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Review Paper

A Comprehensive Review on Nanosuspension: As a Promising Approach for Enhancing Drug Solubility and Bioavailability

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ABSTRACT

Nanosuspension technology has revolutionized drug delivery for poorly water-soluble drugs, which constitute 40-90% of new chemical entities facing bioavailability challenges. Defined as submicron colloidal dispersions (1-1000 nm) of pure drug particles stabilized by surfactants or polymers, nanosuspensions enhance dissolution rate and saturation solubility via increased surface area (Noyes-Whitney equation) and Kelvin effect (Ostwald-Freundlich equation). This review explores their preparation via top-down (media milling, high-pressure homogenization) and bottom-up (precipitation, supercritical fluid) methods, alongside comprehensive characterization including particle size, zeta potential, crystallinity, pH, and bioadhesion.Key advantages encompass universal applicability, high drug loading, route flexibility (oral, parenteral, ocular, pulmonary), reduced variability, and targeted delivery potential. Applications demonstrate improved mucoadhesion for oral bioavailability, IV compatibility for non-injectables, and sustained release via subcutaneous routes. Despite instabilities like Ostwald ripening and aggregation, strategic stabilizer selection ensures long-term physical stability.Nanosuspensions offer a carrier-free, scalable platform superior to conventional techniques (micronization, lipid systems), transforming solubility-limited BCS Class II/IV drugs into viable therapeutics. Future prospects include surface-modified nanocrystals for site-specific delivery and commercial expansion across dosage forms, positioning nanosuspensions as a cornerstone of modern pharmaceutics.

INTRODUCTION

The successful development of pharmaceutical dosage forms largely depends on the physicochemical properties of the active pharmaceutical ingredient (API), among which aqueous solubility and dissolution rate are the

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most critical determinants of oral bioavailability. A substantial proportion of newly discovered drug molecules exhibit poor aqueous solubility, resulting in inadequate dissolution in gastrointestinal fluids and consequently poor systemic absorption following oral administration. It has been estimated that nearly 40–90% of newly developed chemical entities (NCEs) and approximately 40% of marketed drugs possess low aqueous solubility, making poor solubility one of the major challenges in modern drug development. This limitation often leads to reduced therapeutic efficacy, variable pharmacokinetics, increased dose requirements, and poor patient compliance. Therefore, improving the solubility and dissolution characteristics of poorly water-soluble drugs has become a major focus of pharmaceutical formulation research. [1–4]

The Biopharmaceutics Classification System (BCS) classifies drugs according to their aqueous solubility and intestinal permeability. Drugs belonging to **BCS Class II** exhibit low solubility but high permeability, whereas **BCS Class IV** drugs possess both poor solubility and poor permeability. In these categories, drug absorption is primarily limited by the dissolution rate rather than membrane permeability. Consequently, increasing the dissolution rate of poorly soluble drugs is an effective strategy for improving oral bioavailability and therapeutic performance. Conventional approaches such as micronization, salt formation, pH modification, co-solvency, complexation with cyclodextrins, lipid-based formulations, and solid dispersions have been employed to overcome solubility-related limitations. However, these methods often suffer from drawbacks including instability, limited applicability, low drug loading, complex manufacturing processes, and scale-up challenges. [2–6]

Advances in nanotechnology have transformed pharmaceutical drug delivery by providing innovative solutions to overcome solubility-related problems. Among these technologies, nanosuspension has emerged as one of the most effective and versatile formulation strategies for enhancing the dissolution rate and bioavailability of poorly water-soluble drugs. A nanosuspension is defined as a submicron colloidal dispersion of pure drug particles, typically ranging from **1 to 1000 nm**, stabilized by suitable surfactants and/or polymers. Unlike other nanoparticulate systems such as liposomes, polymeric nanoparticles, or lipid carriers, nanosuspensions are essentially carrier-free systems with high drug loading capacity, making them suitable for a broad range of hydrophobic drugs irrespective of their chemical structure. [1,3,5,7]

