



Received on 26 May 2026; received in revised form, 10 June 2026; accepted, 20 June 2026; published 01 October 2026

REDEFINING BIOAVAILABILITY OF ANTIPSYCHOTICS IN SCHIZOPHRENIA THERAPY USING NANOSUSPENSION-BASED APPROACHES

Pooja Gupta ^{*1}, Aditya Narayan ², Shruti Ajitkumar Patel ³, Sejal Vaghela ³, Priyanshi Patel ³ and Falguni Jaiswal ³

Department of Pharmaceutics ¹, Department of Pharmacology ³, Swaminarayan University, Ahmedabad - 382725, Gujarat, India.

Department of Analytical Research and Development ², Troikaa Pharmaceuticals Ltd., Ahmedabad - 380054, Gujarat, India.

Keywords:

Nanosuspension, Schizophrenia, Antipsychotics, Bioavailability enhancement, poorly soluble drugs, Nanotechnology

Correspondence to Author:

Pooja Gupta

Research Scholar,
Department of Pharmaceutics,
Swaminarayan University,
Ahmedabad - 382725, Gujarat, India.

E-mail: poojagupta200212@gmail.com

ABSTRACT: Schizophrenia, a chronic neuropsychiatric disorder, requires long-term administration of antipsychotic drugs, many of which suffer from poor aqueous solubility and low oral bioavailability. These pharmacokinetic limitations often result in subtherapeutic exposure, variable patient responses, and an increased risk of non-compliance. Nanosuspension-based drug delivery has emerged as a promising strategy to overcome these challenges by enhancing the dissolution rate and systemic absorption of poorly water-soluble antipsychotics. This review explores recent advancements in nanosuspension technology, including top-down and bottom-up fabrication methods, surface modification strategies, and targeted delivery approaches. Emphasis is placed on the role of nanosuspensions in optimising the pharmacokinetic profiles of atypical antipsychotics such as risperidone, olanzapine, and quetiapine. Furthermore, we highlight preclinical and clinical data supporting their use, discuss regulatory considerations, and propose future directions for personalised nanosuspension-based schizophrenia therapy. Overall, nanosuspension formulations offer a transformative avenue for improving drug bioavailability, therapeutic efficacy, and patient adherence in schizophrenia management.

INTRODUCTION: Schizophrenia is a chronic and serious neuropsychiatric condition marked by abnormalities in perception, thoughts, emotions, and social interactions. The disease affects roughly 24 million individuals throughout the world and continues to be the major cause of disability among young people.

Schizophrenic patients typically experience positive symptoms, such as hallucinations and delusions, negative symptoms, for example, social isolation and affective flattening, and cognitive deficits, which may include difficulty focusing, remembering information, and planning actions.

Antipsychotics have been the gold standard treatment for schizophrenia until today; however, their efficacy is compromised by poor adherence, toxicity, and inadequate pharmacokinetics ¹. For the last few decades, both conventional and atypical antipsychotic medications have proved successful in the control of psychosis. Nonetheless,

QUICK RESPONSE CODE 	DOI: 10.13040/IJPSR.0975-8232.17(10).2851-66 This article can be accessed online on www.ijpsr.com
DOI link: https://doi.org/10.13040/IJPSR.0975-8232.17(10).2851-66	

numerous antipsychotic drugs present undesirable physicochemical and biopharmaceutical characteristics limiting their therapeutic potential. In particular, such widely used antipsychotic medicines as olanzapine, quetiapine, aripiprazole, lurasidone, ziprasidone, and zotepine lack adequate aqueous solubility and dissolution-limited absorption. These compounds mostly belong to the group of BCS Class II drugs because of low solubility and high permeability. Inability to dissolve rapidly may lead to poor bioavailability, irregular plasma drug levels, delayed action, and poor therapeutic response²⁻³.

Apart from the solubility issues, another problem for many antipsychotics is their extensive first-pass effect, which further limits systemic bioavailability. For instance, olanzapine and quetiapine are extensively metabolised in the liver; aripiprazole displays dissolution-limited absorption as well as considerable pharmacokinetic variability. As a result, it may be necessary to administer an increased dosage or frequency, which may cause adverse events such as sedation, metabolic syndrome, weight gain, cardiovascular effects, and extrapyramidal symptoms. Therefore, the development of more effective drug delivery systems for antipsychotics remains an urgent necessity without compromising their biological efficacy⁴.

Nanotechnology offers exciting prospects for improving poorly soluble drugs' performance by means of innovative drug delivery systems. In particular, nanosuspensions represent a simple, flexible, and effective way to improve drug dissolution rate and bioavailability. Nanosuspensions refer to submicron dispersions containing pure drug crystals or amorphous particles stabilised by surfactants or polymers. In contrast to liposomes, polymeric nanoparticles, solid lipid nanoparticles, nanostructured lipid carriers, and micelles, nanosuspensions do not involve encapsulation of the drug substance into carriers but consist of free particles suspended in a suspension vehicle. Consequently, this approach ensures extremely high drug loading levels while using minimal amounts of other ingredients⁵⁻⁸. Advantages of nanosuspensions as therapeutic agents mainly lie in the reduction in particle size to the nanometre level. The basic premise is that

reduced particle size increases surface area, leads to faster dissolution rates, and increases apparent saturation solubility according to the Noyes–Whitney and Ostwald–Freundlich equations. These benefits contribute together to improved absorption and systemic exposure of the active compound. Several studies have reported the ability of nanosuspensions to increase the dissolution rates, oral bioavailability, and pharmacokinetics efficiency of poorly soluble drugs. Additionally, there is an option to develop nanosuspensions to suit different routes of administration, such as oral, parenteral, ocular, pulmonary, or intranasal administration.

Studies in recent years have investigated the use of nanosuspensions as drug delivery systems for antipsychotic drugs to increase bioavailability, decrease pharmacokinetic variability, increase brain exposure, and develop alternative routes of administration. Despite the positive results obtained during preclinical testing and formulation development, several problems are still relevant, such as stability, large-scale production, regulatory requirements, safety, and translation into the clinic⁹.

In other words, this narrative review aims to critically analyse the importance of the nanosuspension technique for enhancing the delivery of antipsychotics for schizophrenia treatment. Specifically, this review covers aspects such as formulations, modes of increasing bioavailability, physicochemical characteristics, delivery capabilities, safety aspects, limitations, and prospects concerning the application of nanosuspensions of antipsychotics for clinical applications¹⁰.

Limitations of Conventional Antipsychotic Formulations: Several drugs that are used today in the treatment of schizophrenia have very low aqueous solubility and limited dissolution rates as their rate-controlling step. Examples include olanzapine, quetiapine, aripiprazole, ziprasidone, lurasidone, and several others, which are all BCS Class II drugs that have low solubility but high permeability. Lack of adequate solubility may lead to insufficient drug absorption and variability in plasma concentrations¹¹⁻¹².

Moreover, the hepatic first-pass effect results in reduced systemic bioavailability. These factors often lead to increased dosages, which in turn cause various side effects like metabolism problems, drowsiness, and extrapyramidal reactions. One such promising strategy is the use of nanosuspensions. Nanosuspensions reduce the particle size of drugs to the nanometre scale, thus significantly increasing their surface area, rate of dissolution, and apparent saturation solubility while maintaining the unchanged molecular structure of the substance¹³⁻¹⁵.

TABLE 1: BIOPHARMACEUTICAL LIMITATIONS OF COMMON ANTIPSYCHOTIC DRUGS

Drug	Major Limitation	Potential Benefit of Nanosuspension
Olanzapine	Poor solubility, first-pass metabolism	Improved dissolution and absorption
Quetiapine	Extensive hepatic metabolism	Enhanced bioavailability
Aripiprazole	Dissolution-limited absorption	Improved systemic exposure
Lurasidone	Food-dependent absorption	Reduced variability
Ziprasidone	Poor aqueous solubility	Faster dissolution
Zotepine	Low oral bioavailability	Improved absorption

Need for Bioavailability Enhancement:

Enhancing the bioavailability of antipsychotic drugs is a key step towards maximising treatment effectiveness, decreasing dosing intervals, and reducing side effects. Nanotechnology-based drug delivery systems, specifically nanosuspensions, present a strong solution to this problem. Nanosuspensions are colloidal suspensions of sub-micron drug particles stabilised by surfactants or polymers in a water-based medium. They increase the surface area of poorly soluble drugs significantly, resulting in faster dissolution rates according to the Noyes–Whitney equation¹⁶.

