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Review Article

An Overview : Nanotechnology Based Drug Delivery System in Pharmaceutical Science

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ABSTRACT

Nanotechnology has brought a major shift in the field of pharmaceutical sciences by offering new and efficient ways to deliver drugs. It focuses on the use of materials at a very small scale (1–100 nm), where they show unique properties such as increased surface area, better solubility, and improved interaction with biological systems. These features help in enhancing the performance of drugs that otherwise face problems like poor solubility, low bioavailability, and lack of targeted action. A variety of nanocarrier systems such as nanoparticles, liposomes, niosomes, nanosponges, cubosomes, polymeric nanoparticles, dendrimers, carbon nanotubes, quantum dots, ethosomes, and transferosomes have been developed to improve drug delivery. These systems are capable of protecting drugs from degradation, delivering them to specific sites, and releasing them in a controlled manner, which ultimately improves therapeutic outcomes and reduces side effects. Although nanotechnology offers many advantages, certain challenges like high cost, complex preparation methods, stability issues, and safety concerns still exist. However, ongoing research is continuously working to overcome these limitations. Overall, nanotechnology-based drug delivery systems show great promise in improving modern treatment approaches and have the potential to significantly enhance patient care in the future.

INTRODUCTION

Nanotechnology involves the design, development, and application of materials that exist at an extremely small scale, generally extending from 1 to 100 nanometers. At this nanoscale level, materials exhibit exclusive physical, chemical, and biological characteristics not seen in their larger forms. These belongings include a significantly larger surface area, enhanced reactivity, improved solubility, and better interaction with biological systems. Because

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of these special characteristics, Nanotechnology has drawn a lot of interest in many scientific fields, particularly in pharmaceutical sciences. In recent years, it has become especially important in the development of advanced drug delivery systems aimed at improving therapeutic efficiency and patient results. [1]

Traditional or conventional drug delivery systems often face several limitations that reduce the effectiveness of many therapeutic agents. These problems include poor water solubility of drugs, chemical and physical instability, low bioavailability, rapid elimination of drugs from the body, and the inability to deliver drugs specifically to the target site. As a result, higher doses of drugs may be required to achieve the chosen therapeutic effect, which can increase the risk of side effects and toxicity. To address these challenges, researchers have developed nanotechnology-based drug delivery systems that can enhance the overall performance of pharmaceutical formulations. These systems are capable of improving drug solubility, protecting drugs from premature degradation, enabling controlled or sustained drug release, and facilitating targeted delivery of drugs to specific tissues, cells, or organs within the body.[4]

A variability of nanocarriers have been investigated and developed for pharmaceutical applications. These include polymeric nanoparticles, liposomes, niosomes, nanosponges, cubosomes, and microspheres. Each of these nanocarrier systems possesses unique structural and functional characteristics that allow them to encapsulate drugs and deliver them more effectively to the desired site of action. By improving drug stability, bioavailability, and targeting ability, these nanocarriers can significantly enhance therapeutic outcomes while minimizing adverse effects associated with conventional drug therapy.

With the continuous development of science and technology, researchers are gradually focusing on the development of drug delivery systems that are not only active but also safer, cost-effective, and environmentally sustainable. There is also growing awareness regarding the economic feasibility and long-term sustainability of modern technologies, particularly in view of the rapid depletion of natural resources worldwide. Therefore, the development of efficient and sustainable pharmaceutical technologies has become an important research priority. In this context, the present review focuses on the fundamental concepts of nanotechnology, various types of nanocarriers used in drug delivery, their pharmaceutical applications, as well as their advantages, limitations, and potential future prospects in modern medicine.[5]

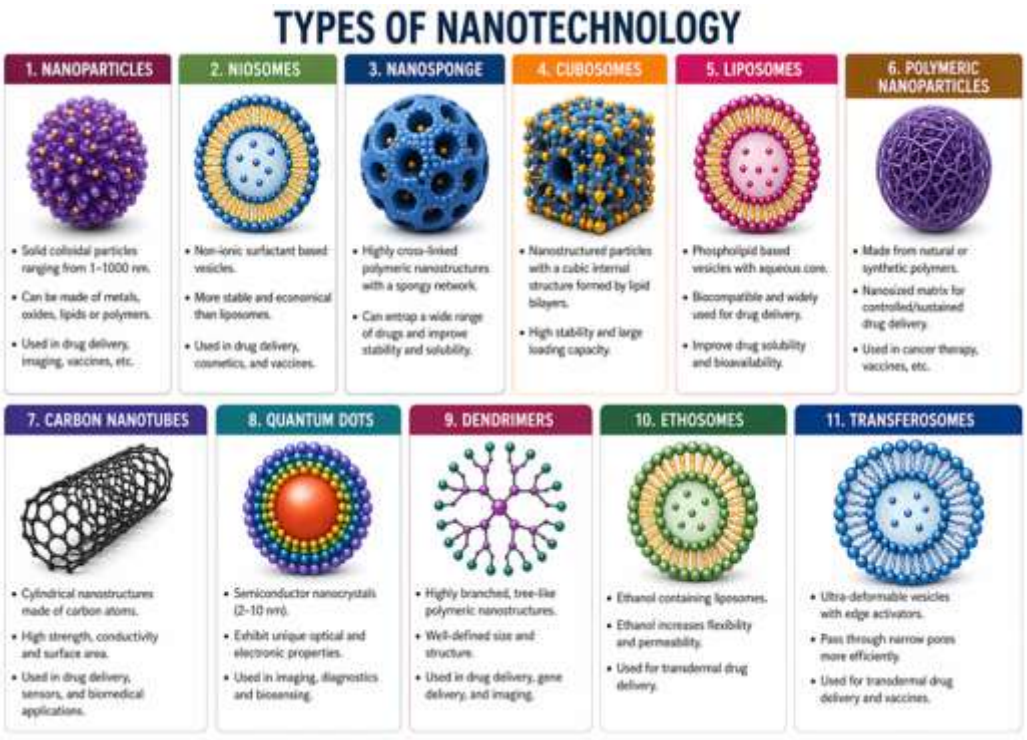
Advantages **Error! Reference source not found.,Error! Reference source not found.**

1. **Improved drug solubility -** Nanocarriers help poorly soluble drugs dissolve better in the body, leading to improved adsorption.
2. **Targeted drug delivery:** Nanoparticles can be designed to deliver drugs directly to specific tissues or cells, reducing damage to healthy cells.
3. **Controlled and sustained release -** Drugs can be released slowly over time, maintaining steady therapeutic levels.
4. **Reduce side effects -** Targeted delivery minimizes drug exposure to non- target organs.

