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**Review Article**

# Advances in Nanoparticle-Based Drug Delivery Systems: A Comprehensive Review of Pharmaceutical Formulations

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## ABSTRACT

A principal drawback of conventional drug delivery approaches lies in their limited capacity to achieve selective targeting, often resulting in diminished therapeutic efficacy and increased systemic toxicity. Nanoparticle-mediated drug delivery systems (DDS) have emerged as a robust alternative, enabling accurate, site-specific transport of pharmacologically active agents while improving their physicochemical stability and bioavailability. This review provides an in-depth examination of the foundational concepts of nanoparticles, their classifications, and their incorporation into various pharmaceutical dosage forms. It encompasses a broad spectrum of nanoparticulate formulations, including tablets, injectables, suspensions, gels, creams, dry powder inhalers, and capsules. Each dosage form leverages distinct classes of nanoparticles—such as polymeric, lipidic, and inorganic carriers—engineered to address specific therapeutic challenges. The convergence of nanotechnology with drug delivery innovations has substantially enhanced drug solubilization, modulated release kinetics, and improved patient adherence. This review emphasizes the expanding utility of nanocarrier systems in pharmaceutical technology and their transformative potential in the advancement of personalized and targeted therapeutic interventions.

## INTRODUCTION

One of the major challenges in treating various diseases is ensuring that therapeutic agents reach their intended target site. Traditional drug administration often suffers from limited efficacy, uneven distribution throughout the body, and poor selectivity[1]. These issues can be addressed through the use of controlled drug delivery systems (DDS), which direct the drug specifically to the site of action. This targeted approach helps minimize unwanted side effects and reduces the impact on healthy tissues. Moreover, DDS can protect the drug from premature breakdown or elimination, increasing its concentration at the desired location and allowing for the use of smaller doses. Such

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advanced therapeutic strategies are especially valuable when there is a mismatch between the administered dose and the desired therapeutic or adverse effects[2]. Nanotechnology, a comparatively recent scientific discipline, has attracted significant interest over the past two decades and is swiftly transitioning from academic research to industrial applications[3]. Nanotechnology involves the deliberate design and manipulation of matter at the nanoscale, specifically between 1 and 100 nanometers, enabling the creation or reconfiguration of nano systems with enhanced functionalities. Nanoparticles represent the culmination of advanced physicochemical manipulation of matter at the molecular level, typically exhibiting dimensions only marginally larger than individual atoms. Arising from precise molecular engineering, these nanostructures demonstrate superior physicochemical properties, including intrinsic thermodynamic stability and self-assembling capabilities[4,5] Their high degree of tunability allows for functionalization to impart targeted characteristics, such as an increased surface-area-to-volume ratio, surpassing that of conventional bulk materials[6]. Nanoparticles possess the capability to significantly enhance the therapeutic effectiveness of drugs by ensuring greater stability and enabling precise delivery to targeted sites of action. A wide range of nanoparticle types— including polymer-based, inorganic, and lipid-based systems—have shown considerable promise in drug delivery applications[7]. The formulation of nanoparticles represents a critical initial step; however, a more significant challenge involves their integration into suitable pharmaceutical dosage forms, followed by the physicochemical and biological characterization of the final nanoparticulate formulation. This review primarily focuses on providing comprehensive information on nanoparticle-based formulations.

