Available online on 15.04.2026 at <http://jddtonline.info>

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

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Review Article

Nanotechnology-Driven Drug Delivery System: Recent Advances, Applications and Future Perspectives

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Article Info:



Article History:

Received 22 January 2026
Reviewed 13 March 2026
Accepted 28 March 2026
Published 15 April 2026

Cite this article as:

Chandola M, Dhaundhiyal K, Ojha A, Singh AK, Bhatt V, Nanotechnology-Driven Drug Delivery System: Recent Advances, Applications and Future Perspectives, Journal of Drug Delivery and Therapeutics. 2026; 16(4):185-194 DOI: <http://dx.doi.org/10.22270/jddt.v16i4.7694>

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Abstract

Purpose: With the ability to solve problems of standard medicine, nanotechnology is presently an innovative technology in advanced pharmaceutical delivery. A wide range of nanocarriers, including lipid-based systems, polymeric nanoparticles, self-assembled structures, and functionalized nanomaterials, provides diverse platforms for the delivery of a range of medicaments, extending from pure substances to genetic therapies like *siRNA* ⁴.

Methods: This review highlights the application of nanotechnology-based systems in drug delivery, including their role in tumour research, bronchial delivery, oral therapeutic formulations, and even integrated techniques such as diagnostic-guided therapy, which blends the assessment and cure.

Results: By presenting the accurate transfer and managed release, nanoparticles can strengthen the therapeutic solubility, durability, and uptake while facilitating the therapeutic results and minimizing the side effects^{2,3}. An additional benchmark has been given to Antitumor therapy, where site-specific nanoparticles and reaction-prone system reduce the harm to nourishing cells while strengthening the treatment reproducibility^{3,8}. Green and sustainable nanomaterials focus on the advancement towards reliable, planet-friendly, and user-friendly formulations⁵.

Conclusion: Regardless of these new methods, hardships remain in assuring large-batch production, prolonged safety, loss prevention, and standardization approval⁶. Currently, investigation prevails to more evident technological approaches, plan efficient carriers, and analyse future opportunities where nano-drug delivery could alter the healthcare on an international scale⁷.

Keywords: nanocarriers, bioavailability, diagnostic-guided therapy, targeted delivery, novel drug delivery system.

INTRODUCTION:

Pharmaceutical drug administration has always been a judgmental aspect of advanced treatment, as the potency of any medicament depends not only on therapeutic activity but also on its capability to achieve the site of therapeutic action in sufficient amounts⁸. Traditional drug delivery systems on the other hand, encounter several problems such as low solubility, formulation instability, enhanced metabolism, undesired distribution and adverse effects^{8,9} as shown in **(Fig1)**. These therapeutic challenges emphasize the immediate requirement of more accurate and effective Novel delivery system⁷.

Nanoscale approaches have emerged as a transformative system that focuses on these limitations by facilitating

the framework of nanoscale carriers with novel molecular and chemical characteristics^{1,2}. With a mean particle diameter typically ranging from 1–100 nm, nanovehicles such as polymeric nanocarriers, lipid-based nanoformulations, dendritic carriers, micellar systems, hydrogel nanoparticles, and metallic nanoparticles offer characteristic benefits because of their extended particle surface area, adjustable surface chemistry, and capability for entrapping both hydrophilic and hydrophobic drugs^{9,12}. These characteristics promote solubility, enhanced stability, sustained drug release, and most notably, site-targeted drug delivery that decreases adverse systemic effects while advancing therapeutic potential^{10,11}.

Conventional vs Nanotechnology-Driven Drug Delivery

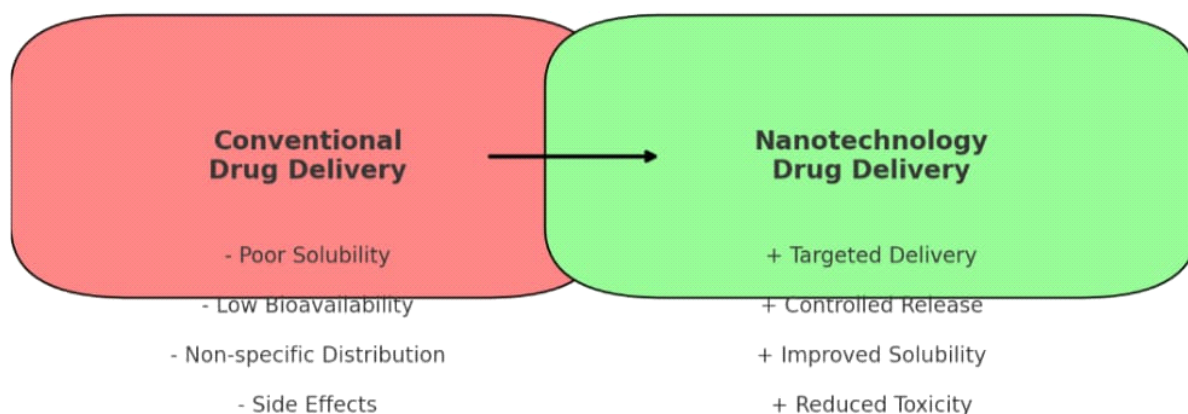


Figure 1: Conventional vs Nanotechnology-Driven Drug Delivery

METHODOLOGY:

This review article was prepared by collecting data from various scientific databases such as PubMed, Google Scholar, and Springer. Applicable research published between 2000 and 2024 were identified using keywords such as "bioavailability", "nanocarriers", "targeted delivery", and "novel drug delivery system".