Nanosuspension technology can be applied to drugs administered through multiple routes, including oral, parenteral, ocular, pulmonary, topical, and transdermal delivery. Oral nanosuspensions improve dissolution, reduce variability associated with food intake, and enhance absorption of BCS Class II drugs. Injectable nanosuspensions enable intravenous administration of drugs that are otherwise poorly soluble, while ocular and pulmonary nanosuspensions prolong residence time and improve local drug availability. Surface-modified nanosuspensions have also demonstrated promising potential for targeted drug delivery, controlled drug release, and treatment of chronic diseases such as cancer, neurological disorders, inflammatory conditions, and infectious diseases. [5–8]

Several preparation techniques have been developed for nanosuspension production, broadly categorized into **top-down**, **bottom-up**, and **combination technologies**. Top-down methods include media milling and high-pressure homogenization, whereas bottom-up approaches involve solvent–antisolvent precipitation and supercritical fluid technology. Recent

developments in continuous manufacturing, Quality by Design (QbD), Process Analytical Technology (PAT), and artificial intelligence-assisted formulation optimization have further improved process reproducibility, scalability, and product quality, facilitating industrial translation of nanosuspension-based drug products. [6–8]

2. Need for Nanosuspension

The increasing number of poorly water-soluble drug candidates emerging from modern drug discovery programs has created significant challenges in pharmaceutical formulation development. It is estimated that approximately 40–90% of newly synthesized chemical entities (NCEs) and nearly 40% of marketed drugs exhibit poor aqueous solubility, resulting in inadequate dissolution and low oral bioavailability. Since oral administration remains the most preferred route of drug delivery due to its convenience and patient compliance, poor drug solubility has become a major obstacle in achieving optimal therapeutic efficacy. Consequently, there is an urgent need for advanced formulation strategies capable of improving the dissolution behavior and absorption of hydrophobic drug molecules. Nanosuspension technology has emerged as one of the most effective and versatile approaches to address these limitations. [1–4]

According to the Biopharmaceutics Classification System (BCS), drugs belonging to Class II are characterized by low aqueous solubility but high membrane permeability, whereas Class IV drugs exhibit both poor solubility and poor permeability. For these drug classes, the rate of dissolution is the primary factor limiting drug absorption following oral administration. Poor dissolution results in slow drug release in gastrointestinal fluids, leading to delayed onset of action, inconsistent plasma drug concentrations, increased interpatient variability, and reduced therapeutic effectiveness. Therefore, enhancing the dissolution rate is essential for improving the oral bioavailability of these compounds. [2–5]

Conventional techniques employed to enhance drug solubility include salt formation, pH adjustment, co-solvency, micronization, solid dispersions, inclusion complexation with cyclodextrins, lipid-based formulations, and surfactant systems. Although these approaches have demonstrated success for selected drugs, each possesses inherent limitations. Salt formation is applicable only to ionizable drugs, while solid dispersions may suffer from recrystallization and physical instability during storageThese shortcomings highlight the need for alternative formulation strategies with broader applicability and superior performance. [3–7]

Nanosuspension technology overcomes many of these limitations by reducing drug particles to the nanometer scale, generally between 1 and 1000 nm. Reduction of particle size dramatically increases the total surface area available for dissolution, as explained by the Noyes–Whitney equation, resulting in a significantly faster dissolution rate. The combination of increased surface area, enhanced wettability, shortened diffusion distance, and elevated saturation solubility produces a higher concentration gradient across biological membranes, thereby facilitating rapid drug absorption and improved bioavailability. [1,4,6]

Beyond improving oral bioavailability, nanosuspensions have demonstrated significant advantages for multiple routes of administration. In parenteral delivery, they facilitate intravenous administration of drugs with poor water solubility without requiring toxic organic solvents. In ocular and pulmonary drug delivery, nanosuspensions improve drug residence time and local absorption, while topical and transdermal formulations benefit from enhanced skin penetration and controlled drug release. Surface modification of nanosuspensions with suitable polymers or ligands

further enables targeted drug delivery to specific tissues, thereby improving therapeutic efficacy and reducing systemic adverse effects. [5–8]

