



**INTERNATIONAL JOURNAL OF  
PHARMACEUTICAL SCIENCES**  
[ISSN: 0975-4725; CODEN(USA): IJPS00]  
Journal Homepage: <https://www.ijpsjournal.com>



## Review Article

# Nanoparticles Based Sustained Release Tablets: A Comprehensive Review

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## ARTICLE INFO

Published: 28 May 2025

### Keywords:

Nanoparticles, Sustained release tablets, Drug delivery, Ionic gelation, Controlled release, Nanotechnology.

### DOI:

10.5281/zenodo.15538501

## ABSTRACT

Nanoparticle-based sustained release tablets represent a transformative advancement in the field of pharmaceutical technology, offering numerous benefits over conventional drug delivery systems. These formulations are designed to release therapeutic agents at a controlled rate over an extended period, thereby improving drug bioavailability, reducing dosing frequency, and enhancing patient adherence. By incorporating drugs into nanoparticles, it is possible to modify pharmacokinetic profiles, ensure consistent plasma drug levels, and minimize peak-trough fluctuations, which can lead to adverse effects or reduced efficacy. Nanoparticles also provide significant advantages such as improved solubility of poorly water-soluble drugs, protection of labile compounds from degradation in the gastrointestinal environment, and targeted delivery to specific sites of action. Among the various strategies employed, ionic gelation and dual ionic gelation have emerged as efficient, mild, and scalable methods for nanoparticle preparation, particularly for hydrophilic and macromolecular drugs. This review comprehensively examines different types of nanoparticles, preparation methodologies, and their integration into sustained release tablets. It further explores the physicochemical and formulation factors affecting drug release profiles. Recent advancements, case studies, and ongoing challenges are also addressed, highlighting the potential and future prospects of nanoparticle-enabled sustained release systems in improving therapeutic outcomes and drug delivery efficiency.

## INTRODUCTION

In recent years, nanotechnology has revolutionized the field of drug delivery, offering innovative

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**Relevant conflicts of interest/financial disclosures:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



solutions for controlled and sustained release formulations. Nanoparticles, due to their unique physicochemical properties, have emerged as promising carriers for enhancing drug bioavailability, stability, and therapeutic efficacy <sup>[1]</sup>. Sustained release formulations aim to maintain consistent plasma drug concentrations, reduce dosing frequency, and minimize side effects associated with peak-trough fluctuations <sup>[2]</sup>. Among these, nanoparticle-based sustained release tablets combine the advantages of both nanoparticulate drug carriers and oral tablet dosage forms, providing a platform for site-specific, prolonged drug delivery <sup>[3]</sup>. Various types of nanoparticles, such as polymeric, lipid-based, and inorganic systems, have been explored for their ability to encapsulate both hydrophilic and hydrophobic drugs, protecting them from enzymatic degradation and premature release in the gastrointestinal tract <sup>[4,5]</sup>. These carriers can be engineered to release their payload in response to physiological stimuli such as pH, temperature, or enzymatic activity, making them suitable for targeted and controlled drug delivery <sup>[6,7]</sup>. One of the key challenges in developing sustained release tablets is ensuring uniform drug distribution and predictable release kinetics. Nanoparticles address these challenges by offering a large surface area for drug adsorption or entrapment, tunable surface characteristics, and the potential for surface modification with targeting ligands <sup>[8,9]</sup>. Additionally, integration of nanoparticles into oral sustained release tablets can improve patient adherence, especially for chronic conditions requiring long-term therapy <sup>[10]</sup>. This review discusses the types of nanoparticles commonly used in sustained release systems, their methods of preparation, and how they can be incorporated into tablet formulations. It also highlights ionic gelation and dual ionic gelation techniques, recent advances in the field, factors affecting drug

release, and the practical challenges faced during formulation development and scale-up.

## NANOPARTICLE TYPES AND ADVANTAGES

Nanoparticles used in sustained release tablets can be broadly categorized into polymeric, lipid-based, inorganic, and hybrid nanoparticles <sup>[11]</sup>. Each type offers distinct advantages in terms of drug loading capacity, release kinetics, biocompatibility, and stability.