Studies relevant to nanotechnology-based drug delivery were included, while those not relevant were excluded. The collected data was then evaluated and arranged in order to provide an organized summary of the topic.

NANOTECHNOLOGY IN DRUG DELIVERY

1-TYPES OF NANOCARRIERS-

LIPOSOMES are nanoscale vesicles formed from lipid bilayer that act as a carriers for transferring the drugs, particularly hydrophobic and hydrophilic compounds to particular sites of the body.

DENDRIMERS are unique tree-like structures consisting of a central core, branched layers (dedrons), and a terminal functional groups, which increases the drug effectiveness and decreases the side effects.

POLYMERIC NANOPARTICLES(PNPs) are nanoscale particles made from polymers that enable controlled and targeted drug release.

MICELLES are the self-assembled spherical structures composed of amphiphilic molecule with a non-polar core and a polar shell.

NANOGELS are three-dimensional, hydrogel nanostructures with controllable particle sizes (20 to 250nm) and high drug-loading capacity.

METALLIC NANOPARTICLES(MNPs) enhance drug delivery due to their increased surface area, improved drug durability and half-life.

2- MECHANISM OF DRUG DELIVERY-

-CONTROLLED RELEASE: In a controlled release system, the drug is developed to be released into the body at a

fixed, slow and continuous rate for a prolonged period of time. Its main aim is to maintain a fixed medicinal concentration in the bloodstream without the need for repeated dosing¹³.

MECHANISM OF CONTROLLED RELEASE:

DIFFUSION- CONTROLLED RELEASE: In this, the drug diffuses slowly from the nanocarrier's core through a polymer layer into biological fluids, providing a sustained release.

DEGRADATION-CONTROLLED RELEASE: In this process, biodegradable polymers(PLGA) break down slowly inside the body, leading to the sustained release of the drug.

STIMULI-RESPONSIVE RELEASE: In this, the nanocarriers release the drug only when they are exposed to specific triggers like pH changes or temperature^{14,15}.

-TARGETED DELIVERY: This approach carries the medicament specifically to the intended site with minimal effect on healthy tissues. This enhances the therapeutic efficiency, reduces side effects and helps in maintaining a steady amount of a drug at the target site¹⁴.

There are mainly two types of delivery:

Permeability-driven targeting, which depends on the Enhanced Permeability and Retention(EPR) phenomenon commonly observed in the tumour site.

Ligand-mediated targeting, which involves surface functionalization of nanoparticles with ligands, antibodies or peptides that help in binding.

-STIMULI-RESPONSIVE DRUG DELIVERY: It is engineered to release the drug in response to the particular biological or environmental stimuli. In this, the nano-scale particles are altered with a polymer matrix that can recognise alterations in the surrounding environment. When the stimulating agent is detected, the carrier matrix experiences a physicochemical change, permitting the medicament to be released at the intended site¹⁵.

TYPES OF STIMULI-RESPONSIVE SYSTEMS:

pH-Responsive delivery platform: Formulated to deliver the medication in acidic or basic conditions.

Thermo-Responsive delivery platform: Some polymeric materials alter their structural framework with temperature.

Catalytic Biomolecules Responsive Systems: These enzymes, present in particular tissues can deteriorate the nanocarrier's matrix, which stimulates the drug release only where those biomolecules are functional.

Oxidation-Reduction Responsive Systems: These react to the redox-regulated environment, leading to site-specific drug release¹⁵.