Aside from enhanced dissolution and absorption, nanosuspensions can be designed for targeted delivery, e.g., intranasal delivery for direct nose-to-brain delivery of drugs, avoiding the blood–brain barrier and first-pass metabolism. This is particularly useful in psychiatric treatment, where quick onset and CNS selectivity are critical. Moreover, nanosuspension formulations can be incorporated into a variety of multiple dosage forms such as oral, injectable, or inhalation systems, and thus offer flexibility in clinical use¹⁷.

Ultimately, the application of nanosuspension technology in schizophrenia pharmacotherapy holds great promise for enhancing drug efficacy, tailoring therapy, and enhancing patient quality of life. Continuing progress in formulation science, surface engineering, and nanocarrier hybrid systems should drive the clinical translation of these emerging therapies into the near future¹⁸.

Clinical Need for Enhanced Antipsychotic Delivery System:

There are several antipsychotic

agents available; however, obtaining a constant therapeutic effect from them in patients suffering from schizophrenia is difficult due to high interindividual differences associated with the pharmacokinetics of the drug and poor patient compliance. Several antipsychotics need to be used over an extended period; moreover, their concentrations in blood plasma experience variations owing to low aqueous solubility, irregular gastrointestinal uptake and extensive first-pass effect. These variations may have an impact on poor therapy results and potential side effects. Hence, developing a system of delivery for an antipsychotic medication that can provide efficient drug dissolution, bioavailability increase, dose standardisation, and alternative ways of drug delivery would be highly beneficial¹⁹⁻²⁰.

Review Methodology: The current manuscript is a narrative review that aims to assess the efficacy of the use of drug delivery based on nanosuspensions as an approach towards enhancing the bioavailability and improving the therapeutic effect of antipsychotic drugs for the treatment of schizophrenia.

Literature Search Strategy: Literature related to this topic was extensively searched across several electronic databases, including PubMed, Scopus, Web of Science, ScienceDirect, Google Scholar, and CrossRef. Literature covering January 2010 – March 2026 was selected through a systematic search process. Keywords and MeSH terms were utilised for conducting the literature search. Some of the key search terms include:

- 1. Antipsychotic nanosuspension

2. Schizophrenia AND nanosuspension
3. Antipsychotic drugs
4. Bioavailability enhancement and nanosuspension
5. Risperidone nanosuspension
6. Olanzapine nanosuspension
7. Quetiapine nanosuspension
8. Aripiprazole nanosuspension
9. Brain delivery of antipsychotics
10. Nanosuspension formulation
11. Drug nanocrystals
12. Intranasal delivery of antipsychotics

Inclusion Criteria: The following studies were included: original articles published in scientific journals, Articles dealing with nanosuspensions or nanocrystals of antipsychotic medications, research related to *in-vitro*, *ex-vivo*, *in-vivo*, pharmacokinetic, formulation development, and stability studies, Papers written in English and Research published from 2010 to 2026.

Exclusion Criteria: The following articles were excluded: Conference papers, editorials, letters, patents, Papers published not in English, Papers describing only nanosuspension content, and duplicate articles. Articles that did not contain enough formulation data.

Searching and Selection: In total, 348 studies were found by database searching. After duplicate removal, 276 articles were considered for title and abstract examination. Then, according to the relevance assessment and inclusion/exclusion criteria, 124 articles were chosen to be read in full-text version. As a result, 97 full-text articles were selected for further review and qualitative study.

Data Extraction: The relevant data, such as drug candidate, technique, particle size, PDI (polydispersity index), zeta potential, stabiliser system, dissolution characteristics, pharmacokinetics results, safety profile, and therapy issues, were obtained from selected articles and reviewed.

Nanosuspension Technology:

Principles and Advantages: Nanosuspensions are colloidal dispersions of pure drug particles between 100 and 1000 nanometres in size, stabilised with surfactants and/or polymers in a water medium. In contrast to other nanocarriers, which involve encapsulating the drug into a matrix or vesicle, nanosuspensions are made up of pure drug crystals that are dispersed homogeneously to avoid aggregation and preserve physical stability²¹.

This technology is especially suited for drugs that are not very water-soluble (BCS Class II or IV), which make up a large percentage of newly synthesised pharmaceutical molecules. Nanosuspensions are designed to increase the rate of dissolution, enhance drug absorption, and ultimately systemic bioavailability, particularly when traditional formulation strategies do not provide therapeutic efficacy²².

Mechanisms for Improving Solubility and Absorption: Nanosuspension technology takes advantage of several physicochemical principles to improve the solubility and bioavailability of poorly water-soluble drugs:

Increased Surface Area: Based on the Noyes–Whitney equation, decreasing particle size results in a tremendous increase in surface area, thus speeding up the rate of dissolution in biological fluids²³.

Increased Saturation Solubility: As a result of the higher surface free energy of nanosized particles, saturation solubility can be increased, leading to a greater concentration gradient and enhanced passive diffusion across biological membranes²⁴.

Increased Adhesion and Mucoadhesion: Nanosuspensions are more likely to adhere to mucosal surfaces (e.g., gastrointestinal lining or nasal mucosa), enhancing residence time and local absorption²⁵.

First-Pass Metabolism Avoidance (in Certain Routes): Alternative routes of administration like intranasal, buccal, or pulmonary delivery by means of nanosuspensions have the potential to avoid hepatic first-pass metabolism, providing improved bioavailability for drugs targeting the CNS, like antipsychotics²⁶.

Stabilised Pharmacokinetics: Through enhancement of solubility and dissolution characteristics, nanosuspensions can minimise variability in plasma levels of drugs and provide more predictable pharmacokinetic profiles ²⁷.

Fabrication Techniques for Antipsychotic Nanosuspensions: Nanosuspension preparation is very important in attaining maximum particle size, stability, and drug release profile. The chosen technique may influence the drug's bioavailability, pharmacokinetics, and scale-up facility. The methods are mainly classified as top-down, bottom-up, and hybrid strategies. All techniques have their own strengths, weaknesses, and appropriateness depending on the drug's physicochemical properties.

Top-Down Approaches: Top-down methods consist of the mechanical breakdown of coarse drug particles into the nanometre size range through external energy. These are the most widely used and scalable processes among pharmaceutical industries ²⁸.

High-Pressure Homogenization (HPH): HPH, a drug suspension is pumped through a thin gap under high pressure (as high as 1500 bar), resulting in particle collision, cavitation, and shear that decrease particle size. Example: HPH-prepared risperidone nanosuspensions have exhibited enhanced dissolution rates and increased drug concentrations in the brain in animal models. Advantages are scalable, reproducible, solventless process; both oral and parenteral use are suitable ²⁹.

Media Milling (Nano-milling): The drug is milled in the presence of grinding media (most commonly zirconium beads) and stabilisers to avoid agglomeration in this process. Example: Wet media-milled olanzapine nanosuspensions have displayed enhanced oral bioavailability and less frequent dosing. Advantages are strong, economical, and appropriate for heat-labile drugs. Limitations include risk of contamination from milling media and longer processing times ³⁰.

Bottom-Up Approaches: Bottom-up approaches include precipitation or crystallisation of drug particles from a supersaturated solution. The methods are founded on controlled nucleation and growth of nanocrystals ³¹.

Antisolvent Precipitation: The drug is dissolved in a water-miscible organic solvent and mixed quickly with an antisolvent (most often water with stabilisers), causing precipitation of nanocrystals. Example: Quetiapine nanosuspensions were successfully prepared through antisolvent precipitation with stabilisers such as poloxamers. Advantages include highly controllable particle formation and less energy demanding compared to top-down processes. Disadvantages are the need for controlled solvent removal and stabilisation, and the chance of uncontrolled crystal growth and aggregation ³².

Controlled Crystallisation Techniques: Applied in thermodynamically stable nanocrystals by fine-tuning temperature, pH, and solvent proportions during precipitation. Less practiced in industry because of the complexity of the formulation ³³.

Hybrid Techniques: Hybrid methods take the advantages of both the top-down and bottom-up methods to overcome the shortcomings of either method. In general, a drug is precipitated (bottom-up) first and followed by mechanical size reduction (top-down) to obtain uniform nanocrystal size distribution and enhanced stability.

Precipitation Followed by Homogenization (Precipitation-HPH): This two-stage technique improves process efficiency with the generation of smaller particles and less mechanical stress. Example: Risperidone studies indicated that the hybrid approach resulted in higher saturation solubility and quicker onset of action, which is important for treating acute episodes of schizophrenia. Advantages are reduced energy requirements, improved final particle size control, and greater reproducibility. Disadvantages are that multi-step processing can be challenging for mass production ³⁴.

