www.wcprj.com 2025 Page: 40-58

Review Article
Volume: 01
Issue: 04

World Current Pharmaceutical Research Journal

SOLUBILITY ENHANCEMENT TECHNIQUES OF POORLY SOLUBLE DRUGS: AN OVERVIEW

Chhavi Nagar, Sneha Pandey, Vipin Kumar, Shabnam Ain*, Qurratul Ain, Nidhi Ruhela, Bhuvnesh, Anshika Sharma and Hiten Khattar

Sanskar College of Pharmacy and Research, Ghaziabad Uttar Pradesh.

Article Received: 31 April 2025
Article Revised: 20 May 2025
Published on: 10 June 2025

***Corresponding Author: Shabnam Ain**
Sanskar College of Pharmacy and Research, Ghaziabad Uttar Pradesh.
Email Id: shabnam.ain@sanskar.org,

ABSTRACT

Solubility is a fundamental physicochemical property that plays a critical role in the development and efficacy of pharmaceutical formulations. It is defined as the ability of a solute—whether solid, liquid, or gas—to dissolve in a solvent, forming a homogeneous solution at a specified temperature and pressure. In pharmaceutical sciences, solubility influences the bioavailability of drugs, particularly in oral dosage forms, where poor solubility can significantly limit therapeutic efficacy. The absorption of a drug depends on its dissolution in aqueous media at the site of absorption, making solubility a key determinant in drug design. Various factors affect solubility, including the structural properties of the compound such as lipophilicity, hydrogen bonding, molecular volume, and crystal energy, as well as environmental conditions like pH, temperature, pressure, co-solvents, and additives. In the pharmaceutical industry, low aqueous solubility remains a major hurdle in the development of new chemical entities and generic formulations. Understanding and improving solubility is essential for enhancing drug absorption, therapeutic performance, and patient outcomes. Strategies to improve solubility and overcome poor dissolution characteristics are continually evolving to meet industry demands.

KEYWORDS: Solubility, Bioavailability, Drug Absorption, Oral Dosage Forms, Pharmaceutical Development, Aqueous Solubility.

INTRODUCTION

The ability of a solid, liquid, or gaseous chemical substance (or referred as *solute*) dissolve in liquid (referred as *solvent)* to form a *homogeneous solution is referred as Solubility*.[1] It is quantitatively defined as the concentration of the solute is saturated in a solution at a specified temperature. Solubility might be examine as the spontaneous collaboration of two or more uniform molecular dispersions.[2] The concurrent and opposing processes of dissolution and phase joining are responsible for solvency during unique equilibrium, resulting in solubility. The solubility of a substance essentially depends on the prone solvent, along with temperature and pressure.[1] It doesn't depend on particle size or other kinetic factors when given sufficient time. Even large particles will eventually dissolve. The given table 1 determines the parts of solvent required to dissolve in per part of solute according to BP and USP solubility criterion.

Table 1: BP and USP solubility Criterion.

Descriptive Terms	Parts of solvent required per part of solute	Solubility range (mg/ml)
Very Soluble	Less than 1	More than 1000
Freely Soluble	1-10	100-1000
Soluble	10-30	33-100
Sparingly Soluble	30-100	10-33
Slightly Soluble	100-1000	1-10
Very Slightly Soluble	1000-10000	0.1-1
Partially Insoluble	10000 or more	Less than 0.1

Oral administration is the most commonly used method for drug delivery due to its ease of use, high patient compliance, cost-effectiveness, minimal sterility requirements, and flexibility in dosage form design. However, the main challenge in designing oral dosage forms is their low bioavailability, which is attributed to poor solubility and permeability. The primary issue encountered in the development of new chemical entities and generic drugs is low aqueous solubility. For a drug to be absorbed, it must be in the form of an aqueous solution at the absorption site.

In Pharmaceutical Industries, solubility plays a crucial role in all dosage forms such as solid, liquid, and semi-solid or semi-liquid forms. It is a crucial factor for formulating different types of drugs. When poorly water soluble drug is given in solid dosage form then in absorption, dissolution rate of poorly water soluble drug can be the rate limiting step. That's

why the poor dissolution characteristics of poorly water soluble drugs are the enormous problem for pharmaceutical industries.[3]

The solubility of a drug significantly impacts its bioavailability. The solubility of a compound is influenced by its structure and the conditions of the solution.[4] The structure of the compound determines its lipophilicity, hydrogen bonding, molecular volume, crystal energy, and ignitability, all of which contribute to its solubility. Solution conditions, including pH, molecular size, co-solvents, additives, ionic strength, pressure, polarity, time, and temperature, can also affect solubility. Compounds with poor solubility can greatly hinder productivity in drug discovery and development.