5. **Enhanced bioavailability -**Drugs delivered through nanocarriers remain in the body longer and reach the target more effectively.

Disadvantages **Error! Reference source not found.**

1. **High production cost -** Some nanocarriers are expensive to develop and manufacture.
2. **Complex formulation process -**Preparation methods require advanced equipment and expertise.
3. **Stability issues -** Certain nanoparticles may aggregate or degrade during storage.
4. **Potential toxicity -** Long – term safety of some nanomaterials is not fully understood.
5. **Environmental concerns -** Disposal of nanomaterials may affect ecosystems.



1.Nanoparticles

Introduction

Nanoparticles are extremely small solid particles, usually ranging from 1to 100 nanometers in size. Because of their very small dimensions, nanoparticles behave differently from larger particles and show unique physical, chemical, and biological properties. One of the most important features of nanoparticles is their large surface area, which allows better interaction with drugs and biological systems. This makes them extremely useful in pharmaceutical drug delivery. **Error! Reference source not found.**

In drug delivery submissions, nanoparticles act as carriers that can hold drugs either on their surface or within their structure. The drug may be dissolved, entrapped, adsorbed or chemically linked to the nanoparticles matrix. By doing so, nanoparticles help protect drugs from degradation, recover the solubility of poorly water soluble drugs, and enhance their absorption in the body**Error! Reference source not found.**. They also allow drugs to be release in a controlled manner and, in some cases, delivered directly to the target site, which reduces unwanted side effects.

Based on their structure, nanoparticles are mainly secret into nanosphere and nanocapsules. Nanospheres consist of a solid matrix in which the drug is uniformly distributed, whereas nanocapsules have a core- shell structure where the drug is enclosed within a cavity surrounded by a polymeric membrane. This structural difference plays an significant role in causal the drug release behavior.

Nanoparticles are commonly prepared using biodegradable and biocompatible materials such as polymers, lipids, and inorganic substances. Polymers like chitosan, PLGA, and alginate are frequently used due to their safety and versatility. Several preparation methods, including solvent evaporation, nanoprecipitation, emulsification, and ionic gelation, are employed to obtain nanoparticles with desired size, stability, and drug-loading efficiency.[5]

In pharmaceutical sciences, nanoparticles have been commonly investigated for various routes of administration such as oral, parenteral, ocular, and transdermal delivery. They are especially important in cancer therapy, vaccine delivery, gene therapy, and the conduct of chronic diseases. Although nanoparticles offer many advantages, challenges related to toxicity, large scale manufacturing, and regulatory approval still exist. Nevertheless, nanoparticles continue to be one of the most promising and widely studied systems in modern drug delivery research

Advantage of Nanoparticles

Nanoparticles offer several important benefits in drug delivery. Their small size tolerates them to increase the solubility of poorly water soluble drugs and improve drug adsorption. They protect the drug from chemical and enzymatic degradation, which enhances drug stability. Nanoparticles can be planned to release drugs in a controlled or sustained manner, reducing dosing frequency and enlightening patient compliance. In addition, targeted delivery using nanoparticles helps concentrate the drug at the disease site while minimizing unwanted side effects. These advantages make nanoparticles highly effective for modern therapeutic application. **Error! Reference source not found.**

Disadvantage of nanoparticles

Despite their benefits, nanoparticles have a number of disadvantages. The preparation process can be costly and difficult, especially in extensive production. Certain nanoparticles may be toxic or cause unwanted immune reactions if they are not properly planned. Particle collection and medication leakage are examples of stability issues that can occur during storage. Furthermore, obtaining regulatory approval for products based on nanoparticles is interesting due to the strict safety and quality requirements. **Error! Reference source not found.**

Applications

Nanoparticles are widely used in many pharmaceutical applications. They play a dangerous role in targeted drug delivery, particularly in the treatment of cancer, where they

help deliver anticancer drugs directly to tumour cells. Nanoparticles are also used to recover oral bioavailability of poorly soluble drugs, as well as drug penetration in ocular and transdermal delivery. Additionally, they are employed in diagnostic imagination, gene therapy, and vaccine delivery. They can be used to treat both chronic illnesses and infectious infections due to their flexibility.[Error! Reference source not found.]

Assessment of Nanoparticles

To guarantee the efficacy, safety, and quality of nanoparticles, evaluation is crucial. Measurements of particle size and size delivery are used to verify the formulation's stability and uniformity. Physical stability is predicted by evaluating surface charge, which is often expressed as zeta potential. To evaluate how much drug is successfully incorporated into the nanoparticles, drug loading and entrapment efficiency are calculated. To realize the drug's release pattern, in vitro drug release investigations are carried out. Particle form and surface structure are investigated through the use of microscopic methods. To assess the performance and shelf life of nanoparticles under various storage circumstances, stability tests are carried out.[**Error! Reference source not found.**]

2. Niosomes

Definition

When hydrated in an aqueous solution, niosomes vesicular drug delivery systems mostly made of non-ionic surfactants and cholesterol—form locked bilayer structures. These vesicles are supple carriers in pharmaceutical drug delivery because they can encapsulate both lipophilic and hydrophilic medications. Niosomes have drawn a lot of interest as a liposome extra since of their stability and biocompatibility.

Summary[**Error! Reference source not found.**]

In an aqueous environment, non-ionic surfactants self-assemble to produce vesicular carriers called niosomes, which are typically stabilized by cholesterol. The system can transport both hydrophilic and lipophilic medications because these surfactants organize into bilayer structures that encircle an internal aqueous core. Niosomes are becoming a vital tool in regulated and targeted drug delivery studies due to their dual drug-loading capability.

They were created to get around some of the drawbacks of liposomes, namely their expensive price and chemical instability. Large-scale pharmaceutical applications find niosomes appealing due to their relative stability, ease of storage, and affordability. Growing interest in their usage in a variety of therapeutic areas has been fueled by their capacity to increase medication bioavailability, extend medicinal activity, and lessen side effects [**Error! Reference source not found.**,**Error! Reference source not found.**]

Niosome Types

The number of bilayers and vesicle size are the primary criteria used to categorize niosomes:

1. **MLVs, or multilamellar vesicles** - These vesicles have an onion-like structure because they are made up of many concentric bilayers encircling an aqueous core. They are often

bigger and better suited for long-term medication release.