**The Basic Necessity and Types of Nanoparticles.**

Owing to their unique physicochemical properties, nanoparticles have emerged as effective carriers for delivering a wide range of therapeutic molecules to specific targets within the body. These site-specific nanomedicines can enhance the therapeutic index of drugs by improving their effectiveness and/or increasing their biocompatibility. Furthermore, nanotechnology offers advantages such as enhancing the solubility and bioavailability of poorly water-soluble drugs, protecting active agents from physiological barriers, facilitating the development of novel bioactive macromolecular therapeutics, and enabling the delivery of large drug payloads[8]. Nanotechnology is primarily divided into two categories: nanodevices and nanomaterials. Nanodevices include advanced components such as respirocytes and NEMS/MEMS (Nanoelectromechanical Systems/Microelectromechanical Systems), which are designed for specific biomedical applications. On the other hand, nanomaterials are further classified into nanostructured and nanocrystalline forms. Nanostructured materials are subdivided into polymeric and non-polymeric systems. Polymeric nano systems consist of nanoparticles, dendrimers, micelles, and drug conjugates, all of which are widely utilized for drug delivery and therapeutic purposes. Non-polymeric nano systems include carbon nanotubes, metallic nanoparticles, silica nanoparticles, and quantum dots, which offer unique physicochemical properties for diagnostic and therapeutic use[9]. Nanocrystalline materials represent another form of nanomaterials characterized by their crystalline structure at the nanoscale. Collectively, these nano systems play a crucial role in advancing pharmaceutical research and improving drug delivery efficiency. The initial generation of

clinically approved nanotechnology-based products primarily consists of liposomal formulations and polymer–drug conjugates. These systems are structurally simple and generally do not possess advanced functionalities such as active targeting capabilities or mechanisms for controlled drug release. In recent years, several innovative and advanced nanoparticle-based techniques for cancer detection have been developed. These engineered nanostructures serve multiple roles, including functioning as fluorescent markers, contrast agents, targeted drug carriers linked with antibodies, and tools for molecular research. Modern advancements in nanoparticulate systems such as quantum dots, paramagnetic nanoparticles, nanosomes and nanoshells are increasingly being utilized in various diagnostic applications[10].

## Nanoparticle Based Formulations

### Nanoparticle Based Tablet

Porous carriers offer a promising way to stabilize amorphous drugs and improve dissolution of poorly soluble compounds. The study aimed to enhance the solubility, dissolution rate, and loading of silymarin by incorporating it into mesoporous silica nanospheres in a lyophilized tablet. Mesoporous silica nanospheres (MSNs) with a 3D-dendritic pore structure were synthesized using a modified one-pot biphase stratification method involving controlled hydrolysis and condensation of a silica precursor. The resulting MSNs were purified, dried, and stored for further physicochemical characterization, including particle size, zeta potential, pore structure, and morphology. The SLM was incorporated into the MSNs through the solvent evaporation technique. A polymeric solution of PVA, sucrose, and PEG was prepared in water, into which the drug-loaded MSNs were added and sonicated until homogeneous. The mixture was poured into blister packs, frozen, lyophilized, and the resulting MSN-based tablets were stored in sealed containers at room temperature[11]. Similarly, a study aimed to develop oral dispersible tablets containing prednisolone-loaded chitosan nanoparticles using Microcrystalline cellulose 101, lactose, and croscarmellose sodium. The nanoparticles were prepared by ionotropic external gelation to improve prednisolone solubility at salivary pH[12]. Chitosan was dissolved in acetic acid and combined with a surfactant and prednisolone in an organic solvent. The organic phase was added dropwise to the chitosan solution, followed by cross-linking with Tripolyphosphate to form nanoparticles through electrostatic interaction. The nanoparticles were then isolated by centrifugation, characterized, and the optimized formulation was used to develop oral dispersible tablets. The formulated nanoparticles were utilized to develop oral fast-disintegrating tablets using the direct compression technique[13]. In a same way, a study focused on developing a colon-targeted oxaliplatin (OP) tablet by combining nanotechnology with fused deposition modeling (FDM) 3D printing to enhance its antitumor efficacy, targeting ability, and safety. OP-loaded alginate nanoparticles were incorporated into Eudragit L100-55 filaments via hot-melt extrusion and 3D printed into tablets, ensuring uniform drug content and targeted release in the colon [14].

