Journal of Pharmaceutical Research and Integrated Medical Sciences (JPRIMS)
ISSN: 3049-1681 | Vol. 03, Issue-07, July-2026 | pp.-01-18

ORIGINALARTICLE https://jprims.in/

Enhancing Oral Bioavailability of Poorly Water-Soluble Drugs: Current Developments in Nanotechnology, Lipid Systems, and Solid Dispersions

Rachana Sagar Dubey[1], Ketaki Kishor Patankar[2], Mukesh Kumar Meena[3], Gourishankar Birtia[4], Mujawar Tamanna Najir[5], Vaishali Nilesh Loharkar[6*]

[1]D Y Patil University Ambi Pune, Maharashtra, India
[2] Shree Sarswati Institute of Pharmacy, Tondavali, Maharashtra, India
[3]Department of Pharmaceutical Sciences, Mohanlal Sukhadia University, Udaipur, Rajasthan 313001, India
[4]Sanaka Educational Trust's Group of Institutions, Malandighi, Durgapur, West Bengal, India, Pin: 713212
[5]GES College of Pharmacy D(pharm)Limb, Satara, Maharashtra, India
[6]Bharati Vidyapeeth Institute of Pharmacy, CBD, Belapur, Maharashtra, India

***Corresponding Email: vaishaliloharkar9@gmail.com**

Abstract:

The oral bioavailability of many medications, especially BCS Class II and Class IV substances, is significantly limited by poor water solubility. Three main options for improving bioavailability are examined in this review: solid dispersions, lipid-based drug delivery systems, and nanotechnology-based methods. Lipid-based systems like SEDDS, SMEDDS, and SNEDDS promote solubilisation and absorption, whereas solid dispersions improve drug dissolution by amorphization and improved wettability. By increasing surface area and improving permeability, nanotechnology-based carriers—such as nanoparticles, nanosuspensions, and nanoemulsions—further boost drug delivery. These technologies considerably increase oral bioavailability, solubility, and dissolution rate, according to the reviewed research. Stability, scalability, production, and regulatory approval are still issues, though. Promising prospects for future developments in oral medication delivery are provided by cutting-edge techniques, including hybrid delivery systems and formulation design aided by artificial intelligence.

Keywords: Oral bioavailability, poorly water-soluble drugs, Solid dispersions, Lipid-based drug delivery systems, SEDDS.

Received: March. 23, 2026 **Revised: April 28, 2026** **Accepted: May. 24, 2026** **Published: July 09, 2026**

DOI: https://doi.org/10.64063/3049-1681.vol3.issue7.000280

1. INTRODUCTION

Because oral drug delivery is convenient, affordable, simple to administer, and has a high patient compliance rate, it is still the most used method of administering drugs[3]. However, poor aqueous solubility frequently limits the effective oral delivery of many pharmaceutical substances, which negatively impacts medication absorption, dissolution, and eventually bioavailability[2]. The frequency of poorly water-soluble medication candidates has significantly increased as contemporary drug development methods continue to produce more complex and lipophilic compounds. Low solubility is a key obstacle to good therapeutic performance, and a large percentage of newly created pharmaceuticals fall into Class II and Class IV categories according to the Biopharmaceutics Classification System (BCS).

Inadequate medication absorption, a delayed onset of action, higher dosage requirements, and significant variability in treatment outcomes can all result from poor oral bioavailability. As a result, one of the main goals of pharmaceutical research is to improve the solubility and dissolution properties of medications that are poorly soluble in water. To overcome these obstacles and improve oral medication absorption, a variety of formulation techniques have been developed over the last few decades[3].

Solid dispersion technologies, lipid-based drug delivery methods, and formulations based on nanotechnology are some of the most promising strategies. Through amorphization, decreased particle size, and increased wettability, solid dispersions facilitate medication solubility. Drug solubilisation and gastrointestinal absorption are enhanced by lipid-based systems, such as self-emulsifying and self-nanoemulsifying formulations. Comparably, carriers based on nanotechnology, like nanoparticles, nanosuspensions, nanoemulsions, and polymeric micelles, offer special benefits by boosting permeability, expanding surface area, and permitting regulated drug release.

A thorough analysis of these technologies' mechanics, benefits, drawbacks, and most recent advancements is crucial given their increasing significance. In order to improve oral bioavailability, this study addresses the difficulties posed by poor water solubility and looks at current developments in solid dispersions, lipid-based systems, and nanotechnology-based methods. The review also analyses the efficacy of various approaches, suggests future prospects for the development of sophisticated oral drug delivery systems, and emphasises important results from the literature.

1.1 Background Information and Context

Because of its ease of use, safety, and high patient compliance, oral medication delivery is the most used method of administration. However, poor water solubility, which lowers drug dissolution and absorption in the gastrointestinal tract, limits the efficacy of many oral medications[4]. Many newly created pharmacological compounds are thought to have limited water solubility, which results in poor oral bioavailability and uneven therapeutic outcomes. In order to overcome this difficulty, a number of formulation techniques have been developed to

improve medication solubility and absorption, including solid dispersions, lipid-based delivery systems, and nanotechnology-based methods.

1.2 Objectives of the Review

The objectives of this review are:

- To talk about the problems with medications that aren't very water-soluble.
- To assess the most current state of the art in bioavailability enhancement using solid dispersion technologies.
- To primary objective is to investigate how lipid-based medication delivery systems can enhance oral absorption.
- To assess methods that make use of nanotechnology to improve the bioavailability and solubility of drugs.
- To weigh the benefits and drawbacks of certain formulation approaches.