Difference between Nanosuspensions and Other Types of Nanocarrier Systems: Nanosuspensions are a type of colloidal dispersion, which comprises only the pure drug dispersed as nanometre-scale crystalline or amorphous particles and stabilised by surfactant or polymer molecules suspended in an aqueous solution. In contrast to many nanocarrier-based systems, the drug molecules are not incorporated in the form of the carrier matrix;

rather, they are present free in a nanoscale dispersion form. This property allows achieving extremely high levels of drug loading without using many other ingredients³⁵. Various nanotechnology-based drug delivery systems for antipsychotics include solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), polymeric nanoparticles, PLGA nanoparticles, micelles,

transferosomes, nano capsules, and cyclodextrin inclusion complexes. However, despite their possible benefits in improving the drug properties, they should be distinguished from the nanosuspensions since the latter are different in composition, method of drug loading, preparation procedure, and release profile³⁶⁻³⁹.

TABLE 2: COMPARISON OF NANOSUSPENSIONS WITH OTHER NANOCARRIER SYSTEMS

System	Drug Location	Carrier Required	Drug Loading	Main Advantage
Nanosuspension	Pure drug nanocrystals	No	Very High	Improved dissolution
SLN	Drug in lipid matrix	Yes	Moderate	Controlled release
NLC	Drug in mixed lipids	Yes	Moderate	Improved stability
PLGA Nanoparticle	Drug in polymer matrix	Yes	Moderate	Sustained release
Micelle	Drug in hydrophobic core	Yes	Low–Moderate	Solubilization
Transferosome	Drug in a deformable vesicle	Yes	Moderate	Skin permeation
Nanocapsule	Drug in polymer shell	Yes	Moderate	Drug protection

These fabrication techniques provide a toolbox for tailoring antipsychotic nanosuspensions depending on the desired therapeutic outcome, drug characteristics, and route of administration. The choice of method ultimately depends on the balance between Efficacy, scalability, and regulatory compliance⁴⁰.

Case Studies on Specific Antipsychotics: Nanosuspension formulations have been extensively explored for various antipsychotic drugs to overcome limitations such as poor aqueous solubility, erratic absorption, and high first-pass metabolism. Below are selected case studies highlighting key findings and outcomes for commonly prescribed antipsychotics⁴¹.

Risperidone:
Background: Risperidone is a second-generation antipsychotic employed in the treatment of schizophrenia, bipolar disorder, and irritability in autism. Risperidone is water insoluble with about 70% bioavailability and is metabolised in the liver to its active metabolite, 9-hydroxy risperidone⁴².

Nanosuspension Results: Formulation techniques are high-pressure homogenization and precipitation ultrasonication methods. Major Findings is risperidone nanosuspension resulted in a 2–3 times increase in dissolution rate, enhanced absorption, and brain delivery in animal models⁴³. Clinical Implication: Enhanced onset of action and possibility of decreased dosing intervals in acute psychotic disorders⁴⁴.

Olanzapine: Olanzapine is a commonly prescribed atypical antipsychotic with limited oral bioavailability (~60%) because of poor water solubility and extensive first-pass metabolism.

Nanosuspension Results: Formulation Technique: Wet media milling and antisolvent precipitation⁴⁶⁻⁴⁷.

Key Results: Investigations demonstrated a remarkable increase in saturation solubility and oral absorption, as well as prolonged plasma levels.

Additional Benefit: Potential to create intranasal olanzapine nanosuspensions for expedited CNS delivery and decreased systemic side effects⁴⁵⁻⁴⁶.

Quetiapine Fumarate:
Background: Quetiapine is a second-generation antipsychotic approved for use in schizophrenia and bipolar disorder. It has low water solubility and is extensively metabolised in the liver⁴⁷.

Formulation Technique: Bottom-up antisolvent precipitation and hybrid nanoprecipitation–ultrasound techniques⁴⁸.

Key Results: Quetiapine nanosuspensions exhibited enhanced dissolution and permeability through intestinal barriers, reflecting an increased C_{max} and AUC *in-vivo*.

Therapeutic Potential: Could improve therapeutic potency with reduced dose-dependent side effects⁴⁹.

Aripiprazole:

Background: Aripiprazole is a partial agonist of dopamine D2 receptors with an unusual mechanism of action. Despite good membrane permeability, poor solubility hampers absorption.

Formulation Technique: Media milling and solvent evaporation-based methodologies.

Major Findings: Attained improved drug solubility and extended release for 24 hours, appropriate for long-term therapy.

Clinical Relevance: Provides the possibility of once-daily or long-acting injectable nanosuspension products⁵⁰⁻⁵⁵.

TABLE 3: REPRESENTATIVE ANTIPSYCHOTIC NANOSUSPENSION FORMULATIONS REPORTED IN THE LITERATURE

Drug	Preparation Method	Particle Size (nm)	PDI	Zeta Potential (mV)	Stabilizer	Major Findings	Pharmacokinetic/I n-vivo Outcome
Risperidone	Nanoprecipitation	215.56 ± 12.65	NR	-19.84 ± 2.55	Pluronic F127	Significantly improved dissolution compared with the pure drug	Approximately a 2-fold increase in oral bioavailability in rabbits compared with marketed tablets
Aripiprazole	Nanoprecipitation /Homogenization based on acid–base neutralisation	350	0.20	NR	Optimized stabilizer system	Enhanced solubility and dissolution rate	Relative bioavailability 123.43% vs commercial tablet and 171.41% vs coarse suspension
Olanzapine	RESS/RESSAS nanosuspension process	150–350	NR	NR	PEG + SLS (best stability)	Significant increase in dissolution rate; stable nanosuspension after freeze-drying	PK data not reported.
Quetiapine Fumarate	Media milling	NR	NR	NR	NR	Developed a nanosuspension for enhancement of solubility and oral delivery of a BCS Class II drug	PK data not reported.

Sustained Release and Nanosuspensions: First and foremost, the main reason why nanosuspensions were developed lies in the possibility of increasing the dissolution rate, saturation solubility, and bioavailability of poorly water-soluble drugs by reducing their particle size. In particular, a decrease in the particles' sizes will allow increasing the surface area of a substance significantly, which will accelerate the process of their dissolution and absorption. Thus, the use of nanosuspensions cannot be automatically associated with creating a sustained-release dosage form because usually, the opposite effect occurs. Namely, sustained and controlled drug delivery typically requires specific strategies related to depot systems, polymeric matrices, extended-action

formulations, implants, liposomes, etc. Moreover, while some forms of nanosuspensions can have sustained release properties under particular conditions, this feature depends solely on the formulation and should not be considered inherent⁵⁶⁻⁵⁹.

At the same time, physicochemical characteristics such as zeta potential impact only the colloid stability and particle aggregation, not the drug-release profile.

Hence, statements about sustained, extended release, prolonged action, and controlled drug delivery require appropriate proof from in-vitro and in-vivo release experiments⁶⁰.

Delivery to CNS and Intranasal Administration:

Current Knowledge and Its Inadequacies: The intranasal route has been of great interest as a novel strategy for the administration of antipsychotic medications because of the extremely rich vasculature in the nasal cavity, along with the possible participation of olfactory and trigeminal nerves in the drug's transport. The use of nanosuspensions may help to enhance the drug's solubility and absorption⁶¹⁻⁶². Still, no certainty using the intranasal route automatically translates into successful nose-to-brain drug delivery. Proving the achievement of the nose-to-brain strategy will involve performing a series of pharmacokinetic studies with the assessment of such factors as the ratio of brain-to-plasma concentration of the drug, the efficiency of drug targeting (DTE%), the percentage of direct transport (DTP%), behaviour changes, and safety for the nasal mucosa. Even though some preclinical studies have shown higher brain levels of the drug after intranasal administration, the evidence in this respect is still insufficient and dependent on the drug formulation⁶³⁻⁶⁵. All in all, antipsychotic nanosuspensions delivered through the nasal route present an interesting topic to explore further, although further studies are needed.

Pharmacokinetics and Pharmacodynamics:

Nanosuspension drug delivery systems have a key function in adjusting the absorption, distribution, and duration of action of antipsychotic medication. Nanosuspensions enhance the physicochemical properties of antipsychotic drugs, which affects both pharmacokinetic (PK) parameters (i.e., C_{max}, T_{max}, AUC) and pharmacodynamic (PD) effects (e.g., symptom control and occupancy of receptors in the CNS)⁶⁶.