Recent advances in pharmaceutical nanotechnology, including Quality by Design (QbD), Process Analytical Technology (PAT), continuous manufacturing, and artificial intelligence-assisted formulation optimization, have significantly improved the reproducibility, scalability, and industrial feasibility of nanosuspension production. In addition, several nanocrystal-based pharmaceutical products have already reached the commercial market, demonstrating the clinical relevance and regulatory acceptance of this technology. These developments further emphasize the growing importance of nanosuspensions as a practical and commercially viable approach for overcoming solubility-related challenges in modern drug delivery. [6–8]

3. Advantages of Nanosuspensions

3.1 Enhanced Solubility and Dissolution Rate

The most significant advantage of nanosuspensions is their ability to improve the apparent solubility and dissolution rate of poorly water-soluble drugs. Reduction of particle size into the nanometer range markedly increases the surface area available for dissolution, thereby accelerating drug release according to the Noyes–Whitney equation. In addition, nanosized particles exhibit higher saturation solubility because of increased surface curvature, as explained by the Ostwald–Freundlich equation. These combined effects result in rapid dissolution and improved drug absorption following administration. This advantage is particularly beneficial for BCS Class II and Class IV drugs, where dissolution is the rate-limiting step for absorption. [1–6]

3.2 Improved Oral Bioavailability

Poor aqueous solubility frequently leads to incomplete gastrointestinal absorption and low oral bioavailability. Nanosuspensions enhance drug absorption by increasing dissolution velocity, improving wettability, and maintaining a higher concentration gradient across the intestinal membrane. Consequently, higher plasma drug concentrations can be achieved using lower doses, reducing interpatient variability and improving therapeutic outcomes. Improved oral bioavailability also contributes to a faster onset of action and more consistent pharmacokinetic profiles. [2–7]

3.3 High Drug Loading Capacity

Unlike polymeric nanoparticles, liposomes, or other carrier-based nanocarrier systems, nanosuspensions consist predominantly of pure drug particles with only small quantities of stabilizers. This carrier-free nature allows exceptionally high drug loading while minimizing the amount of excipients required. High drug loading is particularly advantageous for drugs administered at relatively large doses, as it enables formulation without significantly increasing dosage volume or tablet size. [3–8]

3.4 Broad Applicability to Poorly Soluble Drugs

Nanosuspension technology can be applied to a wide variety of hydrophobic drug molecules irrespective of their chemical structure, molecular weight, or lipophilicity. It is especially useful for compounds that cannot be effectively formulated using salt formation, cyclodextrin complexation, solid dispersions, or lipid-based delivery systems. Therefore, nanosuspensions represent a universal formulation platform capable of improving the delivery of many poorly soluble active pharmaceutical ingredients. [1,4,7]

3.5 Versatility in Routes of Administration

One of the major strengths of nanosuspensions is their compatibility with multiple routes of administration. They can be successfully formulated for oral, parenteral, ocular, pulmonary, topical, transdermal, and intranasal delivery. Oral nanosuspensions improve gastrointestinal absorption, whereas injectable nanosuspensions eliminate the need for toxic organic solvents commonly used for poorly soluble drugs. Ocular and pulmonary nanosuspensions increase residence time at the site of administration and improve local drug availability. Topical formulations enhance skin penetration, while surface-modified nanosuspensions facilitate targeted drug delivery to specific tissues. This versatility greatly expands the therapeutic applications of nanosuspension technology. [2,5–8]

3.6 Rapid Onset of Therapeutic Action

The accelerated dissolution and faster absorption associated with nanosuspensions contribute to a quicker onset of pharmacological action compared with conventional dosage forms. Rapid drug release is particularly beneficial for therapeutic agents requiring immediate clinical effects, such as analgesics, anti-inflammatory agents, and antimicrobial drugs. Faster absorption also improves patient outcomes in acute disease conditions where timely therapeutic intervention is essential. [3–6]

3.7 Reduced Dose and Improved Patient Compliance

Improved bioavailability enables therapeutic drug concentrations to be achieved with lower doses than conventional formulations. Dose reduction minimizes the risk of dose-related adverse effects and may decrease treatment costs. Additionally, smaller doses and less frequent administration improve patient compliance, particularly during long-term treatment of chronic diseases such as hypertension, diabetes, cancer, and neurological disorders. [2–7]