1.3 Importance of the Topic

Reduced oral bioavailability is frequently caused by poor water solubility, which continues to be one of the fundamental challenges in pharmaceutical development. Increased therapeutic efficacy, decreased dosage needs, and better patient compliance can result from increasing the bioavailability of drugs that are poorly soluble in water. Recent developments in lipid systems, solid dispersions, and nanotechnology have offered encouraging answers to problems relating to solubility. Thus, the creation of efficient oral drug delivery systems and upcoming pharmaceutical breakthroughs depend on an understanding of these technologies.

2. ORAL BIOAVAILABILITY AND SOLUBILITY CHALLENGES

The percentage of an oral medication that enters the systemic circulation unaltered and becomes available for therapeutic action is known as oral bioavailability. It is a crucial pharmacokinetic factor that establishes a medication's efficacy[5].

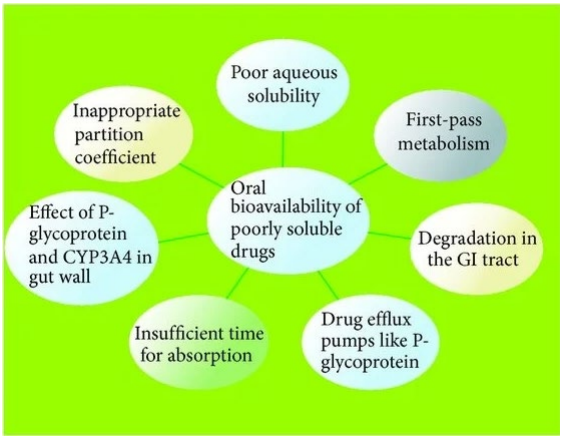

Figure 1: Oral Bioavailability[6]

Drug solubility, gastrointestinal absorption, and first-pass metabolism in the liver all affect oral bioavailability. In general, medications with high oral bioavailability yield more consistent and successful therapeutic results[7].

- **Factors Affecting Oral Bioavailability**

Numerous factors affect the oral bioavailability of drugs. Physical and chemical properties, including solubility, particle size, molecular weight, and lipophilicity, have a significant impact on drug absorption. Bioavailability can also be impacted by physiological variables such as intestinal motility, gastric emptying time, gastrointestinal pH, and enzyme activity. Drug dissolution and absorption are also greatly impacted by formulation-related elements such manufacturing procedures, excipient selection, and dosage form design. Oral bioavailability may be further changed by the presence of meals and interactions with other medications.

- **Biopharmaceutics Classification System**

Drugs are categorised by the (BCS) according to their intestinal permeability and aqueous solubility. This technique aids in formulation development and drug absorption prediction.

Table 1. BCS Classification and Bioavailability Challenges[8]

BCS Class	Solubility	Permeability	Characteristics
Class I	High	High	Rapid absorption and high bioavailability
Class II	Low	High	Dissolution-limited absorption
Class III	High	Low	Permeability-limited absorption
Class IV	Low	Low	Poor absorption and low bioavailability

Because of their poor water solubility, Class II and Class IV medications pose the biggest formulation issues among these classes[9].

- **Challenges Associated with Poorly Water-Soluble Drugs**

The oral bioavailability of poorly water-soluble medications is restricted by a number of obstacles. The amount of medicine available for absorption is decreased by low solubility, which causes sluggish dissolving rates in gastrointestinal fluids. These medications frequently show inconsistent therapeutic responses, delayed beginning of action, and varying absorption profiles. Higher dosages may be necessary in some circumstances to produce the intended therapeutic effect, which could raise the possibility of side effects. Additionally, poor solubility might make formulation development more difficult and lower pharmaceutical products' commercial viability. To increase oral drug absorption, these difficulties have prompted the development of sophisticated formulation techniques such solid dispersions, lipid-based delivery systems, and nanotechnology-based carriers.

2.1 Solid Dispersion Technologies

For drugs that have limited water solubility, solid dispersions are a common way to increase their oral bioavailability and solubility. In a solid dispersion system, an inert carrier matrix contains one or more active pharmaceutical ingredients (APIs) that are disseminated in a solid state. Crystalline, amorphous, or molecularly dispersed forms of the medicine may coexist in the carrier[10].

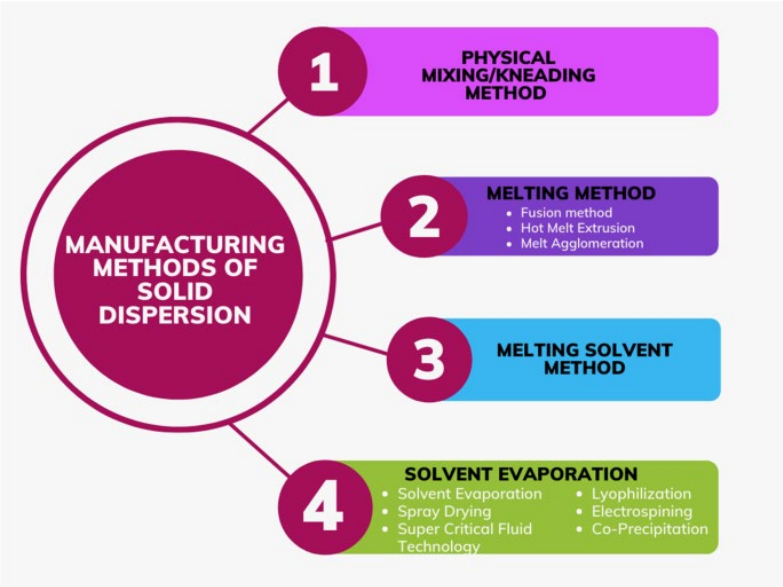

Figure 2: Solid Dispersion Technologies[11]

Solid dispersions' efficacy is mainly ascribed to a number of mechanisms. First, the transformation of crystalline pharmaceuticals into amorphous forms raises the drug's free energy, which improves its apparent solubility and rate of dissolution. Second, by making medication particles more wettable, hydrophilic carriers enable quicker contact with gastrointestinal fluids. Third, the surface area accessible for dissolving is greatly increased when particle size is reduced to the molecular level. Furthermore, some carriers prevent the medication from recrystallising, keeping it in a supersaturated state and enhancing absorption.