Absorption Enhancement: Poor solubility in water is a significant rate-limiting factor for the oral bioavailability of most antipsychotics (e.g., olanzapine, risperidone). Nanosuspensions address this by decreasing particle size, which enhances surface area and dissolution rate. Increasing saturation solubility results in an increased concentration gradient for passive diffusion⁶⁷. Increasing Mucoadhesion enables increased residence time in the gastrointestinal (GI) tract.

Pharmacokinetic Impact:

↑ C_{max} (peak plasma level)

↓ T_{max} (time to achieve peak levels)

↑ AUC (cumulative drug exposure)

↓ Intra- and inter-patient variability⁶⁸⁻⁶⁹.

Pharmacodynamics Issues and Existing

Evidence: The advantages that are being gained from nanosuspension technology are mainly focused on formulation issues, including poor solubility, poor dissolution, and inadequate bioavailability. Even though enhanced pharmacokinetic profiles could lead to better drug exposure at both systemic and tissue levels, pharmacodynamic responses cannot be determined just by achieving higher bioavailability. Issues like D₂ receptor occupancy, modulation of 5-HT_{2A} receptors, improvement of symptoms, avoidance of relapses, cognitive functioning, and extrapyramidal side effects must still be assessed separately⁷⁰. Currently available scientific evidence on antipsychotic nanosuspensions has been mostly derived from formulation studies, physicochemical analysis, dissolution experiments, and preliminary pharmacokinetics. Thus, any claim about better clinical performance, better symptom management, or reduced side effects of antipsychotics in nanosuspensions can only be regarded with caution⁷¹⁻⁷³.

CNS Targeting:**Delivery to the CNS and Intranasal**

Administration: The use of intranasal administration is increasingly gaining prominence as a novel method of delivery of antipsychotic drugs to the central nervous system. Intranasal administration does not necessarily mean that the drug will be transported from the nose directly to the brain. There must be supporting documentation to prove efficacy in terms of brain to plasma ratio, drug targeting efficiency (DTE), direct transport percentage (DTP), pharmacokinetics, bio-distribution, and behaviour⁷⁴⁻⁷⁵. Presently, there is sufficient evidence to prove that intranasal nanosuspensions increase brain exposure to antipsychotic drugs; however, further clinical trials are necessary to prove their efficacy over conventional forms. Sustained release mechanisms are⁷⁶.

Illustrative Example: An intranasally administered risperidone nanosuspension in rats exhibited a 3-fold brain concentration increase over oral tablets, with prolonged plasma levels up to 24 hours. This equated to improved control of behaviour in rodent psychosis models at lower total doses ⁷⁷.

Regulatory and Safety Considerations: The use of nanosuspensions has shown considerable promise in enhancing the bioavailability of poorly soluble antipsychotic drugs; several technical hurdles need to be overcome during the development process.

Particle Size Distribution and Physical Stability: Particle size distribution is an important characteristic of nanosuspensions as it has a direct effect on bioavailability and efficacy. Regulatory bodies typically require extensive particle analysis and assessment in terms of mean particle size, polydispersity index (PDI), and particle size distribution throughout the entire development process. Aggregation, crystal growth, and Ostwald ripening are some phenomena that can have negative effects on product quality ⁷⁸.

Polymorphic Transformation and Crystalline Stability: Crystals in drug nanosuspensions are highly susceptible to transformation due to physical forces applied in particle size reduction processes such as wet milling and high-pressure homogenization. The phenomenon of polymorphic transformation affects the solubility, dissolution characteristics, stability, and bioavailability of drugs. Therefore, characterisation methods such as XRD, DSC, and FTIR should be employed during the formulation development process ⁷⁹.

Stabiliser Selection and Toxicity: Stabilisers are instrumental in inhibiting aggregation and providing long-term nanosuspension stability. Poloxamer 188, Poloxamer 407, PVP, HPMC, and Tween 80 are common stabilising agents. Excessive amounts of surfactants or polymers, or improper selection, can induce toxicity and alter biological response. Hence, safety assessment of excipients is imperative when formulating nanosuspensions ⁸⁰.

Residual Solvents: Organic solvents used for the synthesis of precipitated nanosuspensions need to

be eliminated to reduce toxicity. Appropriate analytical techniques should be considered to ensure that the amount of residual solvent is below recommended maximum limits ⁸¹.

Sterility Criteria: For parenteral or nasal routes of administration, sterility is crucial. Processes should be performed under aseptic conditions to ensure that the product does not contain microorganisms, endotoxins, and other particulate contaminants. Proper sterilisation procedures should be chosen without adversely affecting particle and formulation properties ⁸².

Redispersibility and Stability Tests: Storage causes particle aggregation or sedimentation in nanosuspensions. It is hence essential to conduct tests for redispersibility to ascertain that the suspension is easily reversible. Stability should be assessed for changes in particle size, zeta potential, crystallinity, and solubility ⁸³.

Evaluation of Neurotoxicity and Safety: With the possibility of increased exposure of drugs to the brain, a thorough safety evaluation of antipsychotic nanosuspensions is needed. The effects on neurotoxicity, neuroinflammation, oxidative stress, and tissue accumulation over time should be assessed appropriately *in-vitro* and *in-vivo* before any potential clinical usage ⁸⁴.

TABLE 5: MAJOR REGULATORY AND SAFETY CONSIDERATIONS FOR ANTIPSYCHOTIC NANOSUSPENSIONS

Aspect	Regulatory/Safety Concern
Particle size distribution	Affects dissolution, stability and bioavailability
Polymorphism	May alter drug performance
Stabilizer toxicity	Potential biological and safety concerns
Residual solvents	Toxicity risk if above limits
Sterility	Essential for parenteral and intranasal products
Redispersibility	Important for product usability
Long-term stability	Prevents aggregation and crystal growth
Neurotoxicity	Requires comprehensive evaluation
Scale-up	Manufacturing reproducibility challenges
GMP compliance	Required for commercialisation
Batch-to-batch reproducibility	Ensures consistent product quality

Issues Relating to Up-Scale Production: Despite the successful development at the lab scale,

upscaling nanosuspension fabrication can present several difficulties. Critical parameters for process optimisation include homogenization pressure, milling time, stabilisers' concentration, and batch sizes⁸⁵.

GMP Standards and Batch-to-Batch Consistency: Manufacturing nanosuspensions commercially involves adhering to certain GMP regulations. Achieving batch-to-batch reproducibility in terms of particle properties, dissolution rates, safety, and efficacy becomes mandatory. Advanced QbD concepts and process validation strategies might prove helpful in this respect⁸⁶⁻⁸⁷. In conclusion, while the use of nanosuspensions holds many advantages in antipsychotic drug delivery systems, overcoming several barriers associated with regulation, safety, process design, and quality control can become crucial to success⁸⁸⁻⁸⁹.

Stability, Scalability, and Excipient Safety: Physical stability is a critical parameter, as nanoparticles have a natural tendency to agglomerate due to high surface energy. Stabilisers (e.g., poloxamers, HPMC, PVP) and surfactants (e.g., Tween 80, SLS) are essential to prevent particle growth, sedimentation, and Ostwald ripening. Storage conditions (temperature, light, and pH) significantly affect formulation shelf life. Regulatory guidelines mandate stability testing under ICH conditions for determining product shelf-life and ensuring consistent performance⁹⁰⁻⁹¹.

Scalability Challenges: Top-down processes such as high-pressure homogenization and wet milling are scalable but demanding with respect to process parameter control, e.g., pressure, cycle time, and bead contamination. Bottom-up approaches include the use of solvents and solvent evaporation steps that could be problematic in terms of residual solvent toxicity and reproducibility of the process. Hybrid approaches need to show batch-to-batch reproducibility and could have difficulty securing standard operating procedures that are acceptable for regulatory purposes⁹²⁻⁹⁵.

Excipient Safety: Regulatory bodies demand complete safety information on all inactive ingredients employed in nanosuspensions. GRAS (Generally Recognised as Safe) listing or listed

excipient databases (e.g., FDA Inactive Ingredient Database) are usually referred to as Surfactants and polymers employed in CNS-directed nanosuspensions need to be non-toxic, non-irritating, and must not disrupt the blood–brain barrier or CNS homeostasis⁹⁶.

Regulatory Guidelines for Nanosuspensions in Neurotherapeutics: The regulatory environment for nanosuspensions continues to develop, particularly in the case of neurological or psychiatric drug delivery, where brain penetration, systemic safety, and long-term exposure become key considerations⁹⁷.