3.8 Improved Physical Stability

Appropriate selection of stabilizers such as polymers and surfactants provides steric and electrostatic stabilization, preventing particle aggregation and sedimentation during storage. Optimized nanosuspensions exhibit excellent physical stability while maintaining uniform particle size distribution throughout their shelf life. Modern manufacturing approaches, including Quality by Design (QbD) and Process Analytical Technology (PAT), further improve formulation reproducibility and long-term stability. [5–8]

3.9 Potential for Targeted and Controlled Drug Delivery

Surface modification of nanosuspensions with polymers, ligands, antibodies, or polyethylene glycol (PEG) enables site-specific drug delivery and prolonged circulation time. Targeted nanosuspensions increase drug accumulation at diseased tissues while minimizing exposure to healthy organs, thereby improving therapeutic efficacy and reducing systemic toxicity. This strategy has shown promising applications in cancer therapy, inflammatory disorders, ocular diseases, and central nervous system drug delivery. [4–8]

3.10 Ease of Scale-Up and Commercial Manufacturing

Several industrially feasible manufacturing techniques, including media milling and high-pressure homogenization, enable large-scale production of nanosuspensions with excellent reproducibility. Compared with many advanced nanocarrier systems, nanosuspensions require

relatively simple equipment and well-established processing methods, facilitating technology transfer from laboratory to commercial manufacturing. The successful commercialization of nanocrystal-based pharmaceutical products further demonstrates the industrial applicability and regulatory acceptance of this technology. [2–8]

3.11 Improved Therapeutic Performance

By simultaneously enhancing solubility, dissolution rate, absorption, and bioavailability, nanosuspensions significantly improve the overall therapeutic performance of poorly soluble drugs. Increased drug exposure often translates into improved clinical efficacy, reduced variability in patient response, enhanced safety, and greater treatment success. These advantages have made nanosuspension technology an important platform for developing next-generation pharmaceutical formulations.

5. Characterization of Nanosuspensions

5.1 Particle Size and Particle Size Distribution

Particle size is one of the most important quality attributes of nanosuspensions because it governs dissolution rate, saturation solubility, stability, cellular uptake, and in vivo performance. Generally, nanosuspensions possess particle sizes ranging from 1 to 1000 nm, although an average particle size below 500 nm is often preferred for improved dissolution and enhanced bioavailability.Particle size analysis is commonly performed using Dynamic Light Scattering (DLS), also known as Photon Correlation Spectroscopy (PCS). Other techniques such as Laser Diffraction (LD) and Nanoparticle Tracking Analysis (NTA) are also widely employed. Uniform particle size distribution minimizes sedimentation and aggregation while ensuring reproducible therapeutic performance.

The Polydispersity Index (PDI) indicates the homogeneity of particle size distribution. A PDI value below 0.3 generally represents a uniform nanosuspension with narrow particle size distribution, whereas higher values indicate particle heterogeneity and potential instability. [1,2,6]

5.2 Zeta Potential

Zeta potential is the electrical potential developed at the particle surface and serves as an important indicator of colloidal stability. It reflects the magnitude of electrostatic repulsion between suspended particles.

Higher absolute zeta potential values reduce particle aggregation by increasing repulsive forces. For electrostatically stabilized nanosuspensions, **zeta potential values of ±30 mV or higher** are generally considered sufficient for good stability. In formulations stabilized by both electrostatic and steric mechanisms, values around **±20 mV** may also provide acceptable stability due to the additional steric barrier offered by polymers.

Zeta potential is determined using **Electrophoretic Light Scattering (ELS)** with a zeta potential analyzer. [4,5,17]

Importance

- Predicts physical stability.
- Indicates aggregation tendency.
- Assists in selecting appropriate stabilizers.
- Evaluates long-term storage stability.

5.3 Particle Morphology

Particle morphology refers to the shape, surface characteristics, and structural appearance of drug nanoparticles. Morphological evaluation provides valuable information regarding crystal shape,

surface smoothness, aggregation, and particle uniformity.