2. **LUVs, or large unilamellar vesicles** - LUVs are excellent for encapsulating hydrophilic medicines in higher quantities because they have a single bilayer membrane with a comparatively large internal aqueous capacity.

3. **SUVs, or small unilamellar vesicles** - These are tiny vesicles with a constrained internal volume and a single bilayer. They are helpful when regulated and focused delivery is needed, and they are frequently made using sonication. **Error! Reference source not found.**

Applications and Uses of Niosomes

1. **Sustained and Regulated Drug Release -** Niosomes' bilayer structure makes it possible for medications to be delivered gradually over time, preserving therapeutic heights for extensive periods of time and lowering the frequency of administration.

2. **Oral Medication Administration -** Niosomes can facilitate the absorption of poorly soluble medications and shield them from gastrointestinal tract breakdown, improving their bioavailability.[7]

3. **Topical and Transdermal Administration -** They are helpful in dermatological and cosmetic formulations because they interact with the lipid layers of the stratum corneum to improve drug penetration into the skin.

4. **Parenteral Administration -** Niosomes can extend the duration of circulation and shield medications from the bloodstream's quick degradation.

5. **Vaccination and Antigen Distribution -** By increasing antigen stability and immune cell absorption, they can serve as antigen transporters and boost immunological response. Error! Reference source not found.

Niosome Evaluation Parameters

Niosomes must be well characterized in order to guarantee their stability and functionality.

1) Size Distribution and Vesicle Size- Drug release, stability, and biodistribution are all impacted by particle size. Dynamic light trickle methods are frequently used to measure it.

2) Morphology - Vesicle shape and lamellar structure can be ascertained using microscopic methods like transmission electron microscopy. **Error! Reference source not found.**

3) Efficiency of Entrapment - This measure, which is essential for assessing formulation efficiency, shows how much medication was successfully absorbed into the vesicles.

4) Zeta Potential - Higher absolute values often imply stronger resistance to aggregation, and surface charge assessment aids in the prediction of physical stability.

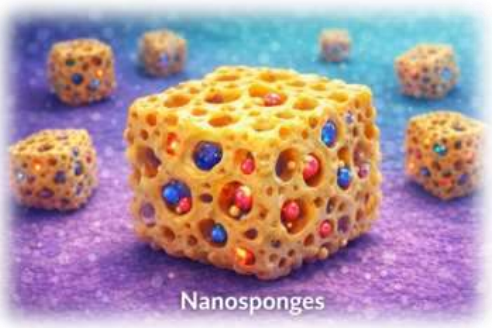
5) Drug Release studies in vitro - These investigations ascertain the release pattern and verify whether the technology offers sustained or controlled drug administration. **Error! Reference source not found.**

3. NANOSPONGES

Overview

A more recent class of porous, nanoscale drug carriers called nanosponges was created to enhance the delivery of medicinal medicines. In

terms of structure, they are networks of three-dimensional cross-linked polymers with microscopic cavities that can hold medicinal molecules. Nanosponges are extremely adaptable carriers in pharmaceutical applications because of these cavities, which enable them to carry both hydrophilic and lipophilic medicines



The majority of medicinal nanosponges are made by cross-linking cyclodextrins with appropriate agents to create stable, sponge-like structures with interior pores. Drug entrapment, degradation protection, and controlled release at the target site are made possible by their porous architecture. Nanosponges improve medication solubility, stability, and bioavailability due to their insignificant size and large surface area. **Error! Reference source not found.**

Nanosponges offer a versatile platform for contemporary drug administration since they may be added to a variety of dosage forms, including tablets, capsules, hydrogels, topical creams, and parenteral systems. **Error! Reference source not found.**

Different Types of Nanosponges

Nanosponges can be categorized according to their content and structure

a) Nanosponges Based on Cyclodextrin -These are the most extensively researched. They are created by cross-linking cyclodextrins with substances like dianhydrides or carbonyl compounds. Their hydrophilic exterior and internal hydrophobic holes enable them to efficiently encapsulate medications that are unwell soluble in water. **Error! Reference source not found.**

b) Nanosponges made of polymers - These are made with biodegradable polymers that create a network that can release drugs under controlled conditions. The polymer-to-crosslinker ratio can be changed to alter the drug release rate. **Error! Reference source not found.**

c) Nanosponges, both crystalline and paracrystalline)

- Drug loading is influenced by the degree of crystallinity:
- Higher drug loading capacity due to crystalline nanosponges
- Comparatively lower loading with paracrystalline nanosponges
- Depending on the structure, drug integration can take the form of inclusion complexes or a mechanical mixing.

Uses for Nanosponges **Error! Reference source not found.**

Nanosponges are widely used in the biomedical and pharmaceutical industries.

a) Improvement of Solubility - By creating inclusion complexes inside their cavities, they greatly increase the solubility & rate of dissolution of medications that are weakly soluble in water. Better bioavailability results from this

b) Sustained and Regulated Drug Release - Because of their porous structure, drugs can diffuse gradually, prolonging therapeutic efficacy and lowering the frequency of doses.

c) Topical Medication Administration - By keeping medications on the skin's surface and releasing them gradually, nanosponges lessen irritation and enhance the local therapeutic effect. They have been investigated for anti-inflammatory and antifungal medications.

d) Delivery of Anticancer Drugs - Anticancer medications can be delivered specifically using nanosponges, increasing drug concentration at tumor locations while reducing systemic side effects.

e) Delivery of Proteins and Enzymes - They aid in preserving the stability of delicate biomolecules during delivery, such as proteins and enzymes.

4. CUBOSOMES

INTRODUCTION:

Cubosomes are nano-sized, self-assembled liquid crystalline particles generated from specific lipids in the occurrence of water and stabilizers. In terms of structure, they have a special bicontinuous cubic phase in which two distinct but connected aqueous channels are formed when a lipid bilayer folds into a three-dimensional periodic structure. Because of this configuration, cubosomes have a remarkably high interior surface area and can load medications with various solubility properties. **Error! Reference source not found.**

Cubosomes are thermodynamically stable and can hold their structure for prolonged periods of time, in contrast to traditional vesicular systems. They are a very flexible nanocarrier system in contemporary pharmaceutical research because of their internal honeycomb-like structure, which enables them to entrap hydrophilic, lipophilic, and amphiphilic medicines. Cubosomes are especially appealing for topical, transdermal, oral, and controlled drug delivery applications because of their nanoscale size and bioadhesive properties.

