composition	Advantages	Clinical Status
1)	Lipid Nanoparticles (LNPs	Spherical vesicles or solid cores made of lipids (phospholipids, cholesterol, ionizable lipids). Includes Liposomes and Solid Lipid Nanoparticles (SLNs).	Highest clinical success; Biocompatible and biodegradable; excellent for delivering mRNA/siRNA (e.g., COVID-19 vaccines); good for hydrophilic/hydrophobic drugs; low immunogenicity.	Multiple FDA-approved formulations (e.g., Doxil, Onpattro, Comirnaty/Spikevax mRNA vaccines). Broad use in infectious disease and oncology.
2)	Polymeric Nanoparticles	Solid colloidal particles (nanospheres/nanocapsules) or self-assembled micelles from biocompatible and biodegradable polymers (e.g., PLGA, PLA, PEG).	Precise controlled/sustained release kinetics; high stability; high drug loading capacity; excellent platform for active targeting through surface functionalization.	Several formulations are FDA-approved (e.g., Abraxane – albumin-bound) or in Phase I-III clinical trials for various cancers and diseases.
3)	Dendrimers	Highly branched, synthetic macromolecules with a central core and numerous, controllable surface functional groups.	Monodisperse (uniform size/shape); high surface area for multi-functionalization (drug, targeting, imaging agent); water-soluble and biocompatible.	Mainly in pre-clinical development, with a few in early Phase I/II clinical trials for drug and gene delivery, and topical microbicides.
4)	Metallic	Solid particles typically made	Excellent stability; unique	Primarily in pre-

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	Nanoparticles	of Gold (Au) or Silver (Ag), often with a functionalized surface coating.	optical/electronic properties for imaging (CT, photothermal) and localized therapy (light/heat conversion); can be used as radiosensitizers.	clinical to early clinical trials (Phase I/II), mainly for cancer diagnosis and treatment (photothermal therapy, radiation enhancement).
5)	Carbon-Based Nanostructures	Structures like Carbon Nanotubes (CNTs) (cylindrical) or Graphene Oxide (GO) (2D sheets) composed entirely of carbon.	Extremely high surface area for drug loading (especially via \pi-\pi stacking); unique mechanical/thermal/electrical properties; efficient photothermal agents (light-to-heat conversion).	Predominantly in pre-clinical research. Safety and long-term biodistribution remain a major focus before widespread clinical entry.
6)	Biomimetic Nanocarriers	Carriers derived from or cloaked with biological materials (e.g., cell membranes like red blood cells, platelets, or cancer cells).	Inherent targeting/stealth properties; long circulation time; reduced immune clearance; can carry biological recognition molecules from the source cell.	An emerging field, primarily in pre-clinical research with some platforms entering early clinical trials for cancer immunotherapy and drug delivery.

MECHANISMS OF CELLULAR UPTAKE & RELEASE

Many nanocarriers gain entry into cells through endocytosis mechanisms, including clathrin-mediated or caveolin-mediated processes (28). The release of contents inside the cell is determined by the design of the carrier:

pH-sensitive release in the acidic environments found in tumors (29). Carriers that respond to enzymes for specific diseased tissue settings (30).Activation through thermo-magnetic or photoresponsive methods (31)

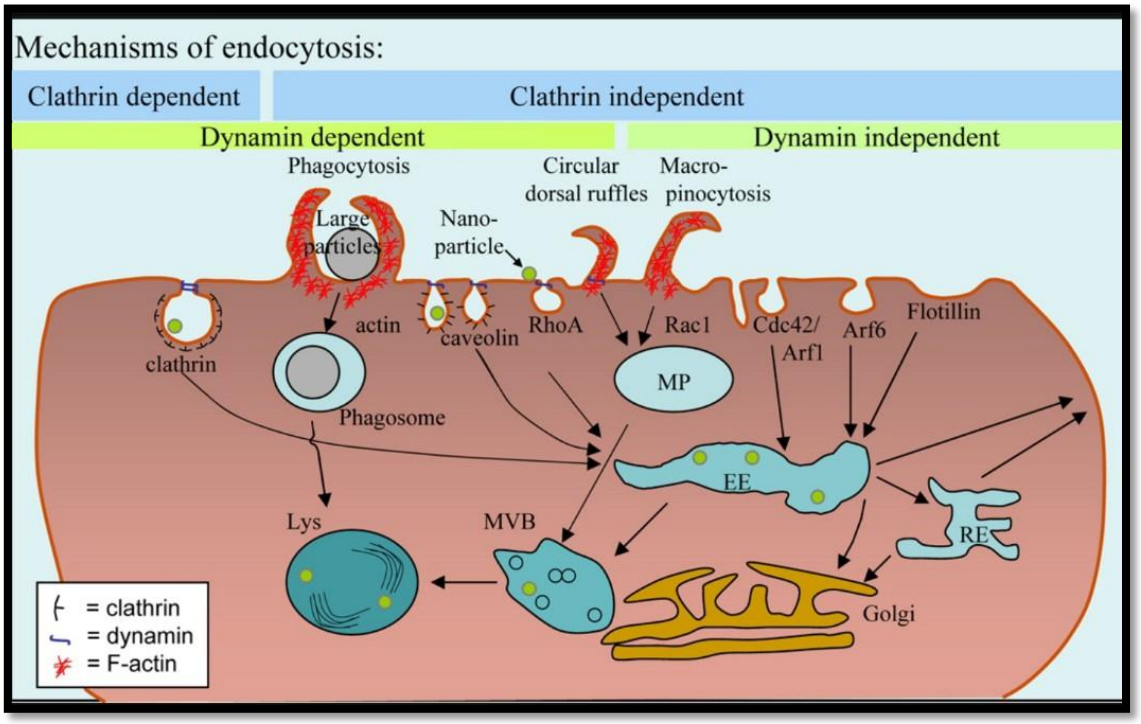

Figure 4: Endocytosis and intracellular release mechanisms of nanoparticles

CLINICAL APPLICATIONS

Cancer

Cancer remains the leading application area for nanomedicine. Clinically approved systems include liposomal doxorubicin and albumin-bound paclitaxel (32). Recent advances integrate diagnosis with therapy (theranostics) (33).

Infectious Diseases

LNP-based COVID-19 vaccines accelerated global investment. Nanocarriers are now being explored for tuberculosis, HIV, malaria, and influenza (34).

Neurological Disorders

Nanocarriers capable of crossing the blood-brain barrier using transferrin or peptide-targeted systems show promise in Alzheimer's and Parkinson's treatment (35,36).

Gene and RNA Medicine

LNPs and polymeric systems are advancing CRISPR, siRNA, and mRNA delivery platforms (37).

2. CHALLENGES AND LIMITATIONS

Regulatory complexity (38)

Limited large-scale reproducibility (39)

Potential long-term toxicity (40)

Variability in immune clearance (41)

3. FUTURE DIRECTIONS

AI-designed nanoparticles

Personalized and organ-specific nanocarriers

Fully biodegradable vectors

Real-time responsive theranostic systems (42–45)

4. CONCLUSION

The last decade has demonstrated remarkable progress in nanotechnology-enabled targeted drug delivery. The clinical translation of nanocarriers has proven their potential in cancer, infectious diseases, neurological disorders, and gene therapy. Continued research, regulatory framework development, and scalable manufacturing will advance nanomedicine toward precision healthcare.

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