BCS Classification System

The BCS is a scientific manifestation for classification of pharmaceutical drugs based on their solubility in water and permeability in intestine. In combination with the in vitro dissolution properties of the formulation, the BCS considers three key factors: solubility, intestinal permeability, and dissolution rate. Each of these factors influences the rate and amount of oral absorption of a drug from a "solid burst release" through oral dosage form.[6]

It was initially included in the guidance document and immediate release solid oral dosage forms: scale up and post approval adjustments, which were part of the regulatory decision-making process.[22]

Drug solubility is determined by the maximum dose strength of an immediate-release medication. While permeability of drug is derived indirectly from the proportion of drug ingredient absorbed in body.[21] BCS is based on the fundamental principle that two drugs that produce the same concentration profile in the GI tract will also produce the same plasma profile after oral administration.[22]

Highly permeable drugs may be documented when

→ The extent of drug absorption in human body should be greater than 90% and intent to be stable in GIT.

→ Intestinal permeability set to be high.

The principles of BCS are widely applied in clinical pharmacology, the creation of new dosage forms, and as a scientific approach to evaluate regulatory clearances and bioavailability exemptions in the pharmaceutical sector.

Mainly drugs which have low Solubility are fall under BCS (Biopharmaceutical Classification System) which are characterized as Class II and Class IV. BCS Classification is classified by USFDA (United State Food and Drug Administration) as shown in the Table 1.2. Class II drugs has low solubility and high permeability while Class IV drugs have low solubility and low permeability as well which leads to low bioavailability.

Table 2: BCS Classification System.

CLASS	SOLUBILITY	PERMEABILITY	EXAMPLES	ARBSORPTION PATTERN
I	High	High	Paracetamol, Theophylline, Metoprolol	Well Absorbed
II	Low	High	Carbamazepine, Danazol Ketoconazole [40&42]	Variable
III	High	Low	Acyclovir, Atenolol, Ranitidine	Variable
IV	Low	Low	Furosemide, Chlorothiazide, Cyclosporin	Poorly Absorbed

Below are the key drugs having low Solubility with some examples:

- NSAIDs (Ibuprofen, Naproxen, Diclofenac, Indomethacin)
- Antifungal Agents (Ketoconazole, Itraconazole, Griseofulvin)
- Antineoplastic Drugs (Paclitaxel, Docetaxel, Etoposide, Erlotinib)
- Antibiotics (Ciprofloxacin, Rifampicin, Tetracycline)
- Cardiovascular Drugs (Amiodarone, Furosemide, Spironolactone)
- Antipsychotic and Antidepressants Drugs (Clozapine, Quetiapine, Olanzapine)
- Antiviral (Ritonavir, Efavirenz, Acyclovir)
- Immunosuppressant (Cyclosporine, Tacrolimus, Sirolimus)
- Lipid lowering Drugs (Atorvastatin, Simvastatin)
- Diuretics (Furosemide, Hydrochlorothiazide)
- Antihypertensive (Nifedipine, Amlodipine)
- Antidiuretic Drugs (Glibenclamide, Glipizide)

- Steroids (Dexamethasone, Hydrocortisone, Prednisolone)
- Proton pump Inhibitor (Omeprazole, Lansoprazole, Pantoprazole)

Factors affecting Solubility

- TEMPERATURE: When a solution absorbs energy, the solubility increases with increasing temperature, and when a solution releases energy, the solubility decreases with increasing temperature.
- pH LEVEL: pH is one of the main effects on the dissolution of most drugs, including ionized groups. Solubility of a drug depends on degree of ionization. The degree of ionization is pH dependent as pH decreases, the solubility increases.[5]
- DRUG PARTICLE SIZE: The solubility of a drug is directly depending on the particle size. Typically, small particles are more soluble and vice versa, especially if the polarity, temperature and pressure for the solutes is the same. Solubility of a drug enables it to undergo effortless diffusion into the bloodstream without requiring energy or carrier proteins for absorption.
- POLARITY: Polarity plays an important role in solubility. A polar solute will dissolve in a polar solvent whereas a non-polar solute will dissolve in a non-polar solvent. If non-polar solute will not dissolve in polar solvent, it remains same without dissolve.
- SOLUTE-SOLVENT INTERACTION: Solute- solvent interactions plays very crucial role in determining solubility. Strong solute-solvent interaction leads to increase in Solubility while weak solute-solvent interaction leads to decrease in Solubility.
- SURFACE AREA: If a particle has smaller size then it causes increasing in surface area leads to increase in solubility.[5]
- PRESSURE: Liquids and solids do not expose any changes in solubility with change in pressure. While as expected, solubility of gases increases with increase in pressure.
- COMMON ION EFFECT: In ionic compounds, if the solvent already contains a common ion, the solubility of the ionic solute decreases. This is a consequence of Le Chatelier's Principle.
- MOLECULAR SIZE: The bigger the molecule or the greater its molecular weight the less soluble the substance. Greater molecules are harder to edge with solvent molecules in direction to solvate the substance.[5]