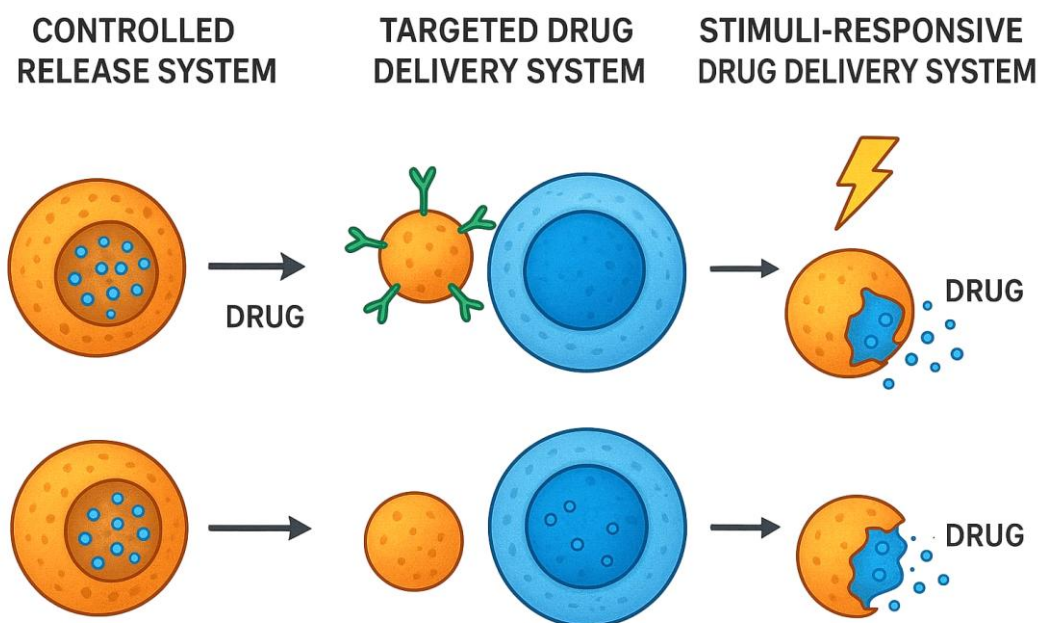


Figure 2: Mechanism of Drug Delivery

APPLICATIONS:

Nanotechnology in pharmaceuticals has improved the way of delivery of drugs are delivered in the body. With the help of nanoscale technology researchers can evaluate and control where, how and when a medicine acts inside the body.

This delivery system increases drug dissolution of the medicament, improving the therapeutic index and biological availability while decreasing the overall side effects of the drug^{18,19,20} as shown in (Table1).

1. Cancer Therapy:

The most potent utilisation of nanotechnology is in cancer treatment. Nano carriers such as phospholipids and polymeric nanoparticles have the ability to detect the cancer cell receptor, which helps in the accumulation of drugs specifically at the tumour site, rather than impacting healthy tissues. Nano-sized drug particles also provides better penetration and prolonged release of anti-tumour medication^{3,16}.

Example: Liposomal doxorubicin (Doxil®) and albumin-bound paclitaxel (Abraxane®) are clinically validated Nano medicines that have improved therapeutic outcomes in cancer patients^{22,23}.

2. Brain-targeting Drug Delivery System:

The treatment of neurological disorders has consistently been challenging due to the presence of the cerebrovascular barrier. Nanocarriers provide a novel method for the transport of medication to the CNS by surface functionalization such as PEGylation or ligand attachment. These tailoring of nanoparticles helps to move through various barriers and reach to the brain tissues^{17,25}.

This delivery system has shown therapeutic capability in regulating seizures, Alzheimer's disease, Parkinson's type disorder and brain tumours²⁶.

Example: Polymeric nanoparticles carrying anti-seizure or anti-Alzheimer's medications have shown enhanced cerebral uptake and sustained release of drug compared to traditional dosage forms²⁷.

3. Antimicrobial Drug Delivery:

Nanotechnology systems have created new opportunities for the treatment of various infections. Lipid-based and polymeric nanoparticles improve the transport and stability of various antibiotics, while metallic nanoparticles like zinc oxide and silver show high effectiveness against microbial infections. They are also helpful in managing drug resistance by ensuring that the medicament remains in the infected site for a longer period of time^{30,31}.

Example: Silver nanoparticles and chitosan-based nanoplatforms have been effectively used for surface decontamination and tissue repair properties³².

4. Gene and Drug Combination Therapies:

Nanotechnology-based delivery systems are platforms capable of diverse applications, including the delivery of

both medicament and hereditary material together. The integration of DNA or siRNA with antineoplastic drugs helps in modulating multiple disease pathways, especially in the conditions like cancer. Nanoparticles preserve the genetic material from degradation and ensure the effective entry into the targeted site^{28,29}.

Table 1: Application of Nanotechnology with examples

APPLICATION AREA	ROLE OF NANOPARTICLES	EXAMPLE
Cancer therapy	Helps in better penetration and prolonged release of drug.	Doxil®, Abraxane®
Antimicrobial drug delivery	Improves drug transport and physiochemical stability.	Silver nanoparticles, Chitosan-based nanoparticles
Gene and drug combination therapy	Modulates multiple disease pathways.	siRNA-based nanoparticles
Central nervous system drug delivery	Nanoparticles helps in moving through various barriers and reaching the brain tissues.	Polymeric nanoparticles

ADVANTAGES AND LIMITATIONS:

Nanoparticle-based drug delivery systems have changed advanced clinical research by increasing drug efficacy, patient compliance, and therapeutic effectiveness. These nano-sized carriers make it feasible to control drug release, increase absorption, and uniform delivery of medicaments to previously unreachable tissues.