- **First-Generation Solid Dispersions:** The earliest generation of solid dispersions used crystalline carriers such as sugars and urea. Eutectic mixes, in which the drug and carrier crystallise separately yet are tightly mixed, are the most common outcome of these systems. Even while the carriers have faster dissolving rates than pure medicines, their crystalline structure limits their enhancement potential[12].
- **Second-Generation Solid Dispersions:** These dispersions use amorphous polymeric carriers such PVP, PEG, and HPMC. By maintaining the medication in an amorphous state, these carriers significantly enhance its solubility and dissolution. This generation's superior performance compared to crystalline carrier systems has led to its widespread acceptance.
- **Third-Generation Solid Dispersions:** Surfactants and polymeric carriers are combined in third-generation solid dispersions. Surfactants prolong supersaturation, prevent

recrystallisation, and increase medication wettability. Tween-based systems, Gelucire®, and poloxamers are a few examples. Compared to earlier generations, these formulations often offer a higher improvement in bioavailability.

- **Fourth-Generation Solid Dispersions:** Fourth-generation solid dispersions are made to improve solubility and offer controlled or prolonged medication release. To enhance stability, boost therapeutic efficacy, and optimise drug release profiles, advanced polymers and multifunctional carriers are employed. The most recent developments in solid dispersion technology are represented by these systems.

Table 2. Classification of Solid Dispersions[13]

Generation	Carrier Type	Key Characteristics
First Generation	Crystalline carriers	Eutectic mixtures, moderate dissolution enhancement
Second Generation	Amorphous polymers	Improved solubility and dissolution
Third Generation	Polymers + Surfactants	Enhanced wettability and stability
Fourth Generation	Controlled-release carriers	Improved bioavailability and sustained release

PVP is a synthetic polymer that dissolves in water and is widely utilised in formulations for solid dispersions. It successfully transforms crystalline medications into amorphous forms and has outstanding solubilising qualities. Additionally, PVP keeps drugs from recrystallising, which sustains improved dissolving performance over time. However, long-term stability may occasionally be impacted by its hygroscopic nature[14].

PEG is a hydrophilic polymer that comes in different molecular weights. Its low toxicity, biocompatibility, and ease of processing make it frequently employed. PEG is very useful for hot melt extrusion and fusion processes and increases medication wettability and dissolving rates. However, at high temperatures, some PEG grades may experience thermal deterioration.

Pharmaceutical formulations frequently use HPMC, a semi-synthetic polymer. It successfully prevents crystallisation during storage and stabilises amorphous medications. By improving wettability and preserving supersaturation in gastrointestinal fluids, HPMC improves medication solubility. It is commonly utilised in hot-melt-extruded and spray-dried solid dispersions.

Table 3. Common Carriers Used in Solid Dispersions[15]

Carrier	Characteristics	Main Benefits
PVP	Water-soluble polymer	Amorphization and recrystallization inhibition
PEG	Hydrophilic polymer	Improved wettability and dissolution
HPMC	Semi-synthetic polymer	Stabilization of amorphous drugs

Soluplus®	Amphiphilic copolymer	Enhanced solubilization and stability

An amphiphilic graft copolymer called Soluplus® was created especially for applications involving solubility augmentation. Drugs that are poorly soluble in water can be stabilised and solubilised thanks to its special structure. Soluplus® has shown exceptional effectiveness in increasing the oral bioavailability of many BCS Class II medications and is especially useful in hot melt extrusion procedures.

2.3 Lipid-Based Drug Delivery Systems

Lipidomic drug delivery systems are an excellent choice for improving the oral bioavailability of drugs that have low solubility in water. By utilising lipids, surfactants, and co-surfactants, these systems enhance solubility and absorption by maintaining a solubilised state for drugs as they travel through the gastrointestinal tract. Improved drug solubilisation, reduced first-pass metabolism, and enhanced lymphatic transport are all ways in which lipid-based formulations might increase the availability of medications throughout the body[16]. Liposomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), self-microemulsifying drug delivery systems (SMEDDS), and self-nanoemulsifying drug delivery systems were the primary lipid-based approaches.

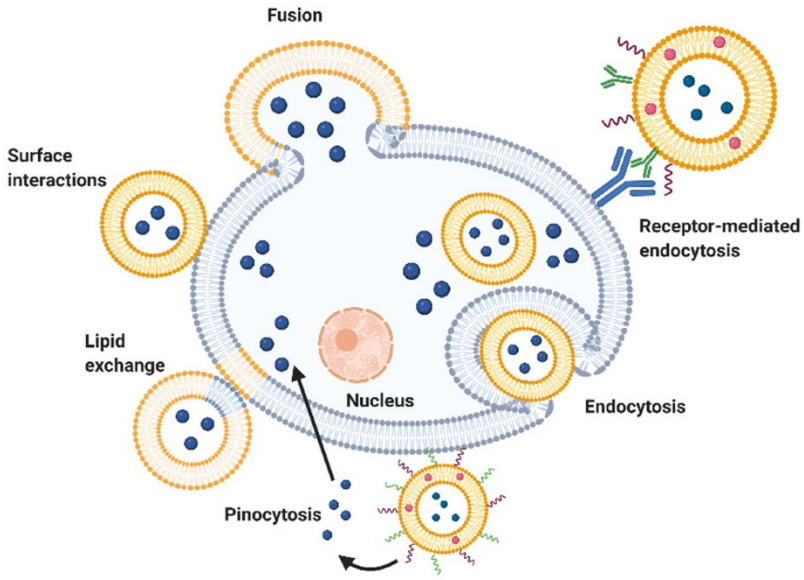

Figure 3: Lipid-Based Drug Delivery Systems[17]