With advent of high screening of potential therapeutic agents has led to an increase in poorly soluble drug candidates, posing a significant challenge for formulation scientists in the oral delivery of such compounds.[3]

To increase the solubility of poor water,[45] soluble drugs Solubilization process is used. It includes salt formation, addition of co-solvent, prodrug design, particle size reduction, use of surface active agents, and complexation. Other physicochemical approaches such as pH adjustment, polymorphs, solvate and hydrates, hydrotrophy, solubilizing vehicles, adsorbents, etc. are used to enhancing oral absorption of poorly water soluble drugs.[3]

Major approaches for Solubility Enhancement

When a drug's solubility in aqueous environment is limited, there are various methods to improve the solubility of poorly soluble drugs. There are some traditional and some novel methods to increase solubility. Solubility enhancement techniques are delineated as,[7]

Physical modification

- Particle Size Reduction
- ♦ Micronization
- ♦ Nano suspension [40 & 41]
- Modification of crystal habit
- Drug dispersion in carriers
- Complexation [39]
- Cryogenic Techniques

Chemical Modification

- pH Adjustment
- Hydrotrophy
- Co- crystallization
- Co-solvency
- Salt formation

Miscellaneous Modification

- Super critical fluid technology
- Micellar Solubilization
- Direct capsule filling

- Electrospinning
- Dropping method Solution

DRUG DISPERSION IN CARRIER

Solid Dispersion

It is used to enhance the solubility and therapeutic effectiveness [39] of poorly soluble drugs. Solid dispersion refers to mixture of hydrophilic matrix and hydrophobic drug to form solid product. The matrix can be crystalline or amorphous.[9 & 16] Due to its simplicity, cost effectiveness and advantages it has been become popular among other techniques. The drug can be molecularly dispersed in either crystalline or amorphous particles using solid dispersion, which is a method of decreasing particle size. It provides improves surface properties and wetting by enabling the distribution of carrier component between and around the medication.[3]

Most often used matrixes are PVP, PEG, Tween 80, Plasdone-S630 and Sodium Lauryl Sulphate.

Due to problems with manufacturing, stability and scale up the solid dispersion technique has not gained transition despite the promising aspects of dissolution enhancement and concept simplicity.[8]

E.g. Celecoxib, Halofantrine, Ritonavir, such drugs solubility can be improved by Solid Dispersion technique using Hydrophilic carriers like

Celecoxib improved its solubility in combination with Povidone while Ritonavir improved its solubility in combination with Gelucire.

Importance of Solid Dispersion:[12]

→ Enhance Solubility.

→ Enhance Bioavailability and Stability of the Drug

→ It also enhances Absorption of the Drug.

→ Improves porosity of drug

→ Decrease crystalline structure of drug into amorphous form to increase dissolution rate and bioavailability.

To improve the dissolution properties of poorly soluble drugs there are numerous techniques are demonstrated in the pharmaceutical literature.[16]

Advantages of Solid Dispersion Technique: [28 &17]

- It is more applicable technique among others to enhance the bioavailability by changing their water solubility.
- It is easier to produce in different formulations
- It can improve wettability of compounds, whether carrier used have surface activity or not. E.g. Urea
- Particles of solid dispersion have high porosity
- Easily applicable when incorporated into fast disintegrating tablet (FDT)

Disadvantages of solid Dispersion Technique:[28]

- Not broadly used for commercial products
- Moisture may increase drug mobility which result in promote drug crystallization.
- Mostly polymers used can cause phase separation, crystal growth or can form metastable crystalline form
- Large scale production is limited due to expensive preparation method

Methods for preparing Solid Dispersion:[14]