Advantages:

1. Targeted and Localized Therapeutic Delivery:

Nanoparticles can be chemically engineered with a particular binding molecule such as antigen-specific proteins, polypeptides or nucleic acid probes that recognise and bind receptors on infected cells. This allows the medicament to arrive at the specific site of action, reducing toxicity to undamaged tissue^{7,14}.

Example: Site-targeting nanoparticles used in cancer therapy accumulated mainly in tumour tissue through the enhanced transmission ability and sustained retention.

2. Increased Absorption and Dissolution Capacity:

Many medicines have poor aqueous solubility, which works as a barrier to clinical effectiveness. Nanoparticle-based formulations increase surface potency and rate of dissolution, which may lead to enhanced absorption and overall drug availability^{9,10}.

3. Long-acting Controlled System:

Nano-sized particles can be manufactured to deliver medicament over a specific time period, helping maintain a particular level of the drug in the body. This sustained release decreases the need of frequent dosing and improves patient compliance¹³.

4. Encapsulation of Degradable Molecules:

Medicaments that are not stable or easily deteriorated by biological catalysts or various environmental factors can

be encapsulated using nanocarriers. This is especially useful for peptides, protein, and gene-targeting therapeutics¹¹.

5. Combination and Multi-purpose Therapy:

Nanotechnology allows the combined delivery of various medicaments or a drug with hereditary material (such as *siRNA*). This approach can overcome complex pathological conditions by working on various pathways at the same time¹⁹.

Limitations:

1. Adverse Effects and Compatibility Issues:

Some nanoparticles can cause adverse effects due to their constituents, surface potential, or aggregation in tissue. Prolonged studies are still essential to validate their overall safety profile¹².

2. Complicated manufacturing and less cost-effective:

The formulation of nanoparticles requires high-quality techniques, environmental management system, and accurate analysis of quality. This makes the production of large-scale medications expensive and technically demanding.

3. Limitations in Stability and Preservative Management:

Nano-sized colloidal suspension particles can undergo chemical degradation or aggregation during product preservation, which may also change their size and effectiveness of the product⁹.

4. Compliance and Ethical Barriers:

As nanotechnology-based drugs are recently developed, compliance requirements for their authorisation, evaluation, and safety assessment are still progressing. This endures their path from laboratory research to medicinal use⁶.

5. Restricted Follow-up Data:

Mostly, the nano-scale based medical procedures are still under evaluation or initial clinical studies. Their

prolonged effects on organs, biotransformation, and the immunological system are not yet clearly understood⁷.

Table 2: Advantages and limitations of Nanotechnology

ADVANTAGES	LIMITATIONS
Targeted drug delivery	Complex regulatory approval
Reduce toxicity	Limited clinical data
Enhance absorption of drug	Limitations in stability
Uniform delivery of drug	Complicated manufacturing
Improved patient compliance	Less cost effective
Increased stability	Limited product preservation

RECENT ADVANCES:

Over the past few years, nanotechnology has changed from basic lab-based research into an effective tool for resolving complicated clinical problems. The focus has transferred from traditional nanocarriers to highly developed nanosystems that targeting, visualising, and sustained release within a combined platform, thereby improving therapeutic outcomes¹⁵.

1. Stimulus-responsive Nanocarriers:

New generation nano-sized particles are now being formulated as a reaction towards the particular

physiological and extrinsic factors such as H⁺ ion concentration, magnetic targeting area, light intensity, thermal energy, or catalytic enzymes. These systems release their medicament only under specific conditions, which precisely target action and decrease systemic effects¹⁵ as shown in (Fig 3).

Example: pH-triggered polymeric Nanoformulations being used for site-specific cancer therapy, where the acidic microenvironment stimulates the drug release, enhancing effectiveness and minimising side effects.