Different Cubosome Preparation Techniques **Error! Reference source not found.**

1. Top-Down Approach- This method starts by combining a lipid (often glyceryl monooleate) with water to create a bulk cubic phase gel. High-energy procedures like probe sonication or high-pressure homogenization are then used to break down this viscous phase into nanoparticles. To stop aggregation, stabilizers like Poloxamer 407 are used. This approach is extensively used because it provides stable dispersions with repeatable particle size.

2. Bottom-Up Method - Using molecular precursors, cubosomes are formed. Hydrotropes are used to dissolve lipids, and then water is carefully diluted to create cubosomes. This method offers for more control over particle creation and uses less energy than the top-down approach. It is a more modern and effective method of producing cubosomes.

ADVANTAGE **Error! Reference source not found., Error! Reference source not found.**

1. High Drug Loading Capacity - Cubosomes possess a vast internal surface area with both aqueous channels and lipid domains, allowing them to encapsulate hydrophilic, lipophilic, and amphiphilic medicines efficiently.

2. Sustained and Regulated Drug Release - Drug diffusion is slowed by the intricate, winding interior structure, which prolongs therapeutic efficacy and lowers dosage frequency.

3. Low Toxicity and Biocompatibility - Cubosomes are typically safe and well tolerated because they are frequently made from biodegradable lipids like glyceryl monooleate.

4. Nature of Bioadhesion - Particularly in topical and mucosal distribution, their ability to stick to biological membranes prolongs their residence time at the site of action.

APPLICATION

1. Oral Medication Administration- By promoting breakdown and shielding medications from deterioration in the gastrointestinal tract, cubosomes increase the bioavailability of poorly water-soluble medications. Additionally, their lipid-based composition may facilitate lymphatic absorption.

2. Systems of Controlled and Sustained Release- Cubosomes release medications gradually over time due to their intricate internal channels. This characteristic lowers the occurrence of dosage and aids in maintaining consistent medication levels in the body.

3. Drug Delivery in the Eyes - Their bioadhesive and controlled-release features make cubosomes appropriate for eye formulations, where prolonged contact time promotes drug absorption.

5. LIPOSOMES

Overview

Liposomes are spherical vesicles with an aqueous core encircled by one or more phospholipid bilayers. They are frequently utilized as medication delivery systems and as models for membrane research because of their structural similarity to actual cell membranes. Liposomes are highly adaptable carriers in medicine, cosmetics, and research because they can carry both fat-soluble medications (inside the lipid bilayer) and water-soluble drugs (within the core). **Error! Reference source not found.**

Liposome Types **Error! Reference source not found.**.**Error! Reference source not found.**

Cubosomes are typically prepared by two major approaches:

The size and quantity of bilayers (lamellae) are the primary criteria used to categorize liposomes:

1. Lamellarity-based

- Unilayer Vesicles (ULV): A single bilayer of phospholipids
- SUVs, or small unilamellar vesicles
- Large Unilamellar Vesicles (LUV) Multilamellar Vesicles (MLV): An onion-like structure made up of several concentric bilayers
- These have different drug loading capacities and release patterns.

2. Considering Function and Composition

- Traditional liposomes: cholesterol plus basic phospholipid
- Polyethylene glycol-coated stealth (PEGylated) liposomes are designed to evade immune recognition and extend circulation.
- Targeted liposomes: ligands (peptides, antibodies) affixed to the surface for delivery to a specified location
- Positively charged cationic liposomes are frequently utilized to transport genes.

Methods of Preparation **Error! Reference source not found.**

The goal of liposome production techniques is to create stable lipid vesicles that effectively entrap drugs.

1. Traditional Techniques

Typically, organic solvents are used in these:

- Thin Film Hydration (Bangham method): MLVs are created by hydrating a lipid film made of organic solvent.
- Reverse Phase Evaporation: Effective for highly encapsulating medications that are soluble in water
- Method of Ether Injection
- Method of Freeze-Thaw

These techniques might leave behind solvent residues, which could lead to problems with stability and toxicity.

2. Innovative/Solvent-Free Techniques

Designed to steer clear of dangerous solvents:

- Heating Method: To create vesicles more quickly and lacking the use of hazardous solvents, lipids are hydrated in an aqueous medium with glycerol and heated.
- The Bubble Method
- Method of Polyol Dilution

These techniques are safer and more suited for medications that are more sensitive, such as proteins and vaccinations.

Uses for Liposomes **Error! Reference source not found.**

There are numerous applications for liposomes:

1. Drug Administration

- Anticancer medications (better targeting, decrease toxicity)
- Delivery of antibiotics and antifungals
- Controlled and sustained drug release

2. Delivery of Vaccines - serve as adjuvants to strengthen the immune system.

3. Gene Transfer -DNA and RNA are delivered into cells by cationic liposomes

4. Examination - utilized as imaging carriers and contrast agents

5. Makeup - Vitamin and antioxidant delivery to the skin

Benefits of Liposomes **Error! Reference source not found.,Error! Reference source not found.**

- Able to transport both lipophilic and hydrophilic medications
- Biocompatible and biodegradable

- Reduce medication toxicity (particularly anticancer treatments)
- Allow for targeted administration
- Prevent the degradation of sensitive drugs (such proteins and nucleic acids)
- Modify size, charge, and surface characteristics

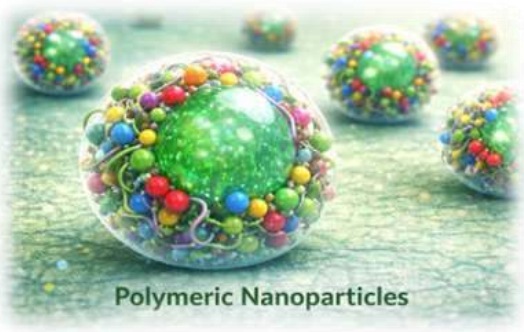
Liposome drawbacks

- Chemical and physical instability (oxidation, fusion, and leakage)
- Short shelf life
- High production costs
- Potentially low drug loading for certain medications
- Difficulties with large-scale manufacturing and sterilization
- Toxic organic solvents are used in some processes

6. Polymeric nanoparticles

Introduction

Polymeric nanoparticles (PNPs) are colloidal systems made of natural or synthetic polymers that are submicron in size, usually ranging from 10 to 1000 nm. To increase medication stability, solubility, bioavailability, and targeted administration, they are frequently utilized in drug delivery systems. The drug may dissolve, entrap, encapsulate, or adhere to the matrix of the nanoparticle. Polymeric nanoparticles can be either nanospheres (matrix system) or nanocapsules (core–shell system), depending on their structure.