### Nanoparticle Based Injectables

The systemic delivery of bisphosphonates, such as sodium alendronate, typically suffers from poor bioavailability and notable toxicity. To address these issues, a novel injectable formulation was developed for direct intra-bone administration of alendronate. This delivery system comprises alendronate-encapsulated nanoparticles incorporated into a gellan gum-based hydrogel matrix. PLGA nanoparticles were prepared using

a double emulsion and solvent evaporation method. Alendronate powder was first emulsified in a PLGA solution to form a primary emulsion, which was then added to an aqueous PVA solution under ultrasonication to create a secondary emulsion. After solvent evaporation, the nanoparticles were collected by centrifugation, washed, freeze-dried, and stored, then redispersed in water for further analysis. Gellan gum was dissolved in ultra-high-quality water at elevated temperature and then cooled before incorporating the nanoparticles- alendronate suspension. To improve injectability, the hydrogel matrix was cross-linked using a calcium chloride solution[15].

**Nanoparticle Based Suspension**

The study aims to develop Omeprazole-loaded nanoparticles for use in a liquid pharmaceutical dosage form. Omeprazole is commonly used to treat gastric hypersecretion disorders in children; however, a liquid formulation suitable for pediatric use is unavailable. Omeprazole-loaded nanoparticles were prepared using the interfacial deposition of preformed polymers method with Eudragit RS100. The organic phase was combined with an aqueous phase containing stabilizers, followed by solvent removal to concentrate the formulation. Enteric coating was applied using Eudragit L100-55 solutions[16,17].

**Nanoparticle Based Gels**

A thermosensitive chitosan-gelatin hydrogel containing 5-fluorouracil -alginate nanoparticles was developed for effective and sustained transdermal delivery of 5-fluorouracil , a commonly used anticancer drug. Due to its short biological half-life (5–10 minutes), 5-fluorouracil clinical application is limited[18]. To enhance its therapeutic efficiency, 5-fluorouracil was encapsulated in alginate nanoparticles via interactions with alginate's functional groups and then incorporated into the hydrogel using a spray drying method[19,20]. Vaginal drug delivery offers localized, long-term release while minimizing systemic side effects. Nanoparticles and nanofibers are promising carriers for this route. This study aimed to develop nanofiber and gel formulations containing benzydamine nanoparticles to ensure prolonged release against vaginal infections. Chitosan nanoparticles were prepared using the ionic gelation method, where benzydamine and ethanol were added to a chitosan solution to enhance drug solubility. Tripolyphosphate (TPP) was added under controlled conditions to form nanoparticles, which were then centrifuged and dispersed in a mannitol solution as a lyoprotectant[21]. The final nanoparticle suspension was freeze-dried to obtain a stable formulation. Then, dispersions containing benzydamine nanoparticles were prepared for nanoparticle-loaded nanofiber formulations. Gel formulations were prepared by dissolving HPMC in water and mixing it with lyophilized nanoparticles using a mechanical stirrer[22,23].

**Nanoparticle Based Cream**

A study formulated day and night cosmeceutical creams using Elaeis guineensis (palm fruit) extract encapsulated in solid lipid nanoparticles (SLNs). The extract, rich in antioxidants like vitamin E, β-carotene, and palmitic acid, demonstrated strong antioxidant activity. The resulting creams showed good physical properties, stability, and were tested for effectiveness on female volunteers. Solid lipid nanoparticles (SLNs) were prepared using the hot homogenization method by mixing *Elaeis guineensis* extract with glyceryl monostearate at elevated temperature until clear. A surfactant solution containing Tween® 80 and Span® 80 was then added and homogenized, followed by cooling in an ice bath. The resulting SLNs were stored in airtight containers for further use. Day and night

creams were formulated using the hot homogenization method with a high-shear mixer. The oil phase, containing various emollients and waxes, was heated and combined with a water phase that included *Elaeis guineensis* SLNs, moisturizers, and stabilizers. After mixing and homogenization, tocopherol acetate and grape seed extract were added; the night cream followed a similar process but excluded sun protection agents and a few specific ingredients[24].

**Nanoparticles Based Dry Powder Inhaler Formulation**

Prothionamide (PTH), a second-line drug for tuberculosis, faces challenges with oral administration due to variable absorption and the need for frequent dosing. To address these issues, pulmonary delivery using nanoparticles was explored to achieve prolonged drug release in the lungs. Chitosan/TPP nanoparticles were formulated using a modified ionic gelation method[25,26]. Prothionamide was incorporated into a chitosan solution, followed by the gradual addition of TPP under continuous stirring. The resulting nanosuspension was centrifuged under controlled temperature to prevent heat-induced instability, washed, and freeze-dried using a cryoprotectant. The flow properties of PTH nanoparticles were first evaluated[27]. To enhance flow, they were manually blended with inhalable-grade anhydrous lactose in varying ratios using the geometrical dilution method[28].

