

# Nano Based Drug Delivery Systems: Recent Developments and Future Prospects

Tejaswini Shinde\*, Kanchan Deshmukh, Vaibhavi Gavali, Shradha Deokar

Mandesh Institute of Pharmaceutical Science and Research Center, Mhaswad, Dr. Babasaheb Ambedkar Technological University, Lonere, Raigad MS India- 415509

## ABSTRACT

Nanomedicine and nano delivery systems are a relatively new but rapidly developing science where materials in the nanoscale range are employed to serve as means of diagnostic tools or to deliver therapeutic agents to specific targeted sites in a controlled manner. Nanotechnology offers multiple benefits in treating chronic human diseases by site-specific, and target-oriented delivery of precise medicines. Recently, there are a number of outstanding applications of the nanomedicine (chemotherapeutic agents, biological agents, immunotherapeutic agents etc.) in the treatment of various diseases. The current review, presents an updated summary of recent advances in the field of nanomedicines and nano based drug delivery systems through comprehensive scrutiny of the discovery and application of nanomaterials in improving both the efficacy of novel and old drugs (e.g., natural products) and selective diagnosis through disease marker molecules. The opportunities and challenges of nanomedicines in drug delivery from synthetic/natural sources to their clinical applications are also discussed. In addition, we have included information regarding the trends and perspectives in nanomedicine area.

**Keywords:** Nanomedicine, Nanomaterials, Drug delivery, Drug targeting, Natural products

## INTRODUCTION

The conventional application of drugs presents challenging problems in the Treatment of many diseases for example: therapeutic effectiveness, poor Biodistribution, stability, solubility and intestinal absorption, lack of selectivity, Side effects and fluctuations in plasma concentration [1-3]. Drug delivery Systems (DDS) have been designed to overcome these limitations and Drawbacks. DDS provide specific drug targeting and delivery, minimizing Undesirable side effects, using lower doses of drug and protecting the drug from degradation. Recent developments in nanotechnology have indicated that Nanoparticles (ranging in size from 1–1000 nm) can be successfully used as Drug carriers with optimized physicochemical and biological properties (small Size, increased drug accumulation and therapeutic effects, ability to cross cell Or tissue barriers, controlled drug release, etc.). The use of nanoparticles as Drug carriers can play an important role in eliminating the challenging Problems associated with conventional drugs used for the treatment of many Chronic diseases such as

cancer, asthma, hypertension, human Immunodeficiency virus (HIV), and diabetes [4-10]. Polymeric nanocarriers, dendrimers, polymeric micelles, liposomes, solid Lipids nanoparticles (SLNs), metallic nanoparticles (magnetic, gold), carbon Nanotubes, nanospheres, nanocapsules and nanogels are examples of Nano-based drug delivery systems that are currently under research and Development [11-15]. Some of them, especially cancer treatments, have been Clinically used and approved by the Food and Drug Administration (FDA). The use of drug delivery systems in cancer treatment consists of two Strategies: passive and active targeting (Figure 1). Each targeting strategy aims to increase the accumulation of the drug within the tumour tissue while Reducing the side effects [16,17].

## Background:

Since ancient times, humans have widely used plant-Based natural products as medicines against various dis-Eases. Modern medicines are mainly derived from herbs on the basis of traditional knowledge and

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practices. Nearly, 25% of the major pharmaceutical compounds and Their derivatives available today are obtained from natural resources Nanotechnology is shown to bridge the barrier of Biological and physical sciences by applying nanostructures and nanophases at various fields of science [11]; Specially in nanomedicine and nano based drug delivery systems, where such particles are of major interest [12, 13]. Nanomaterials can be well-defined as a material with sizes ranged between 1 and 100 nm, which Influences the frontiers of nanomedicine starting from Biosensors, microfluidics, drug delivery, and microarray tests to tissue engineering [14– 16]. Nanotechnology employs curative agents at the nanoscale level to Develop nanomedicines. The field of biomedicine com-Prising nanobiotechnology, drug delivery, biosensors, and tissue engineering has been powered by nanoparticles [17 The use of ideal nano-drug delivery system is decided Primarily based on the biophysical and biochemical properties of the targeted drugs being selected for the treatment [8]. However, problems such as toxicity exhibit by nanoparticles cannot be ignored when considering the Use of nanomedicine. More recently, nanoparticles have Mostly been used in combination with natural products to lower the toxicity issues. The green chemistry route of designing nanoparticles loaded with drugs is widely Encouraged as it minimises the hazardous constituents in the biosynthetic process. Tus, using green nanoparticles for drug delivery can lessen the side-effects of the medications [19]. Moreover, adjustments in nanostructures Size, shape, hydrophobicity, and surface changes can future enhance the bioactivity of these nanomaterials. Thus, nanotechnology offers multiple benefits in treating chronic human diseases by site-specific, and target-Oriented delivery of medicines. However, inadequate Knowledge about nanostructures toxicity is a major Worry and undoubtedly warrants further research to Improve the efficacy with higher safety to enable safer Practical implementation of these medicines. Therefore, cautiously designing these nanoparticles could be helpful in tackling the problems associated with their use. Considering the above facts, this review aims to report different nano based drug delivery systems, significant Applications of natural compound-based nanomedicines, and bioavailability, targeting sites, and controlled release of nano-drugs,

as well as other challenges associated with Nanomaterials in medicines.