1. **Polymeric nanoparticles** are widely employed due to their versatility and ability to encapsulate a wide range of drugs. They are generally prepared from biodegradable polymers like poly (lactic-co-glycolic acid) (PLGA), chitosan, and polycaprolactone, which degrade into non-toxic byproducts <sup>[12]</sup>. These nanoparticles provide controlled and sustained drug release by matrix erosion or diffusion mechanisms, depending on the polymer composition <sup>[13]</sup>.
2. **Lipid-based nanoparticles**, including solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), offer excellent biocompatibility and the ability to incorporate lipophilic drugs. Their lipid matrix protects the drug from degradation and allows modulation of drug release through lipid crystallinity and composition <sup>[14,15]</sup>.
3. **Inorganic nanoparticles**, such as silica, gold, and magnetic nanoparticles, offer unique properties like ease of surface functionalization and stimuli-responsiveness. However, their clinical use is often limited by concerns over long-term biocompatibility and clearance <sup>[16]</sup>.
4. **Hybrid nanoparticles**, which combine polymeric and lipid components, aim to leverage the advantages of both systems,

achieving enhanced drug loading, stability, and targeted delivery <sup>[17]</sup>.

The advantages of nanoparticle-based sustained release tablets include improved drug solubility, enhanced absorption, reduced dosing frequency, and protection of drugs from the harsh gastrointestinal environment <sup>[18]</sup>. Moreover, nanoparticles can be engineered to target specific tissues or cells, improving therapeutic outcomes and reducing systemic side effects <sup>[19]</sup>.

## PREPARATION TECHNIQUES

Several preparation techniques have been developed to fabricate nanoparticles suitable for sustained release tablets. The choice of method depends on the nature of the drug, polymer, and desired release profile.

1. **Emulsion-solvent evaporation** is a widely used method for preparing polymeric nanoparticles. In this technique, the polymer and drug are dissolved in an organic solvent, which is emulsified in an aqueous phase containing stabilizers. Evaporation of the solvent results in nanoparticle formation <sup>[20]</sup>. This method allows control over particle size and drug loading.
2. **Ionic gelation** is a mild, solvent-free technique primarily used for chitosan and other polyelectrolyte polymers. It involves cross-linking polymer chains with multivalent ions, leading to nanoparticle formation under gentle conditions, preserving drug integrity <sup>[21]</sup>. This method is particularly suitable for encapsulating sensitive biomolecules.
3. **Nanoprecipitation** involves the precipitation of polymer and drug molecules from a solvent into a non-solvent, forming nanoparticles upon rapid mixing. It offers simplicity, reproducibility, and narrow size distribution <sup>[22]</sup>.
4. **Supercritical fluid technology** utilizes supercritical CO<sub>2</sub> as a solvent or anti-solvent

to produce nanoparticles with controlled morphology and size without the use of harmful organic solvents <sup>[23]</sup>.

5. **Spray drying and freeze-drying** techniques are often used for drying nanoparticle suspensions into powders suitable for tablet formulation <sup>[24]</sup>. These methods help maintain nanoparticle integrity and improve storage stability.

Combining these techniques or modifying process parameters can tailor nanoparticles physicochemical properties and drug release characteristics, facilitating their incorporation into sustained release tablets <sup>[25]</sup>.

## NANOPARTICLES IN SUSTAINED RELEASE TABLETS

Incorporating nanoparticles into sustained release tablets provides an effective strategy to optimize oral drug delivery. Nanoparticles can be dispersed uniformly within the tablet matrix, enabling controlled drug release by modulating diffusion and erosion mechanisms <sup>[26]</sup>. This integration enhances drug stability, masks unpleasant taste, and improves patient compliance by reducing dosing frequency <sup>[27]</sup>. Nanoparticle-based tablets often utilize matrix systems, where nanoparticles are embedded in polymers such as hydroxypropyl methylcellulose (HPMC), ethyl cellulose, or other hydrophilic/hydrophobic matrices to regulate drug release <sup>[28]</sup>. The drug release rate can be finely tuned by varying the polymer type, concentration, and nanoparticle characteristics such as size and surface charge <sup>[29]</sup>. Furthermore, nanoparticle surface modification with ligands or coatings can impart targeted delivery capabilities to sustained release tablets, ensuring site-specific drug release in the gastrointestinal tract <sup>[30]</sup>. This is especially beneficial for drugs with narrow absorption windows or those requiring localized action <sup>[31]</sup>. The formulation challenges include ensuring

nanoparticle stability during tablet compression, maintaining drug release profiles, and achieving reproducible batch-to-batch consistency [32]. Advances in tablet manufacturing technologies, such as direct compression and wet granulation optimized for nanoparticles, have addressed some of these issues [33].