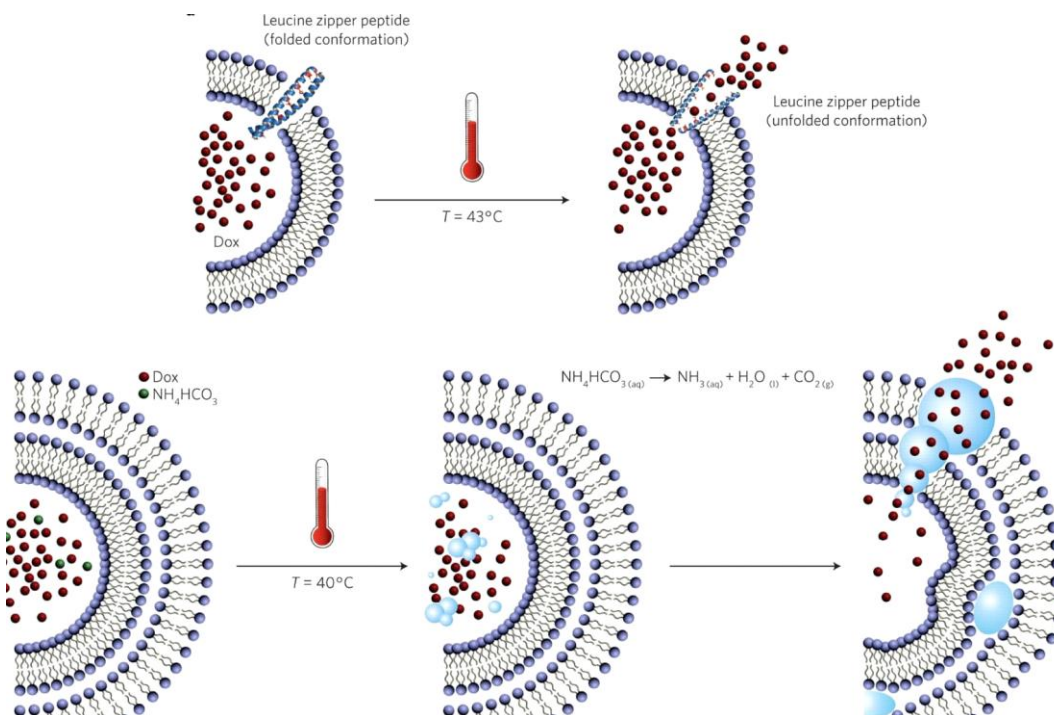


Figure 3: Stimulus-responsive Nanocarriers

2. Lipid-Based Delivery System (LNPs and SLNs):

Lipid-formulated delivery systems, such as lipid nanoparticles (LNPs) or solid-lipid nanoparticles (SLNs), have attained significant acknowledgement due to their enhanced physiological compatibility and ability to

transport both aqueous and fat-soluble effective penetration, increase systemic residence time and prevent deterioration of unstable drugs as shown in (Fig 4).

Example: The effective performance of mRNA-based COVID-19 vaccines Pfizer-BioNTech and Moderna, was largely due to lipid-based nanoparticles that successfully

transported mRNA into cells, presenting the potential of nanotechnology-based medicaments to the world.

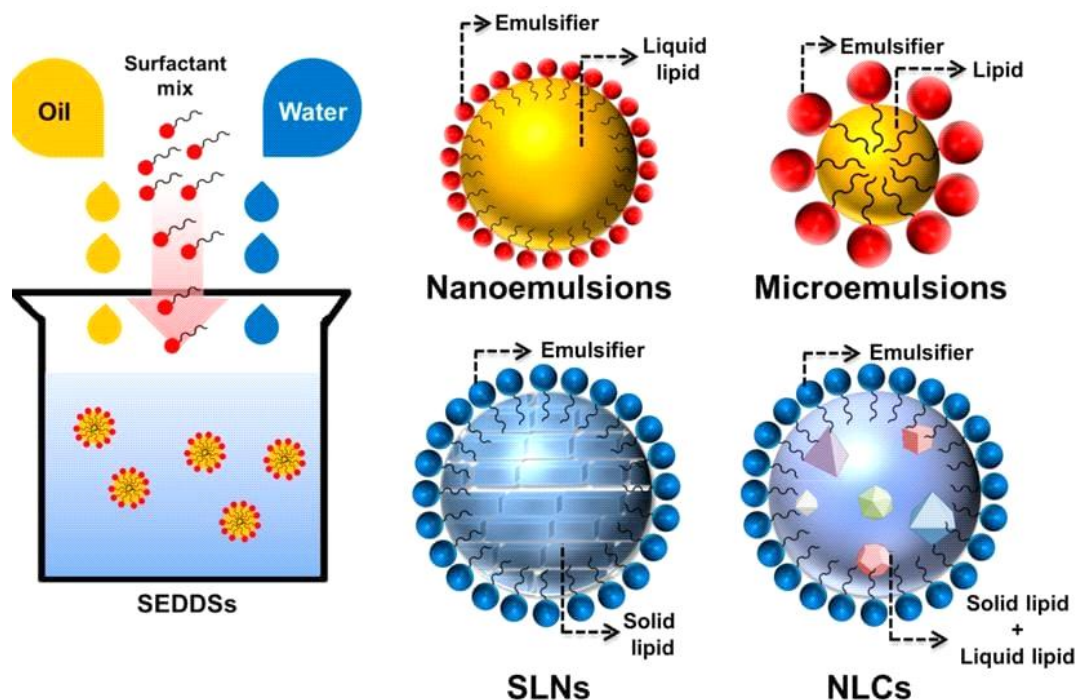


Figure 4: Lipid-Based Delivery System

3. Dendrimer-Based Nanocarriers:

These nanosized polymer, extensively branched tree-structured macromolecules that provide accurate management over polymer morphology, size, and surface functionalization. Due to the adjustable surface chemistry and high drug loading efficiency, they are

particularly helpful in pharmaceutical and gene delivery as shown in (Fig 5).

Example: Poly(amidoamine) (PAMAM) dendrimers have been used to provide antitumor drugs such as methotrexate and doxorubicin, attaining higher efficiency for targeting the cancer-causing cells and minimising the overall toxicity.