The isotropic oil-surfactant mixtures known as SEDDS enhance medication absorption and dispersion by the spontaneous formation of emulsions in the presence of gastrointestinal fluids. The small droplet sizes produced by SMEDDS microemulsions enhance solubilisation efficiency and absorption. SNEDDS creates nanoparticles with enhanced solubility, surface area, and intestinal permeability. Encapsulating hydrophilic and lipophilic drugs in phospholipid vesicles called liposomes increases their bioavailability and protects them from degradation. SLNs provide enhanced stability, controlled release, and protection against degradation by encasing medications in a solid lipid matrix. By offering more drug-loading capacity and improved storage stability, NLCs—which blend solid and liquid lipids—overcome the drawbacks of SLNs.

Because of these benefits, lipid-based systems have drawn a lot of interest in the development of pharmaceutical formulations and have helped a number of oral medication products become successfully commercialised[18].

Table 6. Comparison of Lipid-Based Drug Delivery Systems[19]

System	Typical Size	Major Advantages	Limitations
SEDDS	>300 nm	Improved dissolution and absorption	Formulation complexity
SMEDDS	100–250 nm	Enhanced solubilization and stability	High surfactant content
SNEDDS	<100 nm	Superior bioavailability enhancement	Possible drug precipitation
Liposomes	50–500 nm	Drug protection and biocompatibility	Stability concerns
SLNs	50–1000 nm	Controlled release and protection	Limited drug loading
NLCs	10–500 nm	High drug loading and stability	Complex manufacturing

2.4 Nanotechnology-Based Approaches

By enabling the creation of carriers with specific physicochemical properties and nanoscale dimensions, drug delivery systems based on nanotechnology have revolutionised the formulation of drugs that are poorly water-soluble. Drug absorption and solubility are both enhanced by decreasing particle size to the nanometre range, which substantially increases surface area. Targeted distribution, improved stability, prolonged circulation time, and controlled release are further benefits of nanocarriers[20].

Many approaches based on nanotechnology have been developed to address solubility-related problems. Nanoparticles made of biodegradable polymers protect drugs from degradation by enzymes and chemicals and allow for their release over an extended period of time. Nanosuspensions, which are particularly useful for drugs with low water solubility, are composed of stabilised drug nanoparticles in a surfactant or polymer matrix. Nanoemulsions, which are extremely fine oil-in-water dispersions with droplet sizes in the nanometre range, offer enhanced solubility and absorption capabilities. The hydrophobic core of polymeric micelles is able to dissolve drugs that are insoluble in water, while the hydrophilic shell enhances stability in biological fluids. Dendrimers are large, branching macromolecules that may carry a lot of drugs and dissolve them better because of all the functional groups they contain. These methods hold a lot of potential for improving the therapeutic efficacy and oral bioavailability of a wide range of pharmacological compounds.

Table 7. Nanotechnology-Based Systems for Bioavailability Enhancement[21]

Technology	Size Range	Key Benefits	Major Limitation
Polymeric Nanoparticles	10–1000 nm	Sustained release and protection	Complex manufacturing

Nanosuspensions	100–1000 nm	Enhanced dissolution	Physical instability
Nanoemulsions	20–200 nm	Improved absorption	Surfactant requirement
Polymeric Micelles	10–100 nm	High solubilization capacity	Dilution instability
Dendrimers	1–20 nm	High drug loading	Potential toxicity concerns

2.5 Comparative Evaluation of Enhancement Strategies

The most researched methods for improving the oral bioavailability of weakly water-soluble medications are solid dispersions, lipid-based drug delivery systems, and formulations based on nanotechnology. While increasing medication solubility and absorption is the goal of all three approaches, their methods, benefits, drawbacks, and commercial viability vary[22].

Drug amorphization, improved wettability, and higher dissolution rates are the main ways that solid dispersions boost bioavailability. They are affordable, easy to make, and appropriate for large-scale manufacturing. Amorphous pharmaceuticals' physical instability and the possibility of recrystallisation during storage, however, continue to be significant obstacles. By keeping medications in a solubilised condition and encouraging lymphatic movement, lipid-based systems improve bioavailability. These formulations have shown significant success in commercial pharmaceutical products and are especially advantageous for highly lipophilic substances. However, careful selection of lipid components and surfactants is typically necessary for their formulation and optimisation.

Systems based on nanotechnology significantly increase the solubility, permeability, and controlled release of drugs. Their nanoscale size allows for better absorption and increased contact with biological membranes. Furthermore, tailored drug delivery and long-lasting therapeutic benefits are made possible by nanocarriers. Despite these benefits, their widespread commercialisation may be constrained by high production costs, intricate manufacturing procedures, and regulatory obstacles.

Table 8. Comparative Evaluation of Bioavailability Enhancement Strategies[23]

Parameter	**Solid Dispersions**	**Lipid-Based Systems**	**Nanotechnology-Based Systems**
Solubility Enhancement	High	Very High	Very High
Bioavailability Improvement	High	Very High	Very High
Manufacturing Complexity	Moderate	High	High
Stability	Moderate	High	High

Cost of Production	Low to Moderate	Moderate	High
Commercial Availability	Extensive	Extensive	Emerging
Scalability	High	Moderate	Moderate
Controlled Release Capability	Limited	Moderate	Excellent

All things considered, each approach has unique advantages for getting over poor aqueous solubility. Lipid-based systems are especially successful for lipophilic pharmaceuticals, solid dispersions are preferred for their ease of use and low cost, and nanotechnology-based methods offer sophisticated delivery possibilities. It is anticipated that hybrid systems that combine the advantages of these technologies to produce better therapeutic results would be the main focus of oral medication delivery in the future[24].