### IONIC GELATION AND DUAL IONIC GELATION:

Ionic gelation is a widely employed technique for the preparation of nanoparticles, especially those based on natural polymers like chitosan and alginate. This method involves the cross-linking of polymer chains by multivalent ions (such as tripolyphosphate, calcium, or zinc ions), resulting in the formation of a gel matrix that entraps the drug [34]. The mild processing conditions preserve the bioactivity of sensitive drugs, making ionic gelation particularly attractive for protein, peptide, and nucleic acid delivery [35]. Dual ionic gelation is an advanced modification of the ionic gelation technique, wherein two types of ions or cross-linkers are used sequentially or simultaneously to improve nanoparticle stability and control drug release more precisely [36]. This approach can produce nanoparticles with enhanced mechanical strength, reduced swelling, and sustained drug release profiles [37]. For example, calcium and zinc ions can be used in combination to cross-link alginate and chitosan, respectively, creating interpenetrating polymer networks that provide superior control over drug diffusion [38]. The ionic gelation techniques have been successfully applied in sustained release tablet formulations, offering advantages such as simplicity, scalability, and biocompatibility [39]. However, challenges remain in optimizing gelation parameters (e.g., ion concentration, pH, polymer molecular weight) to achieve reproducible nanoparticle characteristics and desired release kinetics [40].

### FACTORS AFFECTING DRUG RELEASE:

The release of drugs from nanoparticle-based sustained release tablets is influenced by multiple factors related to the nanoparticle properties, tablet matrix, and physiological environment.

1. **Particle size and surface area** play a crucial role; smaller nanoparticles provide a larger surface area, accelerating drug dissolution and release, whereas larger particles tend to sustain release over longer durations [41]. Surface charge influences interaction with biological membranes and can affect mucoadhesion and absorption [42].
2. **Polymer composition and molecular weight** significantly impact the degradation rate and drug diffusion pathways within the nanoparticles. Hydrophilic polymers generally facilitate faster drug release due to swelling and water uptake, while hydrophobic polymers slow release through matrix erosion [43].
3. **Cross-linking density** in nanoparticles prepared by ionic gelation or other methods governs the network tightness, affecting the rate at which the drug diffuses out of the matrix [44]. Higher cross-linking typically results in slower release profiles.
4. The **tablet matrix formulation**, including excipient type and concentration, influences drug release by modifying matrix erosion, swelling behavior, and permeability [45]. Moreover, compression force during tablet manufacture can affect nanoparticle integrity and porosity of the tablet, altering release kinetics [46].
5. Physiological factors such as **pH variations, gastrointestinal transit time, and enzymatic activity** also affect drug release and absorption from sustained release formulations [47].





An in-depth understanding and optimization of these factors are essential for designing nanoparticle-based sustained release tablets with predictable and reproducible drug release profiles [48].

## ADVANTAGES AND CHALLENGES

Nanoparticle-based sustained release tablets offer several significant advantages over conventional formulations. They provide enhanced bioavailability by improving drug solubility and protecting labile drugs from degradation in the gastrointestinal tract [49]. The sustained release profile reduces dosing frequency, thereby improving patient compliance and minimizing side effects related to peak plasma concentrations [50]. Nanoparticles also enable targeted delivery to specific sites within the gastrointestinal tract, which can enhance therapeutic efficacy and reduce systemic toxicity [51]. Moreover, the versatility of nanoparticles allows encapsulation of a wide range of drugs, including hydrophobic, hydrophilic, and biomolecules such as peptides and proteins [52]. The ability to modify surface properties facilitates active targeting and controlled release responsive to physiological stimuli, such as pH or enzymes [53]. Despite these advantages, several challenges hinder widespread clinical application. The stability of nanoparticles during tablet compression and storage remains a major concern, as mechanical stress can cause aggregation or drug leakage [54]. Scale-up of nanoparticle production while maintaining batch-to-batch consistency requires stringent process control and quality assurance [55].