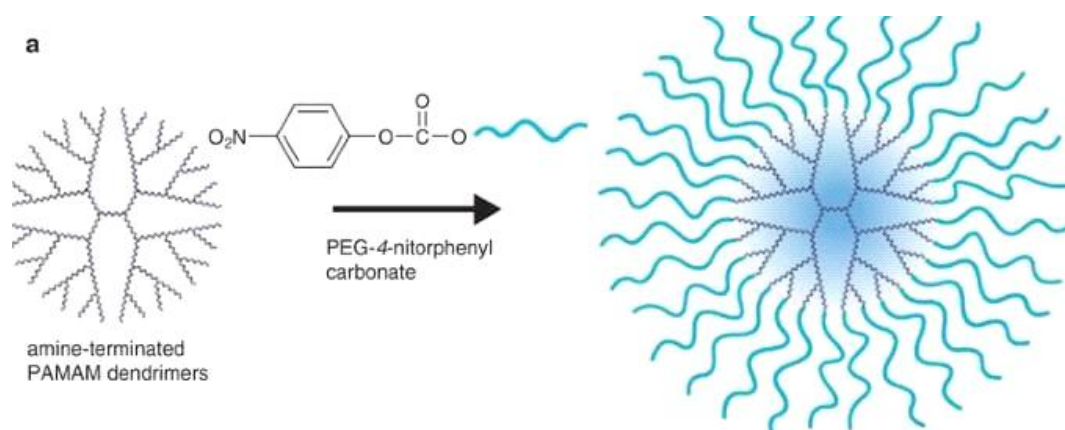


Figure 5: Dendrimer-Based Nanocarriers

4. Nano gels and Hydrogel-Based Nanoparticles:

Nanoscale gel particles are highly swollen, soft and three-dimensional cross-linked hydrophilic polymer matrix in which both low molecular weight as well as high molecular weight compounds are efficiently entrapped. They give their respond to various stimuli like

temperature, pH etc. for targeted and controlled drug delivery with reduced overall toxicity¹⁵.

Example: Temperature-responsive nanoparticles based on chitosan and PNIPAM have been analysed for site-specific tumour therapy and protein delivery, facilitating controlled release at body temperature.

5. Hybrid and Versatile Nanocarriers:

Hybrid nanoscale particles are highly engineered drug delivery system that combine two or more materials such as polymer-lipid or organic-inorganic into a single Nano platform to achieve an improved therapeutic effect. The hybrid structure helps in carrying accurate therapeutic

agents and diagnostic markers for controlled and site-specific drug delivery^{15,16} as shown in (Fig 6).

Example: Gold-liposome hybrid nanoscale particles have been analysed for combined cancer therapy and imaging, allowing concurrent tumour targeting and photothermal therapy (PTT).

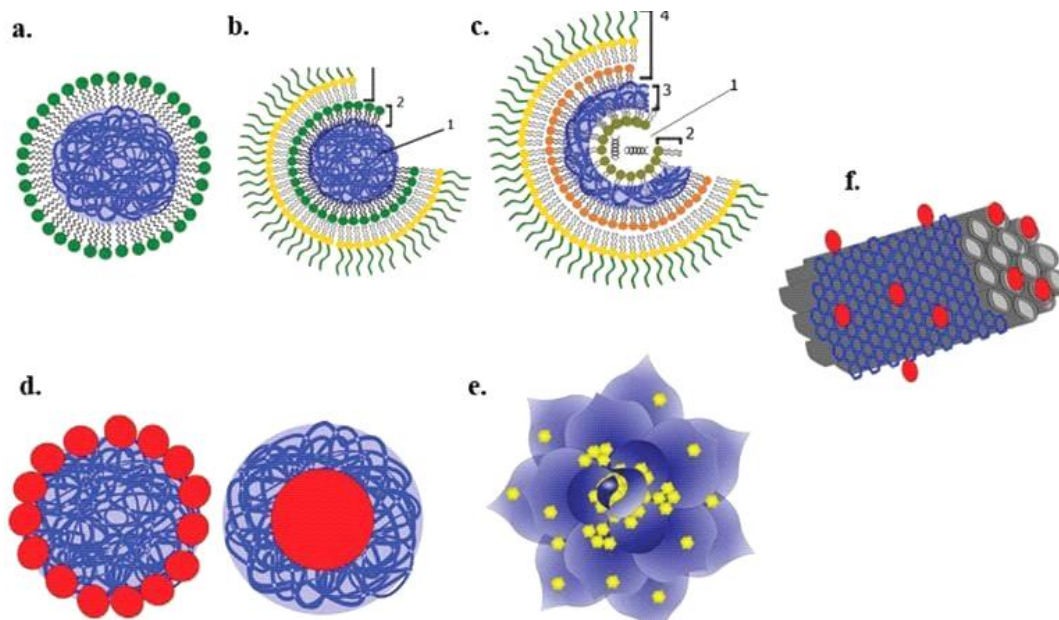


Figure 6: Hybrid and Versatile Nanocarriers

Case Studies of Nano medicines in Clinical Use:

a) Doxil® (PEG-coated liposomal doxorubicin)

Disease: Ovarian and breast cancer, malignant vascular tumour

Nanocarriers: PEG-coated liposomes (~100 nm)

Case study

The traditional doxorubicin experiences a high risk of cardiac toxicity and off-targeted tissue distribution, which leads to the overall systemic toxicity and reduces the therapeutic index.