Because of their capacity to improve therapeutic efficacy while lowering toxicity, shield labile pharmaceuticals from degradation, and provide regulated drug release, polymeric nanoparticles have drawn a lot of interest **Error! Reference source not found.**. They are especially helpful in vaccine delivery systems, gene delivery, and cancer treatment.**Error! Reference source not found.**

TYPES OF POLYMERIC NANOPARTICLES

In general, polymeric nanoparticles are categorized as:

A. Structure-Based **Error! Reference source not found.**

1. Nanospheres

- Systems of the matrix kind
- The medication is evenly distributed throughout the polymer matrix.
- Diffusion or polymer degradation are the methods used for controlled release.

2. Nanoparticles

- The core-shell building
- Medicine enclosed by a polymer membrane in a central chamber
- Fit for safeguarding delicate medications

B. Based on Polymer Type Error! Reference source not found.

1. Natural Polymers

- Chitosan
- Alginate
- Gelatin
- Albumin

2. Synthetic Polymers

- PLGA (Poly lactic-co-glycolic acid)
- PLA (Polylactic acid)
- PCL (Polycaprolactone)
- PEGylated polymers

APPLICATIONS Error! Reference source not found..Error! Reference source not found.

Numerous biomedical uses exist for polymeric nanoparticles:

1. Delivery of Drugs

- Consistent and regulated medication release
- Better solubility of medications that aren't very soluble in water
- Decreased frequency of dosing
- Increased bioavailability

2. Therapy for Targeted Cancer

- Enhanced Permeability and Retention (EPR) impact for passive targeting
- Targeting actively with ligands
- Decreased systemic toxicity

3. Delivery of Genes

- Delivery of RNA-based medicines, siRNA, and DNA
- Preventing enzymatic breakdown of nucleic acids

4. Delivery of Vaccines

- Enhanced stability of antigens
- Immune response regulation

5. Uses for Diagnostics

- Agents for imaging
- Systems for theranostic

ADVANTAGES Error! Reference source not found.

- Consistent and regulated medication release
- Enhanced stability of the medication
- Preventing enzymatic breakdown of labile medicines
- Improved bioavailability of medications with low solubility
- Potential for targeted drug delivery
- Decreased toxicity and adverse consequences

DISADVANTAGES

- Possible harm linked to polymers
- intricate production procedure
- Challenges of industrial production scaling up

- Problems with stability while being stored
- High cost of manufacture

7. CARBON NANOTUBES

INTRODUCTION

Carbon nanotubes (CNTs) are among the most promising carbon nanomaterials for biological applications. which are cylindrical nanostructures made of coiled graphene sheets. Since their discovery by Iijima in 1991, carbon nanotubes (CNTs) have garnered attention because of their outstanding mechanical strength, high surface area, electrical conductivity, chemical stability, and distinctive optical properties.[Error! Reference source not found.] Their ultra-small dimensions (diameter in the nanometer range) and high surface area-to-mass ratio allow them to adsorb or conjugate with a variety of therapeutic molecules, including drugs, proteins, DNA,& antibodies. Because of these characteristics, they can be used in tissue engineering, imaging, medication delivery, and diagnostic applications. But issues with toxicity and exposure at work continue to be major obstacles. [Error! Reference source not found.]

Types of Carbon Nanotubes [Error! Reference source not found.,Error! Reference source not found.]

The quantity of graphene layers, or walls, determines the classification of carbon nanotubes:

1. Carbon nanotubes with a single wall (SWCNTs)

- comprise a single sheet of graphene that has been rolled into a cylindrical shape.
- Usually, the diameter is 0.4–2 nm.
- may behave in a semiconducting or metallic manner.
- Superior electrical qualities and high flexibility

2. DWCNTs, or double-walled carbon nanotubes

- made up of two graphene cylinders that are concentric.
- Mix the characteristics of MWCNTs and SWCNTs.
- Permit functionalization without appreciable conductivity loss.

3. Carbon nanotubes with multiple walls (MWCNTs)

- comprise several layers of concentric graphene.
- The outside diameter could be as much as 100 nm.
- Strong mechanically and more easily functionalized because of its many flaws
- CNTs can also be classified structurally as chiral, armchair, or zigzag based on the direction in which the graphene rolls.

APPLICATIONS [Error! Reference source not found.]

A. Delivery of Drugs

- Therapeutic compounds can be conjugated or adsorbed by CNTs and then transported across cell membranes. Medications can be affixed to the nanotube's surface or placed inside. Diffusion or endocytosis are two possible routes for internalization into cells.
- CNTs have been successfully conjugated with anticancer medications such doxorubicin, paclitaxel, methotrexate, and cisplatin for targeted cancer therapy.

B. Delivery of Genes

- Because CNTs can pass through cell membranes, they make it easier to transport DNA and siRNA into cells, which has potential applications in gene therapy.

C. Uses for Diagnostics

- Biosensors: CNT-based electrochemical sensors have great sensitivity and improved electron transport.
- Imaging: Used in photoacoustic imaging, MRI contrast enhancement, Raman imaging, and NIR fluorescence imaging.

D. Tissue Engineering

- Scaffolds based on CNTs promote cell division and neural development. They are appropriate for tissue regeneration due to their mechanical strength and capacity to create three-dimensional networks.

E. Applications of Vaccines and Immunotherapy

- Functionalized CNTs can act as carriers of antimicrobials or tumor antigens and can also boost immune responses.

Benefits of CNTs **Error! Reference source not found.,Error! Reference source not found.**

1. A great surface area for loading drugs
2. The capacity to pass through cell membranes.
3. The tumor's enhanced permeability and retention (EPR) impact.
4. Outstanding mechanical flexibility and strength
5. Electrical and optical characteristics that are beneficial for imaging and biosensing
6. Stability of chemicals and resistance to deterioration

Risks and Drawbacks of CNTs

1. Possible cytotoxicity based on purity, surface chemistry, shape, and dosage
2. Danger to workers exposed at work during handling and production
3. Potential fibrosis and inflammation of the lungs after inhalation exposure
4. Hydrophobic nature causes dispersion problems
5. High production costs and issues with purity (manufacturing techniques like CVD, laser ablation, and arc discharge

8. QUANTUM DOTS

Introduction-

Zero-dimensional carbon-based nanomaterials called carbon quantum dots (CQDs) are famous for their exceptional photoluminescence, chemical stability, water solubility, and biocompatibility. They are usually smaller than 10 nm. They were identified as a novel class of fluorescent nanomaterials after being initially found during the purification of carbon nanotubes.