Potential toxicity and immunogenicity of some nanoparticle materials also necessitate thorough safety evaluation [56]. Regulatory challenges related to classification, characterization, and quality control of nanomedicines add complexity to their development and approval processes [57].

Overall, overcoming these challenges through advanced formulation strategies and comprehensive evaluation is critical to fully realize the clinical potential of nanoparticle-based sustained release tablets [58].

## RECENT ADVANCES AND CASE STUDIES

Recent years have witnessed remarkable progress in nanoparticle-based sustained release tablets, driven by advances in materials science, formulation techniques, and analytical tools. Novel polymer blends and stimuli-responsive materials have been developed to achieve precise control over drug release kinetics [59]. For example, pH-sensitive polymers enable targeted drug release in specific segments of the gastrointestinal tract, enhancing drug absorption and therapeutic effect [60]. Several case studies demonstrate the clinical potential of nanoparticle-based sustained release tablets. A study on PLGA nanoparticles loaded with the antidiabetic drug Empagliflozin showed improved bioavailability and prolonged glucose-lowering effects in animal models [61]. Similarly, lipid-based nanoparticles encapsulating anticancer agents exhibited enhanced stability and sustained release, leading to improved tumor targeting and reduced systemic toxicity [62]. Advancements in manufacturing techniques, such as microfluidics and 3D printing, have enabled precise control over nanoparticle size and distribution within tablets, improving reproducibility and scale-up potential [63]. Furthermore, combination therapies employing nanoparticles co-loaded with multiple drugs have been explored to enhance treatment efficacy and overcome drug resistance [64]. Despite promising results, translation to clinical practice requires comprehensive evaluation of pharmacokinetics, safety, and patient acceptability. Ongoing clinical trials and regulatory initiatives are paving the way for commercialization of these advanced sustained release formulations [65].



## FUTURE PERSPECTIVES

The field of nanoparticle-based sustained release tablets is poised for significant growth and innovation. Future research will likely focus on the development of multifunctional nanoparticles capable of simultaneous drug delivery and diagnostic monitoring, known as theranostics. Advances in personalized medicine may drive the design of nanoparticle systems tailored to individual patient needs, improving treatment outcomes. Emerging technologies such as artificial intelligence and machine learning are expected to enhance formulation development by predicting optimal nanoparticle properties and release profiles. Furthermore, environmentally friendly and scalable manufacturing processes will be crucial for large-scale production. Integration of novel biomaterials and smart polymers responsive to physiological triggers will enable more precise control over drug release and targeting. Overcoming current challenges related to stability, toxicity, and regulatory approval will accelerate the translation of nanoparticle-based sustained release tablets into widespread clinical use, ultimately benefiting patients through safer and more effective therapies.

## CONCLUSION

Nanoparticle-based sustained release tablets represent a promising advancement in oral drug delivery, offering improved bioavailability, controlled drug release, and enhanced patient compliance. The versatility of nanoparticles allows for the encapsulation of diverse drug molecules and the potential for targeted delivery. Techniques such as ionic gelation and dual ionic gelation provide efficient and scalable methods for nanoparticle preparation, enabling fine-tuning of drug release profiles. Despite existing challenges related to stability, manufacturing, and regulatory hurdles, ongoing research and technological

innovations are steadily addressing these issues. The future of sustained release formulations lies in the integration of smart materials and personalized approaches, paving the way for safer, more effective, and patient-centric therapies.

## ACKNOWLEDGMENTS

The author(s) would like to acknowledge the support and contributions of colleagues and institutions involved in the research and development of nanoparticle-based sustained release drug delivery systems. Gratitude is also extended to the open access publishers and researchers whose work has been instrumental in compiling this review.

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**HOW TO CITE:** Sarthak Keluskar, Rachel Geevarghese, Swapnil Phalak, Nanoparticles Based Sustained Release Tablets: A Comprehensive Review, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 5, 4615-4624. <https://doi.org/10.5281/zenodo.15538501>