Doxil, which incorporates doxorubicin in PEG-coated liposomes, confers a sheath property and avoidance of reticuloendothelial clearance.

Outcome: Extended systemic circulation

Reduced cardiac toxicity

Decrease overall systemic toxicity.

Status: FDA approved

b) Onpatro (Patisiran lipid nanoparticle-based siRNA)

Disease: Hereditary transthyretin amyloidosis (hATTR)

Nanocarriers: Lipid-based nanoparticles

Case study

siRNA is not stable and easily deteriorates in blood. Lipid-based nanoparticles act as a notable development in RNA

interference (RNAi) therapy, which delivers small interfering RNA (siRNA) to the liver.

Outcome: Decreased amyloid protein synthesis

Effective gene suppression

Improved quality of life

Status: 1st FDA-approved small interfering RNA Nano medicine.

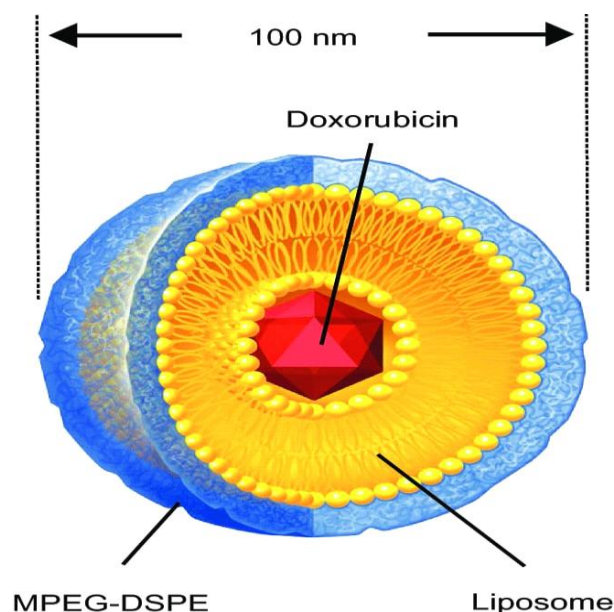


Figure 7: PEG-coated liposomal doxorubicin

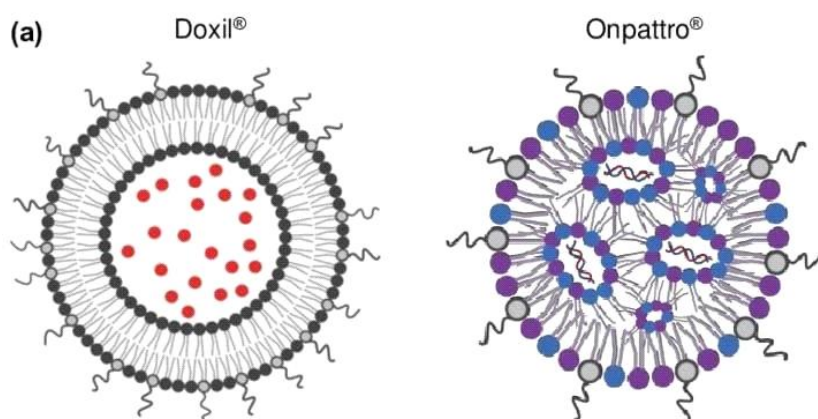


Figure 8: Patisiran lipid nanoparticles-based siRNA

c) Abraxane® (albumin-stabilized paclitaxel)

Disease: Breast cancer, pancreatic cancer and lung cancer.

Nanocarriers: Albumin nanoparticles (~130 nm)

Case study

The solubility of paclitaxel is very low. Traditional formulations use toxic solvents, which cause various hypersensitive reactions in the body.

Abraxane uses nanoparticle-based technology, which delivers paclitaxel without the need for toxic solvents.