FDA and EMA Positions: Although there are no independent guidelines per se for nanosuspensions, both the FDA (U.S.) and EMA (Europe) offer frameworks under nanotechnology-based drug products. Nanosuspensions are assessed as traditional dosage forms, but with added attention to:

1. Particle size distribution (D90, PDI)
2. Surface charge (zeta potential)
3. Dissolution enhancement[98]

Key Documents & Expectations:

FDA Guidance on Nanotechnology (2014): Stresses risk-based evaluations, with full disclosure of particle engineering practices and performance attributes.

ICH Q8–Q11 Guidelines: Relevant for formulation development, process control, and quality risk management of nanosuspensions.

EMA Reflection Paper (2013): Discusses nanomedicine product features, such as toxicology, biodistribution, and risk management⁹⁹.

Special Considerations for CNS Applications: Any nanoparticle destined for CNS delivery must undergo neurotoxicity tests. Preclinical studies would normally require *in-vivo* brain biodistribution, behavioural toxicology, and BBB integrity testing. Long-term neurobehavioral safety, immunogenicity, and accumulation risks must be taken into consideration, particularly for chronic schizophrenia drugs¹⁰⁰.

TABLE 6: EXAMPLES OF REGULATORY APPROVED NANOSUSPENSION/NANOCRYSTAL PRODUCTS (GENERAL)

Product Name	Active Pharmaceutical Ingredient (API)	Indication	Route of Administration	Regulatory Status
Rapamune®	Sirolimus	Prevention of organ transplant rejection	Oral	FDA Approved
Tricor®	Fenofibrate	Hypertriglyceridemia and dyslipidemia	Oral	FDA Approved
Emend®	Aprepitant	Chemotherapy-induced nausea and vomiting	Intravenous	FDA Approved
Megace ES®	Megestrol Acetate	Anorexia and cachexia	Oral	FDA Approved
Zanaflex Capsules®	Tizanidine	Muscle spasticity	Oral	FDA Approved

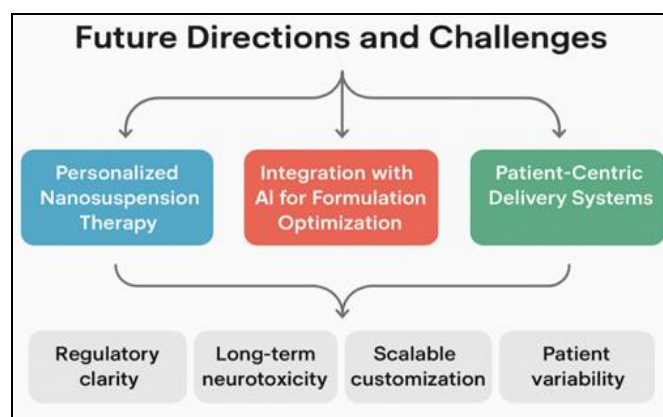
For successful clinical and commercial adoption of nanosuspension-based antipsychotics, formulation developers must focus on:

- Scientific rigour in physicochemical characterisation
- Early and continuous regulatory consultation
- Comprehensive safety and neurotoxicity profiling
- Scalable, GMP-compliant manufacturing processes

These factors ensure that nanosuspension technologies are not only effective but also regulatory-ready and patient-safe for real-world schizophrenia therapy¹⁰¹.

Future Directions and Challenges: The technology of nanosuspensions has remained an interesting approach towards developing antipsychotic drugs with improved deliverability for years now. Future research is expected to revolve around optimising stability properties, scaling up production, designing efficient intranasal and extended-release systems, and implementing reliable methods of quality control. Modern technologies, such as artificial intelligence, machine learning, quality by design principles, and other advances in the field of process analysis, may prove useful in optimising formulations and managing manufacturing procedures. At the same time, they have not been tested extensively and thus should be used with great caution in practice. Personalised drug treatment, digital twins, and three-dimensional printing also have a great deal of potential for further pharmaceutical innovations. Despite that, such approaches still pose serious

technical, regulatory, and economic issues that should be solved at the research level. All future advancements will require close collaboration between experts of different disciplines: formulation scientists, pharmacologists, engineers responsible for production, and many more. Translational research and appropriate regulation will become essential aspects in bringing antipsychotic nanosuspensions into practical use. To summarise, the technology under discussion provides promising opportunities but faces numerous challenges both in terms of science and business. As the therapeutic demands in schizophrenia evolve, the future of nanosuspension technology lies in personalisation, intelligent design, and patient-centric approaches. While nanosuspensions have already shown significant promise, several transformative innovations and ongoing challenges will shape their clinical and commercial trajectory¹⁰².

**FIG. 1: FUTURE DIRECTIONS AND CHALLENGES**

There is still a high potential in nanosuspension technology in improving the delivery of antipsychotics that are highly insoluble in water. The future research would focus on advancing formulations, refining the methods of production,

increasing scalability, and ensuring quality control in order to advance clinical research. Formulation technology will continue evolving, thereby creating opportunities for advancing formulations and manufacturing of nanosuspensions. Moreover, QbD techniques and PATs may assist in controlling the quality attributes during formulation development and scale-up. Innovations, such as AI, machine learning, digital modelling, and 3D printing, are gaining momentum in pharmaceutical research. These technologies can be used for drug formulation optimisation, manufacturing process monitoring, and personalised medicines in the future.

Nevertheless, they require significant validation to be used in the development of antipsychotic nanosuspensions. Advances in this domain would hinge upon rigorous pharmacokinetics, toxicity, and clinical studies, as well as overcoming issues related to manufacturing and regulation. It will be crucial to focus more on translational research to assess if the positive results demonstrated by antipsychotic nanosuspensions in preclinical studies could eventually translate into a safe and efficacious therapy.

Nanosuspensions seem to be a highly promising means of enhancing the delivery of antipsychotics; nevertheless, much more work is needed before their long-term safety, efficacy, and practicality can be assessed¹⁰³.

Patient-Centric Delivery Systems: Modern schizophrenia treatment demands not just efficacy but also convenience and adherence. The future of nanosuspensions lies in formats and routes that minimise invasiveness while maximising therapeutic engagement¹⁰⁴.

Patient Benefits: Lower pill burden and better adherence, less stigma and improved quality of life, better therapeutic alliance and outcome monitoring¹⁰⁵.

Challenge:

Regulatory Clarity: There is a need for harmonised international guidelines dedicated to nanosuspension-based CNS treatments.

Long-term Neurotoxicity: Full safety information over extended use continues to be limited.

Scalable Customisation: Personalisation needs to be GMP and commercial batch-manufacturing-compatible.

Patient Variability: Knowledge about how disease subtype, comorbidities, and lifestyle influence nanosuspension performance. The future of nanosuspension-based antipsychotics is in precision, personalisation, and technology-driven innovation. With the addition of AI, adaptive delivery systems, and patient-specific formulations, these next-generation platforms have the potential to revolutionise schizophrenia management providing quicker relief, fewer side effects, and improved long-term control¹⁰⁶⁻¹⁰⁷.

CONCLUSION: Nanosuspensions have shown great promise in formulating poorly soluble antipsychotic medications that are commonly used for the treatment of schizophrenia. Due to the extremely small size of particles, the use of nanosuspensions could increase the rate of drug dissolution and bioavailability and address important biopharmaceutical challenges related to the pharmacokinetics of certain antipsychotics. The research reviewed in the current article presents promising results in such aspects as formulation development, physicochemical properties of nanoparticles, dissolution rate, and pharmacokinetic performance.

In addition, the ability of nanosuspensions to deliver drugs via various administration routes (oral, parenteral, and intranasal) is worth noting. Despite all these benefits, there is still a lack of scientific data on the use of nanosuspensions for antipsychotics in humans. An improvement in dissolution rate and bioavailability does not prove any therapeutic superiority of the formulations tested in terms of effectiveness, pharmacodynamics, adverse reactions, and other factors. There are still several challenges that prevent antipsychotic nanosuspensions from being used in clinical practice effectively, namely issues of physical stability, scale-up and production processes, consistency between batches, regulations and regulatory affairs, safety considerations, and toxicity studies. It is also necessary to conduct more extensive long-term research into the safety of the nanoparticle formulations.

In conclusion, nanosuspensions have much potential as a drug delivery system in antipsychotic treatment. However, further research should be conducted to validate its efficacy, safety, and usefulness for routine use in the treatment of schizophrenia.