3. METHODOLOGY AND FINDINGS

The approach used to choose and evaluate the pertinent literature is presented in this section, along with the key conclusions drawn from the research that were examined. To assess current developments in increasing the oral bioavailability of poorly water-soluble medications using solid dispersion technologies, lipid-based drug delivery systems, and nanotechnology-based strategies, a comprehensive assessment of published research was carried out. The results show current trends and future prospects in oral drug delivery research and offer insights into the efficacy, benefits, and drawbacks of certain formulation techniques[25].

Literature Search Strategy

The purpose of this literature review was to identify studies that investigated the use of solid dispersions, lipid-based drug delivery systems, and nanotechnology-based approaches to increase the oral bioavailability of drugs that are not highly water-soluble. Google Scholar, PubMed, Scopus, Web of Science, and ScienceDirect were among the scientific databases combed for relevant articles. The following terms were used, either alone or in combination: "oral bioavailability," "poorly water-soluble drugs," "solid dispersions," "lipid-based drug delivery systems," "SEDDS," "SMEDDS," "SNEDDS," "nanoparticles," "nanosuspensions," "nanoemulsions," and "drug solubility enhancement." The search was conducted with a particular emphasis on studies published during the past few years, in order to encompass the most current findings and technical developments in the field[26].

Inclusion and Exclusion Criteria

➢ **Inclusion Criteria**

- Studies on improving the oral bioavailability of poorly water-soluble drugs.
- Research involving solid dispersions, lipid-based systems, or nanotechnology-based approaches.

- Peer-reviewed articles published in English.
- Studies reporting improvements in solubility, dissolution, permeability, or bioavailability.

➢ **Exclusion Criteria**

- Duplicate publications and conference abstracts.
- Editorials, letters, and opinion articles.
- Studies lacking sufficient methodological details.
- Articles unrelated to oral drug delivery or bioavailability enhancement.

3.1 Findings on Solid Dispersion Technologies

Solid dispersion technology is a successful method for enhancing the dissolving behaviour and oral bioavailability of weakly water-soluble medications, as the reviewed literature repeatedly shows. The conversion of crystalline pharmaceuticals into amorphous forms, which have higher free energy and better apparent solubility, was found to significantly increase drug dissolution rates in the majority of investigations. Faster dissolution was made possible by the addition of hydrophilic polymers such PVP, PEG, HPMC, and Soluplus®, which increased medication wettability and decreased particle aggregation[27].

According to research, two of the best preparation techniques for creating stable solid dispersions with improved performance are spray drying and hot melt extrusion. After being incorporated into solid dispersion systems, several studies employing medications like itraconazole, curcumin, celecoxib, and fenofibrate found significant improvements in oral absorption and bioavailability. However, because amorphous medications may recrystallise during storage, thereby diminishing their dissolving advantages, long-term stability is still a problem. Solid dispersions are nonetheless commonly used despite this drawback because of their comparatively straightforward production procedures and commercial viability[28].

3.2 Findings on Lipid-Based Drug Delivery Systems

Lipid-based drug delivery systems have shown in the literature to be very successful platforms for getting around solubility-related obstacles in oral medication delivery. It has been repeatedly demonstrated that SEDDS, SMEDDS, and SNEDDS enhance medication solubilisation in gastrointestinal fluids and keep pharmaceuticals dissolved during the absorption process. Especially for highly lipophilic chemicals, these methods greatly improved intestinal absorption and dissolution rates.

Because SNEDDS may produce nano-sized droplets with a wide surface area for absorption, they often showed the biggest improvement in bioavailability among the several lipid-based techniques. Research on curcumin, tacrolimus, and cyclosporine revealed significant increases in systemic exposure after SNEDDS formulations were administered. By offering regulated medication release, protection from degradation, and improved absorption, (SLNs) and (NLCs) also demonstrated encouraging outcomes. Because of their enhanced stability and greater drug-loading capability, NLCs often performed better than SLNs. Lipid-based methods continue to be

one of the most feasible ways to increase oral bioavailability and have generally seen significant commercial success[29].

3.3 Findings on Nanotechnology-Based Approaches

Drug delivery systems based on nanotechnology have shown great promise for improving the oral administration of medications that are poorly soluble in water[30]. Reducing medication particle size to the nanometre range significantly increases surface area, resulting in faster dissolution and better absorption, according to the reviewed research. It was discovered that polymeric nanoparticles provide improved stability, prolonged drug release, and defence against enzymatic breakdown[31]. Drugs with very low water solubility responded very well to nanosuspensions, which greatly increased dissolving rates[32].

Because of their smaller droplet size and better interaction with biological membranes, nanoemulsions regularly shown increased absorption. Through encapsulation within their hydrophobic core, polymeric micelles successfully enhanced the apparent solubility of hydrophobic medications[33]. The use of nanotechnology-based carriers has been shown in numerous trials to significantly improve bioavailability, pharmacokinetic performance, and therapeutic efficacy[34]. Despite these benefits, issues with cost, scalability, manufacturing complexity, and regulatory approval still prevent some nanocarrier systems from being widely commercialised[35].