→ Solvent Evaporation Method
→ Melting / Fusion Method
→ Spray Drying Method
→ Hot Melt Extrusion Method
→ Super Critical Fluid Method
→ Co-precipitation Method
→ Gel entrapment Method
→ Electrospinning Method
→ Kneading Method
→ Lyophillization Method
→ Co-grinding Method

Solvent Evaporation Method

In this method both the drug and carrier is dissolve in a common organic solvents such as ethanol, chloroform or mixture of ethanol and dichloromethane and then evaporate the solvent of the mixture under vacuum to produce solid solution.[15] Super saturation happens as the solvent is being drained and the constituents precipitate simultaneously, leaving behind a solid residue.[14]

In some cases co-solvents may be used but in large volume as compared to solvents and it required heating to enable complete dissolution of drug and carrier.[15]

Moreover this method has some benefits are that it is ecological method and low temperature is required for decomposition of drug.[12]

E.g. Furosemide is dissolve in Eudragitis (solvent) which has thick consistency that has been powdered, sieved and dried.[10]

Melting / Fusion Method

Sekiguchi and Obi were the first who discovered this method in 1961 to prepare fast release solid dispersion dosage form.[10] In this method both drug and carrier are mixed together using mortar and pestle, the heat is then applied to the mixture until its melting point reaches to each other. Then cool down the mixture with rigorous stirring on ice bath to require solid mass.[9, 10 & 12] The resultant solid mass is then crushed and sieve to form tablet by compressing them with the help of tableting agents.[10]

It has some advantages such that it is quite process and improves the missibility of drug in solvent with no residue left. But, at high temperature it can degrade the drug so this method is applied only when the drug and matrix are compatible with each other.[16]

E.g. Albendazole, Sulfathiazole, Paclitaxel, etc.

Spray Drying Method

It is a versatile and effective technique. The adequate amount of carrier is dissolved in water & the drug is dissolved in an appropriate solvent. The solvent can be water, methanol or organic liquid. After combining solutions using sonication or another appropriate technique, a clear solution is created, which is subsequently spray dried with a spray dryer.[17] Then

Evaporator is used to evaporate the solvent, due to large surface area of droplets after 20-30 min of spray drying, the spray dried mixture with polymer of solid dispersion is obtained.[18]

Polymers which used as carriers are PVP, HPMC, etc.

It improves both bioavailability and solubility of drug with consuming less time and scale-up production is also available in this process but sometimes heat sensitive drugs can causes Thermal degradation and the product may recrystallize on storage. It is mainly applied to enhance the solubility of hydrophobic drugs in oral dosage forms and useful for pulmonary and nasal drug delivery.

E.g. – Spironolactone, Valsartan, Naproxen, etc.

SCF (super critical fluid) Method

It is novel Nano sizing & inventive technique widely used for precipitation & crystallization of materials.[13] It is established in 1980s. Pure liquid and gases which act as intermediate of SCF, helps in product processing by giving them properties.

Non-volatile solvents can be dissolved in super critical fluids with carbon dioxide acting as critical point. A SCF exists as single phase above its critical temperature and pressure.[9]

In this technique, most widely used solvents are ethanol, water, ammonia, nitrous oxide, ethylene, propylene, and n-pentene, etc.[9] CO_2 is used as critical point in SCF due to its properties like it is safer, non-toxic, non-flammable, economical and environmentally stable. It does not cause any damage to Consumer. And the removal of CO_2 from polymer is easier. This technique is also known as Rapid Expansion of Supercritical solution (RESS).

A number of practical firms like lavipharm & ectar therapeutics are experts in particle engineering using SCF technologies to improve solubility and increase particle size.[12 & 25]

E.g. - Ketoprofen, Carbamazepine, Glibenclamide, Carvedilol, etc.

Methods for SCF processing[12]

A. Precipitation with compressed antisolvents process, rapid expansion of supercritical solutions, gas antisolvents recrystallization.
B. Precipitation with impregnation or infusion of polymers with bioactive materials.
C. Compressed fluid antisolvents.

D. Solutions enhance dispersion by SCF.
E. Aerosol supercritical extraction system.
F. Supercritical ant solvents process.