ACKNOWLEDGEMENTS: Nil

CONFLICTS OF INTEREST: Nil

REFERENCES:

- Jawahar N, Meyyanathan SN, Senthil V, Gowthamarajan K and Elango K: Studies on physico-chemical and pharmacokinetic properties of olanzapine through nanosuspension. *J Pharm Sci Res* 2013; 5(10): 196-201.
- Xu Y, Liu X, Lian R, Zheng S, Yin Z, Lu Y and Wu W: Enhanced dissolution and oral bioavailability of aripiprazole nanosuspensions prepared by nanoprecipitation/homogenization based on acid-base neutralization. *Int J Pharm* 2012; 438: 287-295.
- Patel HP, Chaudhari PS and Gandhi PA: Nose to brain delivery of tailored clozapine nanosuspension stabilized using TPGS. *Int J Pharm* 2021; 600: 120474.
- Tashan E, Karakucuk A and Celebi N: Optimization and *in-vitro* evaluation of ziprasidone nanosuspensions produced by a top-down approach. *J Drug Deliv Sci Technol* 2019; 52: 37-45.
- Aldeeb MM, Wilar G, Suhandi C, Mohammed AF, Mahmoud SA, Elamin KM and Wathoni N: Emerging trends in the application of nanosuspension-based biomaterials for anticancer drug delivery. *International Journal of Nanomedicine* 2025; 8587-607.
- Suo Z, Sun Q, Peng X, Zhang S, Gan N, Zhao L, Yuan N, Zhang Y and Li H: Lentinan as a natural stabilizer with bioactivities for preparation of drug-drug nanosuspensions. *International Journal of Biological Macromolecules* 2021; 184: 101-8.
- Salem HF and Kharshoum RM: Nanoprecipitation technique for preparation of sterically stabilized risperidone nanosuspension: *In-vitro* and *in-vivo* study. *International Journal of Pharmacy and Pharmaceutical Sciences* 2016; 8(5): 136-42.
- Pailla SR, Talluri S, Rangaraj N, Ramavath R, Challa VS, Doijad N and Sampathi S: Intranasal zotepine nanosuspension: Intended for improved brain distribution in rats. *DARU J of Pharma Sciences* 2019; 27(2): 541-56.
- Leng D, Chen H, Li G, Guo M, Zhu Z, Xu L and Wang Y: Development and comparison of intramuscularly long-acting paliperidone palmitate nanosuspensions with different particle size. *International Journal of Pharmaceutics* 2014 Sep 10; 472(1-2): 380-5.
- Nguyen HD, Ngo HV, Nguyen VH, Gil MC and Lee BJ: Roles of fatty acid chain length and enzyme-oriented drug controlled release from pH-triggering self-assembled fatty acid conjugated quetiapine nanosuspensions. *International Journal of Nanomedicine* 2023; 18: 7115-31.
- Nguyen HD, Ngo HV and Lee BJ: Novel pH-responsive structural rearrangement of myristic acid-conjugated quetiapine nanosuspension for enhanced long-acting delivery performance. *Advanced Science* 2024; 11(40): 2405200.
- Gol D, Thakkar S and Misra M: Nanocrystal-based drug delivery system of risperidone: Lyophilization and characterization. *Drug Development and Industrial Pharmacy* 2018; 44(9): 1458-66.
- Parmar K and Oza K: Increase in dissolution rate of zotepine via nanomilling process: Impact of dried nanocrystalline suspensions on bioavailability. *AAPS Pharm Sci Tech* 2022; 23(1): 1-12.
- Anup N, Thakkar S and Misra M: Formulation of olanzapine nanosuspension based orally disintegrating tablets (ODT): Comparative evaluation of lyophilization and electrospraying process as solidification techniques. *Advanced Powder Technology* 2018; 29(8): 1913-24.
- Muthu MS and Singh S: Poly (D,L-lactide) nanosuspensions of risperidone for parenteral delivery: Formulation and *in-vitro* evaluation. *Current Drug Delivery* 2009; 6(1): 62-8.
- Jacob S and Nair AB: An updated overview on therapeutic drug delivery using nanosuspension technology. *Current Pharmaceutical Design* 2018; 24(31): 3558-75.
- Rabinow BE: Nanosuspensions in drug delivery. *Nature Reviews Drug Discovery* 2004; 3(9): 785-96.
- Van Eerdenbrugh B, Van den Mooter G and Augustijns P: Top-down production of drug nanocrystals: Nanosuspension stabilization, miniaturization and transformation into solid products. *International Journal of Pharmaceutics* 2008; 364(1): 64-75.
- Van Eerdenbrugh B, Froyen L, Van Humbeeck J, Martens JA, Augustijns P and Van den Mooter G: Alternative matrix formers for nanosuspension solidification: Dissolution enhancement and solid-state characterization. *International Journal of Pharmaceutics* 2007; 338(1-2): 344-9.
- Sinha B, Staufenbiel S, Müller RH and Möschwitzer JP: A novel approach for submicron and nanosized drug delivery systems: Ultra-small nanocrystals. *International Journal of Pharmaceutics* 2021; 609: 121158.
- Keck CM and Müller RH: Drug nanocrystals of poorly soluble drugs produced by high-pressure homogenisation. *European Journal of Pharmaceutics and Biopharmaceutics* 2006; 62(1): 3-16.
- Müller RH, Jacobs C & Kayser O: Nanosuspensions as particulate drug formulations in therapy: Rationale for development and what we can expect for the future. *Advanced Drug Delivery Reviews* 2001; 47(1): 3-19.
- Agrawal YK & Patel VR: Nanosuspension: An approach to enhance solubility of drugs. *Journal of Advanced Pharmaceutical Technology & Research* 2011; 2(2): 81-87.
- Li M, Azad M, Davé R & Bilgili E: Nanomilling of drugs for bioavailability enhancement: A holistic formulation-process perspective. *Pharmaceutics* 2016; 8(2): 17.
- Patravale VB, Date AA & Kulkarni RM: Nanosuspensions: a promising drug delivery strategy. *J of Pharmacy and Pharmacology* 2004; 56(7): 827-840.
- Van Eerdenbrugh B, Van den Mooter G & Augustijns P: Top-down production of drug nanocrystals: Nanosuspension stabilization, product quality and prevention of mitotoxicity. *International Journal of Pharmaceutics* 2008; 353(1-2): 239-247.
- George M & Ghosh I: Identifying the correlation between drug/stabilizer properties and preparation methods of drug nanocrystals: A review. *International Journal of Pharmaceutics* 2013; 444(1-2): 142-154.
- Jacob S, Kather FS, Boddu SHS, Attimarad M & Nair AB: Nanosuspension innovations: Expanding horizons in drug delivery techniques. *Pharmaceutics* 2025; 17(1): 136.
- Verma S, Lan Y, Gokhale R & Burgess DJ: Quality by design approach to understanding the process of