3.4 Comparative Findings and Research Trends

The research listed in Table X show how much progress has been achieved in using sophisticated formulation techniques to improve the oral bioavailability of medications that are poorly soluble in water. Pawar and Barhate (2019) highlighted how solid dispersion technology can increase wettability and decrease crystallinity to improve drug solubility and bioavailability. Jagtap (2025) emphasised the relevance of novel pharmaceutical formulations by highlighting recent advancements in solubility enhancing approaches.

Table 9. Literature Summary of Solubility Enhancement Strategies

Author(s) & Year	Study Focus	Methodology/Approach	Key Findings
Pawar & Barhate (2019)[36]	Solid dispersions for solubility enhancement	Review of solid dispersion technologies and carriers	The dissolving rate and oral bioavailability of pharmaceuticals that are poorly water-soluble are greatly improved by solid dispersions, thanks to their increased wettability and amorphization.
Jagtap (2025)[37]	Recent solubility enhancement	Review of emerging pharmaceutical	Improving medication solubility and therapeutic

	techniques	technologies	performance can be achieved by the use of advanced techniques including solid dispersions, lipid-based systems, and nanotechnology.
Parmar & Patel (2025)[38]	Nanotechnology-based solubility enhancement	Review of novel nanoformulation strategies	Nanomedicines, including nanoparticles, nanoemulsions, nanosuspensions, and nanocarriers, vastly enhance the solubility, absorption, and bioavailability of medications that are not very water-soluble.
Pathak & Raghuvanshi (2015)[39]	Nanoformulations for oral bioavailability enhancement	Comprehensive review of nanotechnology approaches	Nanoformulations enhance oral absorption by increasing surface area, improving permeability, and protecting drugs from degradation.
Deshmukh et al. (2025)[40]	Strategies for enhancing drug solubility	Review of pharmaceutical formulation advances	Modern formulation techniques including solid dispersions, lipid-based carriers, and nanotechnology effectively address solubility-related challenges and improve bioavailability.

Nanotechnology-based methods, such as nanoparticles, nanoemulsions, and nanosuspensions, significantly improve medication absorption and bioavailability through increased surface area and greater permeability, according to Parmar and Patel (2025) and Pathak and Raghuvanshi (2015). In a similar vein, Deshmukh et al. (2025) came to the conclusion that contemporary formulation techniques such solid dispersions, lipid-based systems, and nanocarriers successfully handle solubility-related issues and enhance therapeutic efficacy. Overall, the reviewed literature indicates that incorporating cutting-edge drug delivery technologies presents viable ways to improve oral drug delivery efficiency and overcome poor water solubility.

4. DISCUSSION

Oral bioavailability of drugs that are poorly soluble in water has been greatly enhanced by contemporary formulation techniques, according to this research. Solid dispersions, lipid-based

drug delivery methods, and nanotechnology-based strategies can help overcome the solubility and dissolving restrictions that often impede oral drug absorption. By reviewing the findings reported in the literature, this discussion evaluates the significance, usefulness, and prospective of different technologies. More research is needed in several areas that are already highlighted.

4.1 Interpretation and Analysis of the Findings

Low water solubility is still a major issue that limits the oral bioavailability of many therapeutic compounds, according to this analysis. Solid dispersions, lipid-based drug delivery systems, and nanotechnology-based approaches can dramatically improve the solubility, dissolving rate, and absorption of medications, according to the reviewed research. Contrasted with lipid-based solutions, which maintain medicine solubility and promote lymphatic transport, solid dispersions enhance bioavailability mainly by drug amorphization and better wettability. To further improve pharmaceutical delivery, carriers based on nanotechnology increase surface area, improve permeability, and allow controlled release. To this day, solid dispersions are still popular because of their scalability and user-friendliness, but lipid-based formulations and nanocarriers usually provide a better boost to bioavailability.

4.2 Implications and Significance

Improvements in patient care and new drug discovery are directly tied to increases in oral bioavailability. Reduced side effects, increased therapeutic efficacy, decreased dosage requirements, and improved patient compliance are all possible outcomes of increased bioavailability. Modern drug development is beset by a growing number of therapeutic candidates that are poorly water-soluble; yet, technologies such as SNEDDS, polymeric nanoparticles, and SLNs have shown promise in tackling this problem. Additionally, a number of pharmaceutical items have been successfully commercialised thanks to these formulation processes, indicating their practical and industrial value. It is anticipated that these technologies' ongoing development will be essential to resolving formulation issues with upcoming medicinal compounds.

4.3 Research Gaps and Future Research Directions

- The broad use of cutting-edge bioavailability improvement technology is nevertheless hampered by long-term stability concerns, a lack of clinical validation, and difficulties in large-scale production.
- High production costs and regulatory complexity continue to be major obstacles to the commercialisation of formulations based on lipids and nanotechnology.
- Future studies should concentrate on creating stable, scalable, and affordable delivery methods, such as hybrid formulations that combine the benefits of lipid carriers, solid dispersions, and nanotechnology.
- To increase the safety, effectiveness, and commercial viability of these cutting-edge drug delivery strategies, more extensive clinical research and the application of AI and machine learning for formulation optimisation are required.
-

5. CONCLUSION

Modern pharmaceutical R&D focuses in large part on improving the oral bioavailability of drugs with low water solubility. Significant efforts have been made to create sophisticated formulation procedures that can enhance drug dissolving, absorption, and therapeutic performance due to the growing number of drug candidates with low water solubility. In order to overcome solubility-related obstacles and enhance oral drug delivery results, this review looked at current developments in solid dispersion technologies, lipid-based drug delivery systems, and nanotechnology-based techniques.