Outcome: Enhanced solubility

Decreases hypersensitivity reaction

Improved patient tolerance and overall systemic response

Status: FDA approved

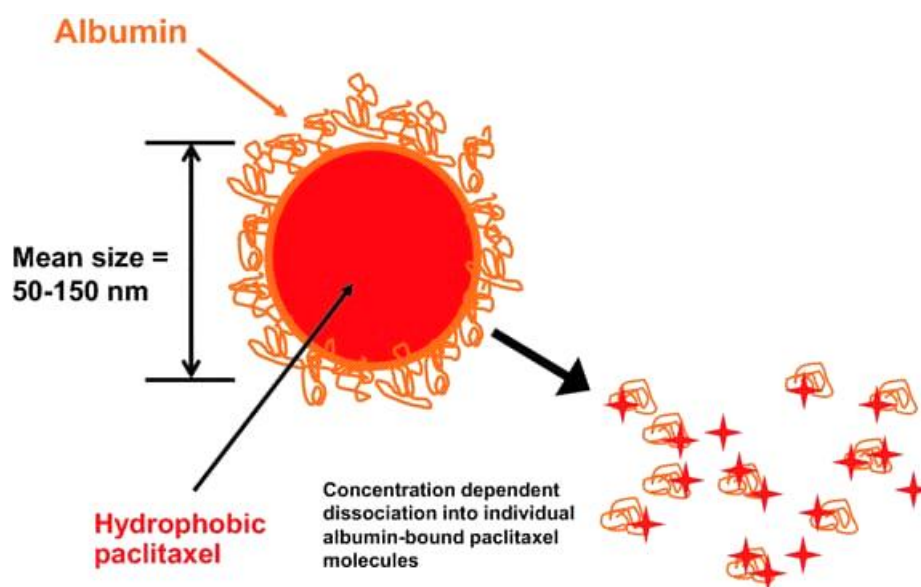


Figure 9: Albumin-stabilized paclitaxel

d) Silver nanoparticle Albumin-stabilised

Application: Burns and long-term wounds

Nanocarriers: Silver nanoparticles

Case study

Antibiotics used traditionally show drug resistance. Silver nanoparticles have been effectively used for antimicrobial activity, surface decontamination and tissue repair properties.

Outcome: Decreased the rate of infection

Enhanced wound healing process

e) COVID-19 Vaccines (Nanoemulsions in the Delivery of Vaccine)

Nanocarriers: Lipid-based nanoparticles

Case study

mRNA is unstable and delicate, which cannot enter cells easily. Lipid-based nanoparticles help in protecting and delivering the genetic material.

Outcome: Strong vaccine effectiveness

Fast immune response

Example: Pfizer-BioNTech (**BNT162b2**)

Moderna (**mRNA-1273**)

CHALLENGES AND FUTURE PROSPECTS OF NANOTECHNOLOGY-DRIVEN DRUG DELIVERY SYSTEM:

Challenges:

One of the major problems is systemic toxicity and biological compatibility. The toxic effect of nanoparticles is due to nanoscale dimensions and enhanced surface reactivity, which results in preferential accumulation in reticuloendothelial organs such as the liver and spleen, causing systemic toxicity^{40,41}.

Another major challenge lies in the large-scale production, stability, and shelf life. The accurate size of the particle, stability, reproducibility, and surface charge at an industrial level are technically challenging and cost-intensive; small variations in material lead to the batch-to-batch alteration, which further reduces the therapeutic efficiency of the product⁴².

Regulatory and approval processes are also major challenges due to their complicated manufacturing procedure. The limited availability of these standardised guidelines is due to the novel approach, which causes problems in the production of safe, effective and stable nanomedicine³⁹.

Future Perspectives:

Despite the various limitations, the future of nanoparticles in drug delivery systems is highly encouraging. Liposomes and polymeric-based nanocarriers show high biological compatibility and flexibility³³.

Future technology systems combine the stimuli-responsive materials that deliver drugs at targeted sites for efficient therapeutic action under specific conditions, such as changes in pH and temperature. This reduces the overall systemic toxicity and enhances the clinical outcomes^{36,37}.

Future nano-sized particles are expected to be biologically compatible, environmentally friendly, and AI-driven precision therapeutics. A customised and stimuli-responsive nanoparticle drug delivery system will further enhance therapeutic outcomes^{34,35}. Moreover, customised Nano medicines could adapt drug formulations to a patient's genetic profile and past disease conditions³⁸.

CONCLUSION:

Nanoparticle-based technology has fundamentally transformed drug delivery systems by enabling precise, sustained, and site-specific delivery of medications^{1,2}.

These developments also open various pathways for effectively treating chronic and complex diseases such as cancer, hereditary diseases, wound healing, neurological diseases, and various microbial infections.

However, ongoing investigations and research focus on the biological compatibility of the materials, customised nanomedicine, and stimuli-responsive nanoparticles, which will enhance the therapeutic efficiency of the nanoparticle delivery system^{5,15}.

Acknowledgement: The authors would like to express their sincere gratitude to the faculty members for their valuable support and guidance throughout the preparation of this manuscript. These authors also acknowledge the efforts of all co-authors in successfully completing this work.

Author Contribution: Manisha Chandola contributed to the concept development, literature review, and drafting of the manuscript. Karuna Dhaundhiyal, Abhijeet Ojha, Arun Kumar Singh, and Vikas Bhatt contributed to guidance, review, and plagiarism checking of the manuscript.

All authors have read and approved the final version of the manuscript.

Conflict of Interest: The authors declare no conflict of interest.

Ethical Approval: Not applicable.

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