- nanosuspension preparation via wet media milling. *International Journal of Pharmaceutics* 2011; 416(1): 329-338.
30. Van Eerdenbrugh B, Vermant J, Martens JA, Froyen L, Van Humbeeck J, Augustijns P & Van den Mooter G: A screening study of surface-active polymers and surfactants for the stabilization of formulation nanosuspensions. *Journal of Pharmaceutical Sciences* 2010; 99(4): 1990-2007.
 31. Choi JY, Yoo JY, Kwak HS, Nam JS & Kim JW: Role of polymeric stabilizers in covalent or non-covalent modification of drug nanosuspensions. *Journal of Controlled Release* 2005; 108(1): 109-117.
 32. Wu L, Zhang J & Watanabe W: Physical and chemical stability of drug nanoparticles and nanosuspensions. *Advanced Drug Delivery Reviews* 2011; 63(6): 456-469.
 33. Deng Z, Chen X & Xu S: Solidification of nanosuspensions by freeze-drying and spray-drying processes. *Powder Technology* 2014; 253: 523-532.
 34. Shariare MH, Blagden N, de Matas M, Leusen J & York P: Influence of formulation parameters on crystallization parameters of nanosuspensions via anti-solvent precipitation. *International Journal of Pharmaceutics* 2012; 434(1-2): 76-84.
 35. Akour YA, Aljaberi A & Migdadi EM: Nanosuspensions: A literature review. *Current Drug Research Reviews* 2026; 18(1): e220126
 36. Aldeeb M, Wilar G, Suhandi C, Elamin K & Wathoni N: Nanosuspension-based drug delivery systems for topical applications. *International Journal of Nanomedicine* 2024; 19: 825-844.
 37. Taneja S, Shilpi S & Khatri K: Formulation and optimization of efavirenz nanosuspensions using the precipitation-ultrasonication technique for solubility enhancement. *Artificial Cells, Nanomedicine, and Biotechnology* 2015; 43(1): 1-7.
 38. Kayser O, Olbrich C, Yardley V, Kiderlen AF & Croft SL: Formulation of amphotericin B nanosuspensions for oral administration in Leishmaniasis. *Antimicrobial Agents and Chemotherapy* 2003; 47(3): 1051-1056.
 39. Pignatello R, Bucolo C, Ferrara P, Maltese A, Puleo A & Puglisi G: Eudragit RS100 nanosuspensions for the ophthalmic controlled delivery of flurbiprofen. *European Journal of Pharmaceutical Sciences* 2002; 16(1-2): 53-61.
 40. Ali HS, Khan S & Serajuddin AT: Preparation, characterization and *in-vivo* evaluation of fluticasone propionate nanosuspensions for pulmonary delivery. *European Journal of Pharmaceutics and Biopharmaceutics* 2011; 78(3): 301-308.
 41. Gigliobianco MR, Casadidio C, Censi R & Di Martino P: Nanocrystals of poorly soluble drugs: Drug bioavailability and physicochemical characterization. *Pharmaceutics* 2018; 10(3): 134.
 42. Xia CR, Gu ZY & Alkan-Onyuksel H: Intravenous formulation of a water-insoluble highly lipophilic antiviral agent using an engineered nanosuspension technique. *International Journal of Pharmaceutics* 2004; 271(1-2): 177-186.
 43. Ahuja M, Dhake AS, Sharma SK & Majumdar DK: Topical ocular delivery of NSAIDs using nanosuspension formats. *Advanced Materials Letters* 2010; 1(3): 185-194.
 44. Lai F, Pini E, Corrias F, Perricci A & Fadda AM: Formulation and characterization of tretinoin nanosuspensions for cutaneous application. *AAPS Pharm Sci Tech* 2013; 14(1): 346-354.
 45. Kesiosoglou F, Panmai S & Wu Y: Nanosizing—oral formulation development and biopharmaceutical evaluation. *Advanced Drug Delivery Reviews* 2007; 59(7): 631-644.
 46. Merisko-Liversidge E & Liversidge GG: Nanosizing for oral and parenteral drug delivery: a perspective on formulating poorly-water soluble compounds using wet media milling technology. *Advanced Drug Delivery Reviews* 2011; 63(6): 427-440.
 47. Chen H, Khemtong C, Yang X, Chang X & Gao J: Nanonization strategies for poorly water-soluble drugs. *Drug Discovery Today* 2011; 16(7-8): 354-360.
 48. Date AA & Patravale VB: Current strategies for engineering drug nanoparticles. *Current Opinion in Colloid & Interface Science* 2004; 9(3-4): 222-235.
 49. Liversidge GG & Cundy KC: Particle size reduction for improvement of oral bioavailability of hydrophobic drugs: I. Absolute oral bioavailability of nanocrystalline danazol in beagle dogs. *International Journal of Pharmaceutics* 1995; 125(1): 91-97.
 50. Peltonen L & Hirvonen J: Drug nanocrystals—Versatile option for formulating poorly soluble materials. *International Journal of Pharmaceutics* 2018; 537(1-2): 73-83.
 51. Kocbek P, Baumgartner S & Kristl J: Preparation and evaluation of nanosuspensions for enhancing the dissolution of poorly soluble drugs. *International Journal of Pharmaceutics* 2006; 312(1-2): 179-186.
 52. Jinno J, Kamada N, Osaki M, Rohera BD & Payne AW: Effect of particle size reduction on dissolution and oral absorption of a poorly water-soluble drug, cilostazol, in beagle dogs. *Journal of Controlled Release* 2006; 111(1-2): 56-64.
 53. Salazar J, Ghanem A, Müller RH & Möschwitzer JP: Nanocrystals: comparison of the size reduction effectiveness of a novel combinative method with conventional top-down approaches. *European Journal of Pharmaceutics and Biopharmaceutics* 2012; 81(1): 82-90.
 54. Ali HSM, York P, Ali AMA & Blagden N: Hydrocortisone nanosuspensions for ophthalmic delivery: A comparative study between microfluidic nanoprecipitation and wet milling. *Journal of Controlled Release* 2011; 149(2): 175-181.
 55. Gao L, Zhang D & Chen M: Drug nanocrystals for the formulation of poorly soluble drugs and its application as a potential drug delivery system. *Journal of Nanoparticle Research* 2008; 10(5): 845-862.
 56. Wang Y, Zheng Y, Zhang L, Wang Q & Zhang D: Stability of nanosuspensions in drug delivery. *Journal of Controlled Release* 2013; 172(3): 1126-1141.
 57. Tuomela A, Hirvonen J & Peltonen L: Stabilizing agents for drug nanocrystals: effect on bioavailability. *Pharmaceutics* 2016; 8(2): 16.
 58. Kakran M, Sahoo NG, Tan IL & Li L: Preparation of nanoparticles of poorly water-soluble antioxidant curcumin by antisolvent precipitation methods. *Journal of Nanoparticle Research* 2012; 14(3): 757.
 59. Kasem OS, Hashim FM & Zaazou MH: Preparation and evaluation of dexamethasone nanosuspension for ocular delivery. *International Journal of Pharmaceutical Sciences and Research* 2012; 3(11): 4165.
 60. Ghosh I, Bose S, Vippagunta R & Harmon F: Nanosuspension for improving the bioavailability of a poorly soluble drug and screening of stabilizing agents to inhibit crystal growth. *International Journal of Pharmaceutics* 2011; 409(1-2): 260-268.
 61. Sigfridsson K, Forssén S, Holländer P, Skantze U & de Verdier J: A formulation comparison, using a solution and different nanosuspensions of a poorly soluble compound.