## POLYMERIC MICELLES

Polymeric micelles that consist of amphiphilic co-polymers in the form of Core/shell nanostructures can be designed to ensure selective delivery of Drugs, especially water insoluble drugs, to their subcellular targets. Polymeric Micelles comprise of two structures: an inner core and an outer shell. Polymeric micelles range in size from 10–100 nm, each type having a narrow Size distribution. This narrow size range is the most important property of Polymeric micelles, ensuring high stability, sterility and long-term circulation in the bloodstream. It is important to point out that polymer chains in the inner core of polymeric micelles affect their stability and it is a key point in drug Delivery to avoid interaction of single polymer chains with the loading drug.

### Production and drug incorporation into polymeric micelles

The production of polymeric micelles can be separated into two techniques: Direct or indirect. What technique will be selected relies on the simple Equilibration of the drug and the type of polymers. While the direct method Includes the direct solubilization of the amphiphile in aqueous medium Followed by encapsulation of the drug, the indirect method depends on the use of water-miscible organic solvents (e.g., acetone, dimethylacetamide) to Co-solubilize the co-polymer and the drug and then to separate organic Solvents by evaporation or dialysis. However, these methods have been improved in recent studies to increase encapsulation capacity and stability and to control drug release kinetics [32-36]. Drugs can be loaded into micelles by chemical conjugation or by physical Entrapment through dialysis or emulsification techniques. The drug loading Procedure may influence the entrapment efficiency and the distribution of a Drug within the polymeric micelles. Chemical conjugation enables the drug to Be incorporated with the hydrophobic polymer by a covalent bond, such as an Amide bond. Thus, the entrapped drug is protected from enzymatic cleavage Due to non-hydrolysis of chemical bonds. The dialysis or oil-in-water emulsion Procedure is used in the physical entrapment of drugs.

**Application:**

Polymeric micelles are primarily used in drug delivery applications, particularly for solubilizing poorly soluble drugs, achieving controlled release, and targeting specific tissues within the body due to their unique core-shell structure, allowing for enhanced bioavailability and reduced side effects by concentrating the drug at the desired site of action; they can be designed to respond to specific stimuli for triggered drug release in targeted areas like tumours. Key applications of polymeric micelles: Cancer treatment: Delivering highly potent anticancer drugs like paclitaxel by encapsulating them within the micelle core, enabling improved tumour accumulation and reduced systemic toxicity. Poorly soluble drug delivery: Solubilizing hydrophobic drugs that have low aqueous solubility, improving their absorption and bioavailability. Sustained drug release: Controlling the release profile of a drug by designing the polymer structure to achieve prolonged therapeutic effects. Targeted drug delivery: Attaching specific ligands or antibodies to the micelle surface to target specific cell receptors, enhancing drug delivery to the desired site. Gene therapy: Delivering nucleic acids like DNA or siRNA to cells using polymeric micelles as carriers. Imaging applications: Incorporating fluorescent dyes or contrast agents into the micelle structure for in vivo imaging and monitoring drug delivery. Key advantages of using polymeric micelles: High drug loading capacity: Ability to encapsulate a large amount of drug within the hydrophobic core. Biocompatibility: Can be designed with biocompatible polymers to minimize toxicity. Stability in circulation: Long blood circulation time due to the hydrophilic outer shell, often achieved by using polyethylene glycol (PEG). Tailored design: Flexibility to modify the polymer structure to achieve desired properties like drug release kinetics and targeting capabilities.

**DENDRIMERS**

Dendrimers are hyperbranched globular shaped particles having a unique Three-dimensional architecture. They can provide perfect control over Molecular structure for a nanosized based drug delivery system due to their Multiple functional surface groups. The first poly(amidoamine) (PAMAM) dendrimer was synthesized by Tomalia in

1985 [109]. Recent studies have focused on improving their application and Functional design as drug or gene delivery systems, especially in cancer Treatment, in order to eliminate their disadvantages. Dendrimers have three different separate components: A core, at the centre of the dendrimer, determines the size and shape of the Dendrimer, Branches, constituted of repeat units lead to a monodisperse, treelike, Star-shaped or generational structure, Terminal functional groups, generally located at the exterior surface of the Dendrimer. These surface groups enable growth of the dendrimer so they Determine the properties of dendritic macromolecules according to their Chemical modification. Dendrimers can be used as a suitable carrier for increasing drug solubilization, enhancing gene or drug delivery and increasing the therapeutic effectiveness of any drug, as well as enabling targeting to specific sites [110-119]