Common techniques include:

- Scanning Electron Microscopy (SEM)
- Transmission Electron Microscopy (TEM)
- Atomic Force Microscopy (AFM)

Well-dispersed spherical or uniformly shaped nanoparticles generally exhibit superior flow properties, enhanced dissolution, and improved formulation stability. [6,10,18]

5.4 Crystal Structure and Crystallinity

Nanoparticle preparation methods may alter the crystalline nature of the drug due to mechanical stress or rapid precipitation. Therefore, evaluation of crystallinity is essential to determine whether the drug remains crystalline or undergoes partial amorphization. [11,13,20]

The principal analytical techniques include:

- X-ray Diffraction (XRD)
- Differential Scanning Calorimetry (DSC)
- Differential Thermal Analysis (DTA)

5.5 pH Determination

The pH of nanosuspensions significantly influences drug stability, particle surface charge, and compatibility with biological tissues. It is measured using a calibrated digital pH meter under controlled temperature conditions.

Maintaining an appropriate pH is particularly important for ophthalmic, injectable, and topical formulations to avoid irritation and maintain drug stability.

5.6 Osmolarity

Osmolarity is particularly important for parenteral and ophthalmic nanosuspensions, where isotonicity is required to minimize tissue irritation and improve patient comfort.

It is measured using an osmometer or calculated theoretically from the formulation composition.

5.7 Surface Hydrophilicity and Hydrophobicity

Surface properties influence nanoparticle interaction with biological membranes, proteins, and cells. Surface hydrophobicity affects plasma protein adsorption, macrophage uptake, biodistribution, and circulation time.

These characteristics are commonly evaluated using Hydrophobic Interaction Chromatography (HIC) or contact angle measurements.

5.8 Drug Content and Entrapment Efficiency

Drug content determines the amount of active pharmaceutical ingredient present in the formulation, whereas entrapment efficiency indicates the proportion of drug successfully retained within the nanosuspension after preparation.

Drug content is commonly determined using:

- UV–Visible Spectrophotometry
- High-Performance Liquid Chromatography (HPLC)

Entrapment efficiency is calculated after separating free drug from nanoparticles by centrifugation or ultrafiltration.

5.9 In Vitro Drug Release Studies

Drug release studies evaluate the dissolution profile of nanosuspensions and compare their performance with pure drug or conventional formulations.

Commonly used dissolution methods include:

- USP Dissolution Apparatus I (Basket)
- USP Dissolution Apparatus II (Paddle)
- Dialysis bag diffusion technique

Samples are analyzed using UV spectrophotometry or HPLC at predetermined time intervals.

5.10 Stability Studies

Stability studies determine whether nanosuspensions maintain their physicochemical properties during storage under various environmental conditions.

Stability studies are generally performed according to **ICH guidelines** under accelerated and long-term storage conditions. [11,13,20]

6. Methods of Preparation of Nanosuspensions

Nanosuspensions are prepared by reducing drug particles to the nanometer range while maintaining their crystalline nature and stabilizing them with suitable surfactants or polymers. The selection of an appropriate preparation method depends on several factors, including the physicochemical properties of the drug, desired particle size, scalability, production cost, and stability of the final formulation. Broadly, nanosuspension preparation techniques are classified into top-down methods, bottom-up methods, and combination technologies, each having distinct principles, advantages, and limitations.

6.1 Top-Down Methods

Top-down methods involve the mechanical size reduction of coarse drug particles into nanoparticles by applying external forces such as shear, impact, collision, or cavitation. These techniques are widely used in the pharmaceutical industry because they are reproducible, scalable, and capable of producing nanosuspensions with uniform particle size distribution. [2,5,6]

6.1.1 Media Milling (Nanocrystal Technology)

Media milling is one of the earliest and most widely employed top-down techniques for nanosuspension preparation. In this method, a coarse drug suspension containing stabilizers is introduced into a milling chamber filled with milling media such as zirconium oxide, glass, or polymeric beads. Rotation of the milling shaft causes continuous collision between the drug particles and the milling beads, resulting in progressive particle size reduction to the nanometer range.