CQDs are structurally composed of an amorphous or graphitic carbon core encircled by several surface useful groups, including amino ($-NH_2$), carboxyl (-COOH), and hydroxyl (-OH) groups. Their optical properties, quantum yield, and chemical reactivity are all greatly influenced by these surface states. Because CQDs are metal-free and less toxic than conventional semiconductor quantum dots (CdSe, CdTe), they are more suitable for use in biomedical applications. **Error! Reference source not found.**

Although the precise emission process is still being studied, their fluorescence is caused by emissive traps, surface imperfections, and quantum confinement phenomena. **Error! Reference source not found.**

Types of Carbon Quantum Dots **Error! Reference source not found.**,**Error! Reference source not found.**

1. Quantum dots of carbon (CQDs) - Size-dependent fluorescence in quasi-spherical nanoparticles with mixed sp^2/sp^3 carbon structures

2. Quantum dots of graphene (GQDs)The optical characteristics are influenced by tiny pieces of crystalline graphene sheets with strong edge effects.

3. CNDs, or carbon nanodots -Amorphous carbon nanoparticles in which surface defect states are the primary source of fluorescence

4. Doped Quantum Dots of Carbon - Heteroatoms like nitrogen, sulfur, or phosphorus can be added to CQDs to improve their conductivity, catalytic activity, and fluorescence intensity.

Methods of Synthesis **Error! Reference source not found.**,**Error! Reference source not found.**

There are two main methods used to synthesis CQDs:

1. Top-Down Techniques -These entail dissolving bulk carbon compounds using methods including electrochemical oxidation, arc discharge, and laser ablation.[26]

2. Bottom-Up Approaches- These entail employing hydrothermal, solvothermal, microwave-assisted, or pyrolysis techniques to carbonize tiny organic compounds.[24]

Better control over particle size and surface functionalization is possible with bottom-up methods.[25]

APPLICATION **Error! Reference source not found.**,**Error! Reference source not found.**

1. Bioimaging- CQDs are appropriate for cellular imaging and diagnostic applications because of their bright, consistent fluorescence and low cytotoxicity.

2. Delivery of Drugs - They can conjugate with medications and targeting ligands for regulated and targeted delivery because of their nanosize and functional surface groups.

3. Chemical Sensing and Biosensing - Metal ions, proteins, glucose, and environmental contaminants can all be found using CQDs as fluorescent probes.

4. Solar power - In solar cells and other energy devices, CQDs enhance light gathering, charge transport, and overall efficiency.

5. Devices That Emit Light - CQDs are utilized in LEDs and display technologies because of their adjustable emission wavelengths.

6. Environmental Applications and Catalysis Because of their electron transfer capabilities, CQDs participate in redox reactions and improve the photocatalytic destruction of contaminants.

Benefits **Error! Reference source not found.,Error! Reference source not found.**

1. Outstanding photoluminescence with adjustable emission
2. High biocompatibility and low toxicity
3. Surface functional groups provide good water solubility.
4. Photostability and chemical stability
5. Eco-friendly and economical synthesis
6. Simple surface alteration for specific uses

Drawbacks **Error! Reference source not found.**

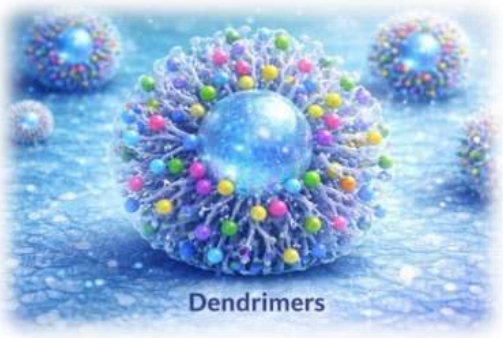
1. A lack of knowledge on the mechanisms underlying fluorescence
2. The challenge of attaining a consistent size distribution
3. Differences in quantum yield across batches
4. Difficulties in large-scale manufacturing

9. DENDRIMERS

Introduction

Dendrimers are three-dimensional, monodisperse, highly branching macromolecules having a distinct structure and nanoscale dimensions. Since of their tree-like construction, the word "dendrimer" arises from the Greek words dendron (tree) and meros (part).

They were initially created by Vögtle in 1978, and then by Hawker & Fréchet (convergent synthesis) and Tomalia (divergent synthesis). **Error! Reference source not found.**



The components of dendrimers are:

1. Core
2. Repeating Branching units (generations G0–G12)
3. Surface functional groups

They typically have : **Error! Reference source not found.,Error! Reference source not found.**

1. Their molecular weight is usually between 5,000 and 500,000 g/mol.

2. Minimal polydispersity

3. Globular shape

4. High functionality of the surface

Structure of Dendrimers

There are mainly 3 structure **Error! Reference source not found.**

1. Core

- The central molecule or atom
- Identifies the pattern of branching
- May offer unique characteristics (e.g., porphyrin core → fluorescence).

2. Interior Layers, or Branches

- Units of repeated monomers
- In charge of porosity, stability, and flexibility
- Generations (G1, G2, G3, etc.)

3. Functional Groups at the Terminal

- Found on the surface
- May be neutral, cationic, or anionic.
- Regulate biological contact, reactivity, and solubility

Types of Dendrimers **Error! Reference source not found.**,**Error! Reference source not found.**,**Error! Reference source not found.**

In accordance with Chemical Composition

1. Polyamidoamine, or PAMAM

- The most researched
- created using a different approach
- utilized in the delivery of drugs and genes

2. Polypropylene Imine, or PPI

- Elevated density of amines
- used in gene delivery and antitumor

3. PLL, or poly-L-lysine

- Biodegradable
- utilized in microbicidal and antiviral applications

4. Dendrimers made of polyester

- Biodegradable
- Decreased toxicity

B. Modern/Advanced Types

- Janus dendrimers
- supramolecular Dendrimers
- Shape- persistent Dendrimers
- Rotaxane Dendrimers

Methods of synthesis **Error! Reference source not found.**,**Error! Reference source not found.**