5.1 Summary of Main Insights and Conclusions

This study emphasises how difficult it is to administer poorly water-soluble medications orally and how important formulation technologies are to getting around these restrictions. Drug solubility, dissolution rate, and oral bioavailability have all been significantly improved by solid dispersions, lipid-based drug delivery systems, and nanotechnology-based methods. Lipid-based solutions enable drug solubilisation and absorption through the gastrointestinal tract, whereas solid dispersions improve drug performance through amorphization and improved wettability. Additional benefits of nanotechnology-based carriers include enhanced permeability, more surface area, and regulated drug release. When taken as a whole, these methods have increased the potential for creating efficient oral formulations of medications that are poorly soluble in water.

5.2 Importance of the Review

Bioavailability augmentation has become a key field of research because to the growing number of poorly water-soluble medication candidates in pharmaceutical development. This article offers a thorough summary of the most extensively researched and commercially significant methods used to solve issues connected to solubility. The study is a useful tool for researchers, formulation scientists, and the pharmaceutical industry looking for efficient oral drug delivery methods because it summarises recent developments in solid dispersions, lipid systems, and nanotechnology.

5.3 Recommendations

- To reduce drug recrystallisation and storage-related instability, create more stable formulations.
- For commercial production, concentrate on scalable and economical manufacturing methods.
- Investigate hybrid delivery strategies that incorporate nanotechnology, lipid-based carriers, and solid dispersions.
- Make use of machine learning and artificial intelligence to optimise formulations and forecast drug performance.
- To determine the long-term safety and effectiveness of cutting-edge formulations, carry out more clinical research.

- To promote effective product development and commercialisation, academic institutions, business, and regulatory bodies should work together more closely.

REFERENCES

1. Rocha, B., de Morais, L. A., Viana, M. C., & Carneiro, G. (2023). Promising strategies for improving oral bioavailability of poor water-soluble drugs. *Expert opinion on drug discovery*, *18*(6), 615-627.
2. Liu, Y., Liang, Y., Yuhong, J., Xin, P., Han, J. L., Du, Y., ... & Ma, Y. (2024). Advances in nanotechnology for enhancing the solubility and bioavailability of poorly soluble drugs. *Drug design, development and therapy*, 1469-1495.
3. Zhang, X., Xing, H., Zhao, Y., & Ma, Z. (2018). Pharmaceutical dispersion techniques for dissolution and bioavailability enhancement of poorly water-soluble drugs. *Pharmaceutics*, *10*(3), 74.
4. Shah, P., Goodyear, B., & Michniak-Kohn, B. B. (2017). A review: Enhancement of solubility and oral bioavailability of poorly soluble drugs. *Adv Pharm J*, *2*(5), 161-173.
5. Kumari, L., Choudhari, Y., Patel, P., Gupta, G. D., Singh, D., Rosenholm, J. M., ... & Kurmi, B. D. (2023). Advancement in solubilization approaches: a step towards bioavailability enhancement of poorly soluble drugs. *Life*, *13*(5), 1099.
6. Sharma, M., Sharma, R., & Jain, D. K. (2016). Nanotechnology based approaches for enhancing oral bioavailability of poorly water soluble antihypertensive drugs. *Scientifica*, *2016*(1), 8525679.
7. Bhalani, D. V., Nutan, B., Kumar, A., & Singh Chandel, A. K. (2022). Bioavailability enhancement techniques for poorly aqueous soluble drugs and therapeutics. *Biomedicines*, *10*(9), 2055.
8. Mahmood, T., Sarfraz, R. M., Ismail, A., Ali, M., & Khan, A. R. (2023). Pharmaceutical methods for enhancing the dissolution of poorly water-soluble drugs. *ASSAY and Drug Development Technologies*, *21*(2), 65-79.
9. Tran, P., & Park, J. S. (2021). Recent trends of self-emulsifying drug delivery system for enhancing the oral bioavailability of poorly water-soluble drugs. *Journal of Pharmaceutical Investigation*, *51*(4), 439-463.
10. Kazi, M. (2017). Lipid-Based Nano-Delivery for Oral Administration of Poorly Water Soluble Drugs (PWSDs): Design. *Adv. Technol. Deliv. Ther*, *3*, 31.
11. Bhatt, S., Sharma, J., Singh, M., & Saini, V. (2018). Solid lipid nanoparticles: a promising technology for delivery of poorly water-soluble drugs. *Acta Pharm. Sci*, *56*(3), 27-49.
12. Kesharwani, R., Jaiswal, P., Patel, D. K., & Yadav, P. K. (2023). Lipid-based drug delivery system (LBDDS): An emerging paradigm to enhance oral bioavailability of poorly soluble drugs. *Biomedical Materials & Devices*, *1*(2), 648-663.
13. Bakrey, H., Abdu, A., Shivgotra, R., Soni, B., Sharma, M., Bakrey, A., & Jain, S. K. (2025). Innovative strategies and advances in drug delivery systems to address poor solubility: a comprehensive review. *Current Drug Targets*.
14. Da Silva, F. L. O., Marques, M. B. D. F., Kato, K. C., & Carneiro, G. (2020). Nanonization techniques to overcome poor water-solubility with drugs. *Expert opinion on drug discovery*, *15*(7), 853-864.