The milling process may be performed in batch or recirculation mode under controlled temperature conditions to avoid thermal degradation of the drug. The stabilizers adsorb onto the newly generated particle surfaces and prevent aggregation during milling.

Advantages

- Suitable for poorly water-soluble drugs.
- Simple and reproducible process.
- Scalable for industrial manufacturing.
- Produces narrow particle size distribution.
- Applicable to high drug concentrations.

6.1.2 High-Pressure Homogenization

High-pressure homogenization is one of the most commonly used industrial methods for producing nanosuspensions. The drug suspension is forced through a narrow homogenization gap under extremely high pressures (typically **500–1500 bar**). As the suspension passes through the homogenization valve, intense cavitation, turbulence, shear stress, and particle collision break down the coarse drug particles into nanoparticles.

Multiple homogenization cycles are generally required to obtain the desired particle size. This method is particularly suitable for thermally stable drugs and is widely used because it does not require toxic organic solvents.

Advantages

- Solvent-free process.
- Suitable for large-scale manufacturing.
- Produces uniform nanoparticles.
- High reproducibility.

- Can be used under aseptic conditions. [4,5,7,17]

6.1.3 Emulsion Diffusion Method

The emulsion diffusion method utilizes emulsions as templates for nanosuspension formation. Initially, the poorly soluble drug is dissolved in a volatile organic solvent that is partially miscible with water. This organic phase is emulsified into an aqueous phase containing surfactants to form a stable oil-in-water emulsion. Subsequent dilution with water facilitates diffusion of the organic solvent into the external phase, leading to supersaturation and precipitation of nanosized drug particles.

The particle size of the nanosuspension largely depends on the droplet size of the initial emulsion, making emulsification conditions critical for successful formulation.

Advantages

- No specialized equipment required.
- Easy control of particle size.
- Suitable for laboratory-scale preparation.
- Good reproducibility.

6.2 Bottom-Up Methods

Bottom-up methods build nanoparticles from molecular or dissolved drug states through controlled precipitation. In these techniques, the drug is first dissolved in a suitable solvent and then rapidly precipitated by adding an antisolvent. Proper control of nucleation and crystal growth is essential to obtain uniform nanoparticles. [6,10,16]

6.2.1 Supercritical Fluid Technique

Supercritical fluid technology is an advanced particle engineering method that utilizes fluids above their critical temperature and pressure, most commonly **supercritical carbon dioxide (CO_2)**. Under supercritical conditions, carbon dioxide exhibits both gas-like diffusivity and liquid-like solvating properties, allowing rapid precipitation of nanoparticles.

Several approaches have been developed, including:

- Rapid Expansion of Supercritical Solution (RESS)
- Precipitation with Compressed Antisolvent (PCA)
- Supercritical Antisolvent (SAS) Process

These methods produce nanoparticles with narrow particle size distribution while minimizing residual organic solvents.

Advantages

- Minimal solvent residues.
- Environmentally friendly process.
- High purity products.
- Uniform particle size. [14,18,24]

6.2.2 Precipitation Technique (Solvent–Antisolvent Method)

The solvent–antisolvent precipitation method is one of the simplest and most widely used bottom-up techniques for nanosuspension preparation. The poorly soluble drug is first dissolved in a water-miscible organic solvent. This solution is then rapidly introduced into an aqueous antisolvent containing stabilizers under continuous stirring.

Rapid supersaturation causes immediate nucleation followed by controlled crystal growth, resulting in nanosized drug particles. The effectiveness of this technique depends on the rate of mixing, solvent-to-antisolvent ratio, temperature, and stabilizer concentration.

Advantages

- Simple and economical.
- Rapid particle formation.
- Suitable for heat-sensitive drugs.
- Easy laboratory-scale preparation. [16,17,22]

6.2.3 Emulsification–Solvent Evaporation Technique

In this method, the drug is dissolved in a volatile organic solvent and emulsified into an aqueous phase containing stabilizers. Continuous stirring or homogenization forms fine emulsion droplets. Subsequent evaporation of the organic solvent results in precipitation of nanosized drug particles within the aqueous medium.

The final particle size depends on droplet size, solvent evaporation rate, homogenization speed, and stabilizer concentration.