1. Divergent Method (Tomalia)

- Growth starts from core outward
- Stepwise generation addition

- Risk of structural defects due to incomplete reactions

2. Convergent Method (Hawker and Frechet)

- Dendrons prepared first
- Then attached to core
- More precise and homogeneous

3. Click Chemistry

- High yield
- Fewer by-products
- Efficient and rapid synthesis

Advantage **Error! Reference source not found.,Error! Reference source not found.**

- Improve solubility of poorly soluble drugs
- Enhance bioavailability
- Targeted drug delivery
- Controlled release
- High drug loading capacity
- Ability to cross biological barriers
- EPR effect in tumors
- Monodispersity and defined structure
- Multivalency interactions

Disadvantage **Error! Reference source not found.,Error! Reference source not found.**

- Cytotoxicity (especially cationic dendrimers)
- Toxicity increase with higher generation
- Hemolytic activity (damage to RBCs)
- Possible immunogenicity
- Complex multi-step synthesis
- Structural defects in divergent method
- Steric hindrance in convergent method
- High production cost
- Difficult large- scale manufacturing
- Limited clinical approval

Applications of Dendrimers **Error! Reference source not found.,Error! Reference source not found.,Error! Reference source not found.**

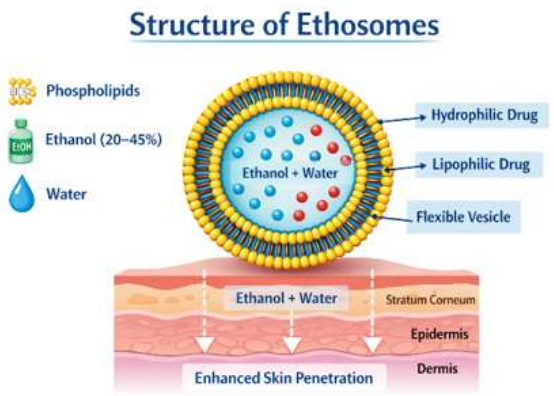
1. Targeted drug delivery
2. Antibacterial therapy
3. Anti-inflammatory therapy
4. Controlled and sustained release
5. Improvement of drug solubility
6. Enhancement of bioavailability
7. Antiviral therapy
8. Anticancer therapy

10.ETHOSOMES

Ethosomes are a modern and highly current drug delivery system designed to enhance the penetration of therapeutic agents through the skin. They are soft, flexible vesicular carriers primarily composed of phospholipids, a high concentration of ethanol, and water. Unlike conventional liposomes, ethosomes contain a significant amount

of ethanol, which plays a crucial role in improving their ability to deliver drugs across the skin barrier.

The concept of ethosomes was introduced to get around the drawbacks of conventional transdermal medication delivery methods, particularly the difficulty of crossing the stratum corneum—the outermost layer of the skin that acts as a strong protective barrier. Ethanol, being a key component, disrupts the lipid structure of the skin, increasing its permeability. At the same time, it imparts flexibility to the vesicles, allowing them to deform and penetrate deeper layers of the skin more effectively.**Error! Reference source not found.**



Structurally, ethosomes are vesicles formed by phospholipid bilayers that encapsulate both hydrophilic and lipophilic drugs. The presence of ethanol not only enhances drug solubility but also reduces the size of vesicles and increases their stability. This dual action significantly improves drug loading and delivery efficiency.

One of the major advantages of ethosomes is their ability to deliver drugs to deeper skin layers and even into systemic circulation, making them suitable for both local and systemic therapy. They have been effectively explored for the delivery of a wide range of drugs, including anti-inflammatory agents, antifungal drugs, antiviral drugs, and hormones. Additionally, ethosomes have shown promising results in cosmetic applications such as anti-aging and skin hydration treatments.

Ethosomes provide a number of advantages over traditional medication delivery methods, such as enhanced drug permeation, enhanced bioavailability, non-invasive administration, and better patient compliance. However, they also have some limitations, such as potential skin irritation due to high ethanol content and challenges in large-scale production.

In conclusion, ethosomes represent a significant advancement in transdermal drug delivery technology. Their unique composition and mechanism of action make them a promising carrier system for improving the therapeutic effectiveness of various drugs. Ongoing research continues to explore their potential in overcoming skin barrier limitations and expanding their applications in pharmaceutical and cosmetic fields.

Advantage of Ethosomes **Error! Reference source not found.**

- High skin penetration ability due to ethanol effect
- Suitable for both hydrophilic and lipophilic drugs
- Non-invasive drug delivery (no injections required)
- Improved bioavailability
- Flexible vesicles allow deep tissue penetration
- Better patient compliance
- Can be used in cosmetics and pharmaceuticals

Disadvantage of Ethosomes

- High ethanol concentration may cause skin irritation
- Limited stability compared to some other carriers
- Risk of drug leakage during storage
- Scale-up and industrial production can be challenging
- Not suitable for all drugs (especially ethanol-sensitive drugs)

Methods of Preparation of Ethosomes Error! Reference source not found.,Error! Reference source not found.

Ethosomes can be prepared using different techniques, but the most commonly used methods are the cold method and the hot method. These methods are designed to produce soft, flexible vesicles with high drug-loading capacity and enhanced skin penetration ability.

1. Cold method

The cold method is the simplest and most frequently used technique for preparing ethosomes.

- In this method, phospholipids are first softened in ethanol at room temperature. The drug to be incorporated is also added to this ethanolic solution, ensuring complete mixing. Since ethanol is a good solvent, it helps in dissolving both the lipid and, in many cases, the drug.
- After obtaining a uniform solution, distilled water is added slowly in a fine stream under continuous stirring. This step is very important because the gradual addition of water leads to the spontaneous formation of vesicles. During this process, phospholipids arrange themselves into bilayer structures, entrapping the drug within the vesicles.
- To obtain a uniform and smaller vesicle size, the dispersion is usually subjected to sonication or extrusion. This helps improve stability and enhances drug delivery efficiency.

2. Hot method

The hot method is used when better control over vesicle formation is needed or when dealing with certain formulation conditions.

- In this technique, phospholipids are first dispersed in water and heated to a moderate temperature (usually around 40–50°C). At the same time, ethanol and the drug are heated separately to the same temperature.
- Once both phases reach the desired temperature, the ethanolic phase is slowly added to the aqueous phase with continuous stirring. This controlled mixing results in the formation of ethosomal vesicles.
- After mixing, the system is allowed to cool down to room temperature. Similar to the cold method, sonication or homogenization may be carried out to reduce vesicle size and improve uniformity.

3. Mechanical Dispersion method

This method is similar to traditional liposome preparation but modified by incorporating ethanol.