**Nanoparticle Based Capsule**

Cantigi extract possesses several beneficial properties, including antioxidant activity. Although various dosage forms have been developed, a capsule formulation has not yet been explored. Nanoparticles were synthesized through the nanoprecipitation method using gelatin as the polymer and glutaraldehyde as the cross-linker. They were subsequently analyzed for their particle size, polydispersity index, functional groups, surface charge, morphology, and drug entrapment efficiency[29,30]. The capsule formulation was formulated by manually blending the active compounds with suitable fillers and a glidant, followed by filling into hard gelatin capsules. Before encapsulation, the mixture was assessed for parameters such as moisture content, particle size distribution, bulk and tapped density, and flow characteristics. Post-filling, the capsules underwent evaluation for mass uniformity, disintegration time, and dissolution performance[31].

**Regulatory Considerations**

Nanoparticle-based medicines are complex, multi-component systems, making their regulation far more challenging than conventional drugs. Unlike standard formulations with a single active agent and inert excipients, nanomedicines often contain multiple functional components that influence pharmacological behavior.

**Currently, agencies like the FDA and EMA assess nanomedicines case by case, as there are no universal standards. Key regulatory concerns include:**

1. **Physicochemical characterization** – Ensuring critical product attributes are consistently reproduced during manufacturing.
2. **Biodistribution** – Evaluating unusual tissue accumulation or prolonged persistence of nanoparticles.
3. **Clinical safety** – Assessing immune responses and long-term toxicity.
4. **Definition** – Establishing clear criteria for what qualifies as a nanomedicine.

The emergence of generic nanomedicines adds further complexity. Unlike small-molecule generics, demonstrating equivalence in nanomedicines requires more than standard bioequivalence testing. Failed attempts to replicate formulations such as nab-paclitaxel highlight risks of instability, poor reproducibility, and unsafe impurity levels when critical physicochemical parameters are not matched. Regulators have begun developing product-specific guidance, for example with liposomal doxorubicin, but broader frameworks are still needed. Standard PK and toxicity studies may not adequately predict nanoparticle behavior at target sites, and conventional animal models may fall short in mimicking human responses. To ensure safety and efficacy, regulatory approval must rely on comprehensive characterization, advanced disease models, and long-term monitoring. Personalized approaches, where nanomedicines are directed toward specific biomarkers (e.g., tumor receptors), may reduce trial size and cost while improving patient outcomes—an approach regulators are increasingly supportive of.[32]

## CONCLUSION

Nanoparticle-based drug delivery systems (DDS) represent a significant advancement in pharmaceutical technology, offering enhanced therapeutic outcomes through targeted, controlled, and efficient delivery of drugs. These systems address key limitations of conventional dosage forms, such as poor bioavailability, rapid degradation, and systemic side effects. By leveraging the unique physicochemical properties of nanoparticles—such as high surface-area-to-volume ratio, tunability, and biocompatibility—researchers have developed a wide variety of innovative formulations, including tablets, injectables, suspensions, gels, creams, dry powder inhalers, and capsules. Each dosage form serves distinct therapeutic needs and routes of administration, from oral fast-dissolving tablets to colon-targeted 3D-printed formulations and thermosensitive gels for sustained transdermal or vaginal drug delivery. Incorporating nanoparticles into these forms not only improves drug solubility and stability but also ensures precise delivery to the intended site of action. The progress outlined in various studies highlights the transformative potential of nanotechnology in drug delivery, especially for poorly soluble drugs and complex therapeutic agents. With continued research and technological refinement, nanoparticle-based pharmaceutical formulations are poised to redefine treatment paradigms across multiple therapeutic areas, contributing to more effective, safer, and patient-friendly healthcare solutions.

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