Advantages

- Simple and cost-effective.
- Suitable for hydrophobic drugs.
- Good particle size control.
- High drug loading.

6.3 Combination Technologies

To overcome the limitations associated with individual preparation methods, combination technologies integrate bottom-up and top-down approaches. One such strategy involves initial precipitation of the drug to generate fine particles followed by high-pressure homogenization to further reduce particle size and improve uniformity. This hybrid approach enhances process efficiency, minimizes crystal growth, and produces stable nanosuspensions with narrow particle size distribution. [5,18,26]

7. Applications of Nanosuspensions

7.1 Oral Drug Delivery

Oral administration is the most widely preferred route for drug delivery due to its convenience, cost-effectiveness, and patient compliance. However, many orally administered drugs exhibit poor aqueous solubility, resulting in low dissolution rates and limited gastrointestinal absorption. Nanosuspensions overcome these limitations by reducing particle size to the nanometer range, thereby increasing the surface area available for dissolution and improving saturation solubility.The enhanced dissolution rate creates a higher concentration gradient across the gastrointestinal membrane, leading to improved absorption and oral bioavailability. In addition, nanosuspensions exhibit increased mucoadhesion, which prolongs gastrointestinal residence time and facilitates greater drug absorption. These formulations also reduce variability associated with food intake and provide faster onset of therapeutic action. Numerous poorly soluble drugs, including fenofibrate, itraconazole, and sirolimus, have demonstrated significantly improved oral bioavailability when formulated as nanosuspensions. [2,5,10,13]

7.2 Parenteral Drug Delivery

Parenteral administration is essential for drugs requiring rapid systemic action or those exhibiting poor gastrointestinal absorption. However, many hydrophobic drugs cannot be formulated as injectable preparations because of their low aqueous solubility. Traditionally, toxic organic solvents or surfactants have been employed to increase solubility, often causing adverse reactions.

Nanosuspensions provide an effective alternative by dispersing pure drug nanoparticles in an aqueous medium stabilized with suitable surfactants or polymers. Their small particle size permits intravenous administration while avoiding the need for harmful solubilizing agents. Following injection, the increased surface area accelerates dissolution, resulting in rapid therapeutic action. Injectable nanosuspensions have been investigated for anticancer agents, antifungal drugs, corticosteroids, and anti-inflammatory drugs. Furthermore, nanosuspensions enable controlled drug release and prolonged systemic circulation, improving therapeutic outcomes. [2,6,17,18]

7.3 Ocular Drug Delivery

Ocular drug delivery remains challenging because of physiological barriers such as tear turnover, blinking, nasolacrimal drainage, and the corneal epithelium, all of which reduce drug residence time and bioavailability. Conventional eye drops often exhibit bioavailability below 5%.

Nanosuspensions improve ocular drug delivery by increasing drug solubility and maintaining prolonged contact with the ocular surface. Their nanosized particles provide a larger contact area with corneal tissues, resulting in enhanced drug penetration and improved therapeutic effectiveness. In addition, the small particle size minimizes irritation and enhances patient comfort. Nanosuspensions have shown promising applications in the treatment of glaucoma, fungal keratitis, bacterial eye infections, and inflammatory ocular disorders. [13,20]

7.4 Pulmonary Drug Delivery

The lungs possess an extensive alveolar surface area, rich vascularization, and thin epithelial membranes, making pulmonary administration an attractive route for both local and systemic drug delivery. Nevertheless, poorly soluble drugs often exhibit slow dissolution within pulmonary fluids, limiting their therapeutic effectiveness.

Nanosuspensions significantly improve pulmonary drug delivery by enhancing drug dissolution in lung fluids and facilitating uniform deposition throughout the respiratory tract. They may be administered using nebulizers, metered-dose inhalers, or dry powder inhalers after appropriate formulation modifications. Pulmonary nanosuspensions have been investigated for corticosteroids, antibiotics, bronchodilators, and antifungal agents, offering improved treatment of asthma, chronic obstructive pulmonary disease (COPD), pulmonary infections, and lung cancer. [10,16,20]

7.5 Targeted Drug Delivery

Targeted drug delivery aims to selectively concentrate drugs at diseased tissues while minimizing exposure to healthy organs. Owing to their nanoscale dimensions, nanosuspensions exhibit enhanced cellular uptake and can accumulate in target tissues through passive or active targeting mechanisms.