**Types of dendrimers:**

Different types of dendrimer having different functionalities have been Developed using recent advances in synthetic chemistry and characterization Techniques to overcome limitations and improve applications. The most Commonly used types of dendrimer

1. PAMAM Dendrimers
2. PPI Dendrimer
3. Liquid crystalline (LC) Dendrimers
4. Core shell (tecto) dendrimer
5. Chiral dendrimers

**Application of dendrimers:**

Dendrimers have a wide range of applications due to their unique structure and properties. Here are some applications of dendrimers:

**1. Drug Delivery**

Dendrimers can be used as carriers for drugs, genes, and other therapeutic agents. Their branched structure allows for high drug loading and controlled release.

**2. Cancer Treatment**

Dendrimers can be designed to target cancer cells specifically, reducing the harm to healthy cells. They

can also be used to deliver chemotherapy drugs directly to the tumour site.

### 3. Gene Therapy

Dendrimers can be used as vectors for gene delivery, allowing for efficient transfection of cells with minimal toxicity.

### 4. Imaging and Diagnostics

Dendrimers can be labelled with imaging agents, such as fluorescent dyes or radioactive isotopes, for use in medical imaging and diagnostics.

### 5. Cosmetics and Personal Care

Dendrimers can be used in skincare products to deliver active ingredients, such as antioxidants and moisturizers, deep into the skin.

### 6. Sensors and Detection

Dendrimers can be used to create sensors for detecting biomolecules, such as proteins and DNA.

### 7. Catalysis

Dendrimers can be used as catalysts for chemical reactions, offering improved efficiency and selectivity.

### 8. Environmental Remediation

Dendrimers can be used to remove pollutants from water and soil by binding to heavy metals and other contaminants.

### 9. Tissue Engineering

Dendrimers can be used to create scaffolds for tissue engineering, providing a framework for cell growth and differentiation.

### 10. Biomedical Research

Dendrimers can be used as tools for studying biological systems, such as protein-protein interactions and cellular signalling pathways. These are just a few examples of the many applications of dendrimers. Their unique properties make them

versatile molecules with a wide range of potential uses.

### SOLID LIPID NANOPARTICLES (SLNs): -

SLNs which are in the size range of 10–1000 nm, are attracting major attention as a novel colloidal drug carrier with the potential to overcome limitations in Drug delivery including poor drug loading capacity, size problems, unstable Properties, uncontrolled drug release associated with polymeric nanoparticles, Dendrites and liposomes. SLNs offer unique properties such as small size, Large surface area, high drug loading and entrapment efficiency, low toxicity, Excellent physical stability, controlled drug release, protection of drugs from Degradation, and avoidance of the use of organic solvents. The structure of SLNs based on lipids that are solid at room temperature. The Lipid structure of SLNs is important to determine whether or not a loaded Molecule can be strongly encapsulated within a delivery system. Therefore, the Lipids that form the SLNs core structure could be important for high-rate drug Loading. Additionally, most lipids that form the structures of SLNs are Biodegradable, so SLNs show excellent biocompatibility and have less toxic Effects. When the use of SLNs is investigated, it seems that SLNs have often Been selected for lipophilic and hydrophilic drug compatibility with lipids that Do not have toxic effects as carriers. However, in recent years, increasing Attention has also been paid to the coating of SLNs in order to load lipophobic and hydrophilic drugs in the lipid structure and also to provide gene delivery. Different methods are being developed to prepare SLNs, such as high-pressure Homogenization (hot and cold homogenization), microemulsion, solvent Emulsion diffusion, solvent evaporation, ultrasonication/high speed Homogenization, and spray drying methods. However, it is very important to Choose the best methods to avoid drug degradation and lipid crystallization According to the properties of the incorporated substances. After production, the second most important step is the characterization of nanoparticles. Analytical methods can be used to characterize SLNs in terms of particle size, ZP, PCS, surface characteristics (TEM/SEM), crystallinity [differential scanning Calorimetry (DSC), XRD], chemical shift, NMR, drug entrapment efficiency, and In vitro drug release studies (UV spectroscopy,



HPLC). After SLNs are Characterized, the third most important step is their application according to the desired properties. Different applications have been studied in the Literature, especially in cancer treatment:

- (i) chemotherapeutic drugs Incorporated into SLNs to eliminate their disadvantages and overcome MDR,
- (ii) Gene therapy (delivery of peptides, genes, miRNA, siRNA into cells),
- (iii) Drug targeting, new adjuvants for vaccines, treatment of infectious Diseases, cosmetic and dermatological preparations and agricultural application.