15. Hosszú, Z., Pártos, P., Mahdavi, M., Ujhelyi, Z., Fehér, P., Haimhoffer, Á., ... & Pető, Á. (2026). The Role and Potential of Nanotechnology in Improving Solubility and Enhancing Bioavailability. *Pharmaceutics*, *18*(4), 478.
16. Pant, N. C., & Juyal, V. (2022). Enhancing oral bioavailability of poorly water soluble drugs through solid lipid nanoparticles: recent advancements. *Asian Pac J Health Sci*, *9*, 10-15.
17. Kalepu, S., & Nekkanti, V. (2015). Insoluble drug delivery strategies: review of recent advances and business prospects. *Acta Pharmaceutica Sinica B*, *5*(5), 442-453.
18. Kumar, M., Kumar, D., Kumar, S., Kumar, A., & Mandal, U. K. (2022). A recent review on bio-availability enhancement of poorly water-soluble drugs by using bioenhancer and nanoparticulate drug delivery system. *Current Pharmaceutical Design*, *28*(39), 3212-3224.
19. Bhalani, D. V., Nutan, B., Kumar, A., & Singh Chandel, A. K. (2022). *Bioavailability enhancement techniques for poorly aqueous soluble drugs and therapeutics. Biomedicines. 2022; 10: 2055*.
20. Banerjee, S., & Pillai, J. (2019). Solid lipid matrix mediated nanoarchitectonics for improved oral bioavailability of drugs. *Expert opinion on drug metabolism & toxicology*, *15*(6), 499-515.
21. Zhou, Y., Du, J., Wang, L., & Wang, Y. (2017). Nanocrystals technology for improving bioavailability of poorly soluble drugs: a mini-review. *Journal of nanoscience and nanotechnology*, *17*(1), 18-28.
22. Yang, M., Gong, W., Wang, Y., Shan, L., Li, Y., & Gao, C. (2016). Bioavailability improvement strategies for poorly water-soluble drugs based on the supersaturation mechanism: an update. *Journal of Pharmacy & Pharmaceutical Sciences*, *19*(2), 208-225.
23. Guo, S., Pham, K., Li, D., Penzak, S. R., & Dong, X. (2016). Novel in situ self-assembly nanoparticles for formulating a poorly water-soluble drug in oral solid granules, improving stability, palatability, and bioavailability. *International Journal of Nanomedicine*, 1451-1460.
24. Tran, T. T., & Tran, P. H. (2020). Insoluble polymers in solid dispersions for improving bioavailability of poorly water-soluble drugs. *Polymers*, *12*(8), 1679.
25. Tran, P., Pyo, Y. C., Kim, D. H., Lee, S. E., Kim, J. K., & Park, J. S. (2019). Overview of the manufacturing methods of solid dispersion technology for improving the solubility of poorly water-soluble drugs and application to anticancer drugs. *Pharmaceutics*, *11*(3), 132.
26. Chaudhary, A., & Shambhakar, S. (2024). Nanotechnology in drug delivery: overcoming poor solubility challenges through nanoformulations. *Current Nanomedicine (Formerly: Recent Patents on Nanomedicine)*, *14*(3), 200-211.
27. Tran, P. H., & Tran, T. T. (2020). Nano-sized solid dispersions for improving the bioavailability of poorly water-soluble drugs. *Current Pharmaceutical Design*, *26*(38), 4917-4924.
28. Danish, K. A., & Lubhan, S. (2016). Various techniques of bioavailability enhancement: a review. *J. Drug Deliv. Ther*, *6*(3), 34-41.
29. Sri Rekha, M., Sangeetha, S., & Seetha Devi, A. (2023). Solid lipid nanoparticles: a potential option for enhancing oral bioavailability of highly soluble and poorly permeable (BCS Class III) drugs. *Current Drug Delivery*, *20*(3), 223-236.
30. Narmada, I. (2023). Contemporary Review on Solubility Enhancement Techniques. *Journal of Drug Delivery & Therapeutics*, *13*(2).

31. Chandramohan, K., Nepolean, R., Karthikeyan, K., Anbarasu, D., & Jayaram, N. (2026). Strategies for Improving Solubility and Dissolution of Poorly Water-Soluble Drugs: Current Developments and Pharmaceutical Applications.
32. Siddiqui, K., Waris, A., Akber, H., Munir, K., Mir, M., Khan, M. W., & Aman, W. (2017). Physicochemical modifications and nano particulate strategies for improved bioavailability of poorly water soluble drugs. *Pharmaceutical nanotechnology*, *5*(4), 276-284.
33. Joshi, K., Chandra, A., Jain, K., & Talegaonkar, S. (2019). Nanocrystalization: an emerging technology to enhance the bioavailability of poorly soluble drugs. *Pharmaceutical nanotechnology*, *7*(4), 259-278.
34. Majekodunmi, S. O. (2016). Enhancement of the solubility, bioavailability and absorption of poorly soluble drug candidates through nanotechnology-a review. *West African Journal of Pharmacy*, *27*(2), 78-88.
35. Dahma, Z., Álvarez-Álvarez, C., & de la Torre-Iglesias, P. M. (2025). A mini-review on enhancing solubility in topical hydrogel formulations using solid dispersion technology for poorly water-soluble drugs. *Colloids and Interfaces*, *9*(2), 17.
36. Pawar, S. R., & Barhate, S. D. (2019). Solubility enhancement (Solid Dispersions) novel boon to increase bioavailability. *J. Drug Deliv. Ther*, *9*(2), 583-90.
37. Jagtap, M. (2025). Recent Trends in Solubility Enhancement Techniques for Poorly Water-Soluble Drugs. *International Journal of Scientific Research and Technology*.
38. Parmar, K., & Patel, R. (2025). Novel nano-technologies to enhance drug solubility, dissolution and bioavailability of poorly water-soluble drugs. *Biomaterials Connect*, *2*(1), 1-10.
39. Pathak, K., & Raghuvanshi, S. (2015). Oral bioavailability: issues and solutions via nanoformulations. *Clinical pharmacokinetics*, *54*(4), 325-357.
40. Deshmukh, T. M., Ingole, G. P., Sharma, R. M., & Gite, N. T. (2025). Enhancing the Solubility of Poorly Soluble Drugs: Strategies and Advances in Pharmaceutical Formulations. *Asian Journal of Pharmaceutical Research*, *15*(3), 309-315.