- First, phospholipids are dissolved in an organic solvent and a thin lipid film is formed by evaporating the solvent under reduced pressure. This film is then hydrated using a hydroethanolic solution containing ethanol and the drug.

- As hydration proceeds, vesicles are formed and subsequently reduced in size using sonication or extrusion techniques.

Application of Ethosomes

Transdermal drug delivery

- Delivers drugs into systemic circulation through skin
- Avoids first-pass metabolism

Topical drug delivery

- Enhances drug retention in skin layers
- Used for local treatment

Antiviral drug delivery

- Improves penetration of antiviral drugs
- Example: Acyclovir

Antifungal drug delivery

- Enhances treatment of fungal infections
- Examples: Clotrimazole, Ketoconazole

Anti-inflammatory drug delivery

- Used for pain and inflammation
- Examples: Diclofenac, Ibuprofen

Cosmetic applications

- Used in anti-aging, anti-wrinkle, and skin hydration products

Delivery of large molecules

- Suitable for peptides and proteins

Hair and scalp treatment

- Targets drug delivery to hair follicles
- Example: Minoxidil

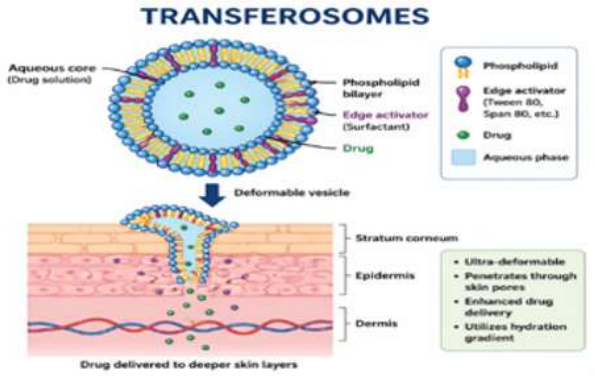
11. Transferosomes

Transferosomes are highly flexible and deformable vesicular drug delivery systems designed to enhance the transport of drugs through the skin. They are also known as ultra-deformable liposomes because of their ability to squeeze through very small pores in the skin without breaking.

These vesicles are mainly composed of:

- Phospholipids
- Edge activators (surfactants like Tween 80, Span 80)
- Water

The presence of edge activators is the key feature that differentiates transferosomes from conventional liposomes. These agents destabilize the lipid bilayer slightly, making it highly flexible and elastic.



Transferosomes work by utilizing the natural hydration gradient of the skin. They move from the dry outer layer (stratum corneum) to the deeper

hydrated layers, carrying the drug along with them **Error! Reference source not found.**

Composition

- Phospholipids → form vesicle structure
- Edge activators → provide flexibility (e.g., Tween 80, Span 80, Sodium cholate)
- Aqueous phase → hydration medium
- Drug → hydrophilic or lipophilic

Method of preparation Error! Reference source not found.

A. Thin film hydration method

1. Dissolve phospholipids and edge activator in organic solvent
2. Evaporate solvent → form thin lipid film
3. Hydrate film with aqueous phase containing drug
4. Sonicate to reduce vesicle size

B. Modified Hand Shaking

1. Similar to thin film hydration
2. Gentle shaking used during hydration

C. Reverse Phase Evaporation Method

1. Prepare water-in-oil emulsion
2. Remove solvent under reduced pressure
3. Vesicles are formed

A. Thin film hydration method

- This is the most common and reliable method for preparing transferosomes.
- First, phospholipids and edge activators (such as Tween 80 or Span 80) are dissolved in an organic solvent like chloroform or methanol. This ensures uniform mixing of all lipid components.
- The organic solvent is then removed using a rotary evaporator under compact pressure, which results in the formation of a thin, dry lipid film on the walls of the flask.
- Next, this lipid film is hydrated using an aqueous phase containing the drug. During hydration, the lipids swell and peel off, forming vesicles.
- To obtain smaller and more uniform vesicles, the dispersion is subjected to sonication or extrusion

B. Modified Hand Shaking

- This method is a variation of the thin film hydration technique.
- In this process, lipids and edge activators are dissolved in an organic solvent and a thin film is formed as before. Instead of using advanced equipment, the hydration step is carried out by gentle hand shaking.
- The aqueous drug solution is added, and continuous shaking helps in the formation of vesicles.

C. Reverse Phase Evaporation Method

- In this method, both aqueous and organic phases are used to form vesicles.
- First, phospholipids and edge activators are dissolved in an organic solvent. Then, the aqueous phase containing the drug is added to form a water-in-oil emulsion.

- This emulsion is subjected to evaporation under reduced pressure. As the solvent is removed, vesicles are formed.

Advantages Error! Reference source not found.

- Extremely high deformability
- Excellent skin penetration
- Suitable for large molecules (proteins, peptides)
- Improves bioavailability
- Non-invasive drug delivery
- Can deliver drug to deeper tissues

Disadvantages

- Expensive raw materials
- Stability issues (oxidation of phospholipids)
- Difficult large-scale production
- Possible drug leakage

Application Error! Reference source not found.

- Transdermal drug delivery
- Delivery of proteins and peptides
- Anti-inflammatory drugs (diclofenac)
- Hormonal delivery (insulin, corticosteroids)
- Anticancer drug delivery
- Vaccination (transdermal immunization)
- Cosmetic applications
- Local anesthetic delivery

CONCLUSION

Nanotechnology has emerged as a powerful tool in improving drug delivery systems and overcoming a number of restrictions related to traditional formulations. The development of various nanocarriers such as nanoparticles, liposomes, niosomes, nanosponges, cubosomes, polymeric nanoparticles, dendrimers, carbon nanotubes, quantum dots, ethosomes, and transferosomes has opened new possibilities in pharmaceutical research.

Each of these systems offers specific advantages, including improved drug solubility, enhanced stability, better bioavailability, targeted delivery, and controlled release of drugs. These benefits not only increase the effectiveness of therapy but also help in reducing side effects and improving patient compliance.

Nevertheless, despite their encouraging promise, difficulties like as toxicity risks, high production costs, formulation complexity, and difficulties in large-scale manufacturing still need to be addressed. With continuous advancements in technology and research, these issues are probable to be minimized in the future.

In conclusion, nanotechnology-based drug delivery systems represent an important advancement in modern medicine. They have the potential to make treatments more precise, effective, and safer, and are likely to play a significant role in the future of healthcare and personalized medicine.

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