- European Journal of Pharmaceutics and Biopharmaceutics 2007; 67(2): 540-547.
62. Erreira MD, Duarte J, Veiga F, Paiva-Santos AC & Pires PC: Nanosystems for Brain Targeting of Antipsychotic Drugs: An Update on the Most Promising Nanocarriers for Increased Bioavailability and Therapeutic Efficacy. *Pharmaceutics* 2023; 15(2): 678.
 63. Rathi R, Mehrete N, Goyal S, Singh I, Huanbutta K & Sangnim T: Advanced Drug Delivery Technologies for Enhancing Bioavailability and Efficacy of Risperidone. *International Journal of Nanomedicine* 2024; 19: 12871-12887.
 64. Singh S & Muthu MS: Preparation and Characterization of Nanoparticles Containing An Atypical Antipsychotic Agent. *Nanomedicine* 2007; 2: 233-240.
 65. Verma S, Gokhale R & Burgess DJ: A comparative study of top-down and bottom-up approaches for the preparation of micro/nanosuspensions. *International Journal of Pharmaceutics* 2009; 380(1-2): 216-222.
 66. Keck CM & Müller RH: Size analysis of submicron particles of pharmaceutical relevance: A review. *International Journal of Pharmaceutics* 2008; 355(1-2): 150-163.
 67. Lindfors L, Skantze P, Skantze U, Rasmusson M, Zackrisson A & Olsson U: Amorphous drug nanoparticles in aqueous suspensions with stable particle size or Controlled growth. *Langmuir* 2006; 22(3): 906-910.
 68. Van Eerdenbrugh B, Baird JA & Taylor LS: Crystallinity assessment of formulations containing drug nanocrystals: Comparison of different techniques. *The AAPS Journal* 2010; 12(4): 566-575.
 69. Xia D, Quan P, Piao H, Piao H, Sun S, Yin Y & Cui F: Preparation of pure drug nanoparticles by an eco-friendly self-assembly method. *International Journal of Pharmaceutics* 2010; 392(1-2): 240-247.
 70. Liu Y, Sun C, Sun J & Zhang T: Preparation, characterization, and *in-vivo* evaluation of a nitrendipine nanosuspension. *International Journal of Pharmaceutics* 2010; 398(1-2): 244-251.
 71. Zhang X, Guan J, Ni R, Li LC & Mao S: Preparation and evaluation of solid nanosuspensions of a poorly soluble drug in oral administration. *European Journal of Pharmaceutics and Biopharmaceutics* 2014; 86(3): 464-472.
 72. Yue PF, Li GX, Wan J, Yang M, Zhu WF & Wang CH: Process optimization, characterization, and evaluation of a curcumin nanosuspension stabilized by a natural protein. *International Journal of Pharmaceutics* 2013; 441(1-2): 35-44.
 73. Wu W, Lu Y & Qi J: Oral delivery of nanocrystals: Challenges and opportunities. *Journal of Controlled Release* 2013; 172(3): 1126-1141.
 74. Wang Z, Li M & Davé R: Influence of process parameters on the preparation of surfactant-free drug nanocrystals by wet media milling. *Advanced Powder Technology* 2015; 26(3): 967-975.
 75. Lu Y, Wang Y & Qi J: Formulation design and manufacturing of nanocrystals for oral bioavailability enhancement. *Current Pharmaceutical Design* 2014; 20(3): 323-336.
 76. Merisko-Liversidge EM & Liversidge GG: Drug nanoparticles for formulation of poorly soluble compounds. *Toxicologic Pathology* 2008; 36(1): 43-48.
 77. Shariare MH, de Matas M & York P: Effect of polymorphism on the production of nanosuspensions using high-pressure homogenization. *International Journal of Pharmaceutics* 2012; 426(1-2): 272-278.
 78. Sarnes A, Kovalainen M, Häkkinen MR, Laaksonen M, Herfindal L & Peltonen L: Nanocrystals for precise pulmonary drug delivery: Evaluation of processing parameters. *Industrial & Engineering Chemistry Research* 2014; 53(38): 14753-14760.
 79. Kumar BS & Singh SK: Formulating poorly water-soluble anti-inflammatory agents using customized high-shear homogenization approaches. *Drug Development and Industrial Pharmacy* 2016; 42(5): 780-791.
 80. Leng D, Chen H & Li G: Continuous production of drug nanosuspensions using microfluidics-assisted technology. *Chemical Engineering Journal* 2015; 270: 312-322.
 81. Hecq J, Siepmann F, Amighi K & Siepmann J: Development and evaluation of nanocrystals for systemic intravenous targeting of potent low-solubility chemotherapeutics. *Journal of Controlled Release* 2005; 110(1): 51-62.
 82. Zhao YX, Hua HY & Chang M: Nanocrystals in topical ophthalmic drug delivery: Enhancing ocular retention and transcorneal permeation. *AAPS Pharm Sci Tech* 2013; 14(4): 1210-1219.
 83. Dong Y, Ng WK, Shen S, Kim S & Tan RB: Solid state characterization of nanocrystalline pharmaceutical suspensions upon spray-drying stabilization. *Powder Technology* 2011; 212(1): 242-249.
 84. Shegokar R, Al Shaal L & Müller RH: Production of nevirapine nanosuspensions by high pressure homogenization: Characterization and toxicity studies. *Pharmazie* 2011; 66(7): 482-489.
 85. Baert L, van 't Klooster G, Dries W, François M, Wouters A, Basstanie E & Meuldermans W: Development of a long-acting injectable formulation with nanoparticles of paliperidone palmitate. *International Journal of Pharmaceutics* 2009; 375(1-2): 73-82.
 86. Darville N, van Heeswijk J, Vynckier A, De Meester M, Vandervoort J, Annaert P & Van den Mooter G: Macrophage uptake and processing of paliperidone palmitate nanocrystals. *Journal of Controlled Release* 2014; 195: 115-126.
 87. Darville N, van Heeswijk J, Vynckier A, De Meester M, Vandervoort J, Annaert P & Van den Mooter G: Intramuscular administration of paliperidone palmitate nanocrystals: *In-vivo* dissolution and tissue response. *European Journal of Pharmaceutics and Biopharmaceutics* 2014; 88(3): 734-744.
 88. Turncliff RZ, Hard ML, Du Y, Sadler BM, Risinger RC & Wehr A: Pharmacokinetics of aripiprazole lauroxil, a novel long-acting injectable intramuscular formulation of aripiprazole, in healthy subjects. *Clinical Therapeutics* 2015; 37(7): 1533-1545.
 89. D'Souza S, Faraj JA, Giovagnoli S & DeLuca PP: Formulation and characterization of risperidone LAI formulations. *Journal of Controlled Release* 2013; 168(3): 3.
 90. Lu S Yu PP, He JH, Zhang SS, Xia YL, Zhang WL and Liu JP: Enhanced dissolution and oral bioavailability of lurasidone hydrochloride nanosuspensions prepared by antisolvent precipitation-ultrasonication method. *RSC Advances* 2016; 6(54): 49052-49059.
 91. Mohammed AA and Abd Alhammid SN: Preparation, characterization and *in vitro* evaluation of clozapine nanosuspension. *Iraqi Journal of Pharmaceutical Sciences* 2024; 33(1): 43-56.
 92. Kumar AR: Development and evaluation of lurasidone hydrochloride nanosuspension incorporated orally disintegrating tablets. *Asian Journal of Pharmaceutics* 2017; 11(4): 873-881.

93. Kakran M, Sahoo NG and Li L: Fabrication of drug nanoparticles by anti-solvent precipitation method for enhanced drug dissolution. *Powder Technology* 2012; 223: 59-64.
94. Zhang D, Tan T, Gao L, Zhao W and Wang P: Preparation of azithromycin nanosuspensions by high pressure homogenization and its physicochemical characterization studies. *DDIP* 2007; 33(5): 569-575.
95. Mauludin R, Müller RH and Keck CM: Development of an oral rutin nanocrystal formulation. *International Journal of Pharmaceutics* 2009; 370(1-2): 202-209.
96. Gao L, Zhang D, Wang M, Zheng T and Wang S: Studies on formulation and evaluation of oridonin nanosuspensions. *International Journal of Pharmaceutics* 2007; 355(1-2): 321-327.
97. Hu J, Johnston KP and Williams RO: Nanoparticle engineering processes for enhancing the dissolution rates of poorly water-soluble drugs. *Drug Development and Industrial Pharmacy* 2004; 30(3): 233-245.
98. Müller RH and Peters K: Nanosuspensions for the formulation of poorly soluble drugs: Preparation and characterization. *International Journal of Pharmaceutics* 1998; 160(2): 229-237.
99. Xia D, Quan P, Piao H, Sun S, Yin Y and Cui F: Preparation of stable nitrendipine nanosuspensions using the precipitation-ultrasonication method. *AAPS Pharm Sci Tech* 2010; 11(3): 1526-1533.
100. Liu Y, Wang L, Zhao Y, He M and Zhang X: Preparation and characterization of baicalein nanosuspensions for dissolution enhancement. *Drug Development and Industrial Pharmacy* 2011; 37(4): 438-444.
101. Yue PF, Yuan HL, Li XY, Yang M and Zhu WF: Preparation and characterization of itraconazole nanosuspensions by precipitation-homogenization method. *Drug Development and Industrial Pharmacy* 2009; 35(5): 628-635.
102. Boraey MA, Hoe S, Sharif H, Miller DP and Lechuga-Ballesteros D: Improvement of the dissolution rate of fenofibrate by nanosuspension formulation. *Drug Development and Industrial Pharmacy* 2013; 39(10): 1569-1579.
103. Shah SU, Shah KU, Rehman AU and Khan GM: Investigating the effect of production techniques on megestrol acetate nanosuspensions. *AAPS Pharm Sci Tech* 2011; 12(3): 857-864.
104. Jacobs C, Kayser O and Müller RH: Nanosuspensions as a new approach for formulation of poorly soluble drugs. *Pharmaceutical Research* 2001; 18(2): 189-194.
105. Ganta S, Paxton JW, Baguley BC and Garg S: Formulation and pharmacokinetic evaluation of paclitaxel nanosuspensions. *International Journal of Pharmaceutics* 2009; 367(1-2): 179-186.
106. Wang Y, Zheng Y, Zhang L, Wang Q and Zhang D: Stability studies of drug nanocrystals and nanosuspensions. *J of Cont Rele* 2013; 172(3): 1126-1141.
107. Radtke M and Müller RH: Nanostructured lipid carriers: The new generation of lipid drug carriers. *New Drugs* 2001; 2(1): 48-52.

How to cite this article:

Gupta P, Narayan A, Patel SA, Vaghela S, Patel P and Jaiswal F: "Redefining bioavailability of antipsychotics in schizophrenia therapy using nanosuspension-based approaches". *Int J Pharm Sci & Res* 2026; 17(10): 2851-66. doi: 10.13040/IJPSR.0975-8232.17(10).2851-66.

All © 2026 are reserved by International Journal of Pharmaceutical Sciences and Research. This Journal licensed under a Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License.

This article can be downloaded to **Android OS** based mobile. Scan QR Code using Code/Bar Scanner from your mobile. (Scanners are available on Google Playstore)