Surface modification using polymers, polyethylene glycol (PEG), antibodies, peptides, or specific ligands further improves tissue specificity and prolongs systemic circulation. These modifications reduce uptake by the reticuloendothelial system and enhance drug accumulation at desired sites. Targeted nanosuspensions have shown promising applications in cancer chemotherapy, brain drug delivery, inflammatory diseases, and infectious disorders. Tween 80-coated nanocrystals have also demonstrated enhanced transport across the blood–brain barrier, improving central nervous system drug delivery. [4,18,24]

7.6 Topical and Transdermal Drug Delivery

Topical and transdermal drug delivery offers localized therapy while avoiding gastrointestinal degradation and hepatic first-pass metabolism. However, the highly organized structure of the stratum corneum presents a major barrier to drug penetration.

Nanosuspensions enhance topical drug delivery by increasing the contact surface between drug particles and skin, improving dissolution within skin fluids, and facilitating penetration through hair follicles and appendages. Their small particle size also enables localized drug accumulation within the epidermis and dermis, improving therapeutic effectiveness while minimizing systemic absorption. Topical nanosuspensions have been investigated for corticosteroids,

antifungal agents, nonsteroidal anti-inflammatory drugs, and dermatological treatments. [21,23]

7.7 Intranasal Drug Delivery

Intranasal administration provides rapid drug absorption due to the highly vascularized nasal mucosa and offers the potential to bypass the blood–brain barrier through the olfactory pathway. Nanosuspensions improve intranasal drug delivery by enhancing dissolution and increasing residence time on the nasal mucosa. Mucoadhesive stabilizers further improve drug retention and absorption, making this approach particularly attractive for central nervous system disorders, peptide delivery, and emergency medications requiring rapid onset of action. Although research is still evolving, intranasal nanosuspensions represent a promising strategy for future pharmaceutical development. [18,24]

8. FUTURE OUTLOOK

Nanosuspension technology has emerged as one of the most promising nanotechnology-based approaches for improving the solubility, dissolution rate, and bioavailability of poorly water-soluble drugs. Although several nanosuspension-based products have already reached the pharmaceutical market, continuous advancements in nanotechnology, material science, and pharmaceutical engineering are expected to further expand their therapeutic applications.

One of the most significant future trends is the integration of **Quality by Design (QbD)** and **Process Analytical Technology (PAT)** into nanosuspension development. These approaches facilitate systematic optimization of critical formulation variables and process parameters, ensuring consistent product quality, enhanced reproducibility, and easier regulatory approval. Continuous manufacturing technologies are also expected to replace conventional batch production, enabling cost-effective large-scale manufacturing while maintaining uniform particle characteristics. Overall, future innovations in formulation strategies, advanced manufacturing technologies, nanomaterials, and regulatory science are expected to further strengthen the role of nanosuspensions as a versatile and commercially viable drug delivery platform.

CONCLUSION

Poor aqueous solubility continues to be one of the major challenges in pharmaceutical formulation development, limiting the bioavailability and therapeutic efficacy of many drug molecules. Nanosuspension technology has emerged as an effective and versatile strategy for overcoming these limitations by reducing drug particle size to the nanometer range, thereby enhancing saturation solubility, dissolution rate, and drug absorption.Compared with conventional solubility enhancement techniques, nanosuspensions offer several important advantages, including high drug-loading capacity, minimal use of excipients, improved physical stability, compatibility with multiple routes of administration, and suitability for both newly developed and existing poorly soluble drugs. Various preparation methods, including media milling, high-pressure homogenization, solvent–antisolvent precipitation, and supercritical fluid technology, enable the production of stable nanosuspensions with desirable physicochemical properties. Comprehensive characterization of particle size, polydispersity index, zeta potential, morphology, crystallinity, drug content, and dissolution behavior plays a crucial role in ensuring formulation quality, stability, and therapeutic performance.

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