## • PRODUCTION METHODS OF SLNS: -

### 1. High-pressure homogenization:

nanoparticles (SLNs) using high pressure homogenization, a mixture of molten lipid (containing the drug), a suitable surfactant, and aqueous phase are subjected to high pressure through a narrow orifice in a homogenizer, causing the lipid to break down into tiny particles, forming a stable SLN dispersion; this method is considered efficient for producing small, uniformly sized nanoparticles with good stability.

### 2. Microemulsion method:

The microemulsion method for producing solid lipid nanoparticles (SLNs) involves creating a stable microemulsion containing the desired drug loaded into a molten lipid phase, which is then dispersed into an aqueous phase, causing the lipid to solidify into tiny nanoparticles, essentially “trapping” the drug within the solid lipid matrix.

### 3. Solvent emulsification/evaporation:

The solvent evaporation method is a technique used to create nanoparticles by emulsifying a polymer in water and dispersing it in a volatile solvent. The solvent is then evaporated to form solid particles.

### 4. Supercritical fluid (SCF) technique:

Nanoparticles primarily refers to the use of supercritical fluids (SCFs), which are substances at a temperature and pressure above their critical point, allowing for unique properties like high diffusivity and low viscosity, making them ideal for precise nanoparticle synthesis and manipulation.

### 5. Ultrasonication:

Ultrasonication is a non-thermal technique that uses sound waves to extract bioactive compounds from plant and animal materials, such as nutraceuticals. It's a green technology that can be used to create new products and purify bioactive components.

### 6. Spray-Drying:

Particles is a technique that uses a spray dryer to create particles in the nanometre range. This process is used to create powders from solutions, emulsions, or dispersions.

### Characterization of SLNs: -

SLN characterization:

- (i) Particle size and size distribution: Measured using dynamic light scattering (DLS) to assess the average particle size and uniformity of the SLN dispersion; a narrow size distribution is desirable for optimal performance.
- (ii) Zeta potential: Indicates the surface charge of the SLNs, which influences their stability in suspension; a high zeta potential (positive or negative) generally provides better colloidal stability.
- (iii) Morphological analysis: Transmission electron microscopy (TEM) is used to visualize the shape and size of individual SLNs, confirming their spherical morphology.
- (iv) Drug loading efficiency: Determined by calculating the amount of drug encapsulated within the SLNs compared to the initial drug concentration, indicating the effectiveness of the drug loading process.
- (v) Thermal analysis (DSC): Differential scanning calorimetry is used to study the melting

behaviour of the lipid matrix within the SLNs, confirming the solid nature of the lipid core at body temperature.

- (vi) In vitro drug release studies: Evaluation of the rate and extent of drug release from the SLNs under controlled conditions to assess the controlled release profile.

#### Other Important Considerations:

1. Lipid selection: The choice of lipid (e.g., tristearin, stearic acid, cetyl palmitate) significantly impacts the properties of the SLNs, including their melting point and stability.
2. Surfactant selection: The type and concentration of surfactant used to stabilize the SLNs influences their particle size, zeta potential, and overall stability.
3. Production method: Different methods like high-pressure homogenization, microemulsion techniques, and solvent evaporation can impact the characteristics of the final SLN formulation.

#### • Applications Of SLNS

Solid lipid nanoparticles (SLNs) are used in drug delivery, cancer therapeutics, and other biomedicine applications.

#### Applications

- Drug delivery: SLNs can deliver a variety of drugs, including antibiotics, chemotherapeutic drugs, and nucleic acids. They can be used in oral, parenteral, transdermal, intranasal, ocular, and pulmonary drug delivery.
- Cancer therapeutics: SLNs can help overcome physiological barriers and multidrug resistance pathways in cancer therapy. For example, SLNs can be used to deliver paclitaxel to treat breast cancer cells.
- Gene therapy: SLNs are being considered for use in gene therapy, including in vivo gene therapy.
- Clinical trials: SLNs are used in clinical trials.
- Cosmetics: SLNs are used in cosmetics.

#### Advantages

- SLNs are biocompatible
- SLNs can encapsulate hydrophilic and hydrophobic compounds
- SLNs can improve solubility, cellular uptake, and stability
- SLNs can reduce enzyme degradation
- SLNs can prolong the circulation time of various drugs.

#### CONCLUSION: -

This review has highlighted recent advances in nanomedicine, encompassing technological progress in delivering both established and novel drugs, as well as innovative diagnostic methodologies. While initial applications of nanotechnology focused primarily on improving drug solubility, absorption, bioavailability, and controlled release, the field has expanded significantly. Despite the inherent uncertainties associated with nanodrug discovery and development, the potential benefits of nanomedicine, including enhanced therapeutic efficacy and reduced side-effects, are substantial. Further research and development in this rapidly evolving field promise to revolutionize disease diagnosis and treatment.

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