Hot melt extrusion Method

It is most widely used method. The first person who discovered this technique was *Speiser* & *Huttenrach* for pharmaceutical purpose to overcome some limitation of poorly soluble drugs. Such limitations can be challenging in sustained and controlled release, difficulty in combining multiple functions in single formulations, limited stability of some drugs and so on.[25]

It is the process of forming new materials by forcing the material through orifice under certain conditions such as temperature, mixing, pressure and feed rate.
In this process polymer, drug & excipients are blend thoroughly in molten state for granulation without any use of solvent. It uses co-rotating twin screw extruder, carriers and active pharmaceutical ingredients are combined with drug concentration for hot stage extrusion. The drug concentration is 40% w/w.[15 & 10] Hot melt extrusion technologies have been limited due to the temperature sensitive drugs.

E.g.:- sustained released pellets, Ritonavir, Tamoxifen, Itraconazole, etc.

Co-precipitation Method

It is a recognition method for increasing dissolution, bioavailability and solubility of poorly soluble drugs.

In this technique, a certain quantity of drug must be combined with the carrier solution while being continuously stirred for 1 hour by magnetic stirrer. The precipitate is separate out from the mixture by vacuum filtration and allowed to dried at room temperature to prevent the loss of water structure from inclusion complexes.[13 & 25]

This method is suitable for heat sensitive materials because it requires less amount of Energy. Use of Organic solvents makes this process cost effective and ecofriendly. It has some drawbacks that it leads to particle aggregation due to non-uniformity in drug and carrier mixture and sometimes it can also leads to phase separation.
E.g. – Celecoxib, Silymarin

Kneading Method

It is a simple method to prepare an inclusion complex. In this method the polymer or carrier is dispersed with water or small amount of hydrophilic solvent, the mixture is then triturated and transformed the mixture into thick paste by kneading process for specific time. The mixture is then placed in an oven at 45^0 C for drying in a specific time period. When the mixture is completely dried, pass the mixture through sieve no. 30 if required. The dried mass is then stored in a vacuum desiccator and packaged in an air tight container for further use.[12,23,24]

For small scale or laboratory scale; kneading process is done by using Mortar and Pestle while for large scale; kneading process can be done by using extruders and other machines.[12]

It is an appropriate method for formulation of Solid dispersion as it reduces the risk of phase separation and improves the wettability, solubility and bioavailability of drug. However it is a time consuming process which require labor intensives. If overheating is applied during the process then it can cause production loss and affect its stability.[24]

E.g. Cefixime, Domperidone, Efaviren

Co-grinding Method

It is a physical process for preparing solid dispersion to enhance solubility and bioavailability of the poorly soluble drugs.

In this method, drug and carrier both are chosen according to their compatibility and solid enhancing properties and weigh accurately. Then physical mixture of drug and carrier is formed which is then subjected to a blender for some time at a particular speed. The mixture is then introduced in a chamber of vibration ball mill in which steel balls are added for grinding.[23,10]

Solid dispersions are obtained then collected the sample and kept at room temperature in a screw capped glass vial until it is next used. It is a simple and cost effective method which increases the solubility and bioavailability of poorly soluble drugs. This method also helps in decreasing particle size and aggregation.[12]

E.g. Chlordiazepoxide, Mannintol

Gel – entrapment Method

Drug is encompass in a gel like structure formed by hydrophilic polymer with specific solvent, then tapered the drug within a matrix to create a stable, amorphous dispersion that enhance dissolution and adsorption of drug.[25]

In this method firstly prepared a polymer matrix with dissolving a hydrophilic polymer in a solvent which can be water or any other suitable organic solvent. A gel like matrix is formed in which drug is entrapped. Then pass the mixture through drying process, it can be done by freeze drying or spray drying to remove the solvent and solidifies the mixture. After drying the solid dispersion is often in the form of powder and further proceeds it into granules, tablets or other dosage forms.[10 &12]

It is a beneficial process for controlling the release rate of drug and enhances drug stability by reducing recrystallization of drug product.

Lyophillization Method

It is a molecular mixing technique where carrier and drug are dissolved in common solvent. It involves transfer of mass and heat to and from the product.

In this method, the physical mixture of polymer is prepared by mixing hydrophilic carrier with suitable solvent. Hydrophilic carriers used in this method are PEG, PVP, Mannintol, etc. Then freeze the prepared mixture at -50^0 to -80^0 C. A solidified frozen matrix with drug and carrier undergoes primary drying under vacuum to vaporize the solvent from the mixture. Then it undergo freeze drying by Freeze Dryer to remove residual solvent molecules. The dry, porous lyophilized solid dispersion is collected and formulated into various dosage forms such as capsules, tablets, etc.[26]

This method have some upsides such as it has great acceleration of sublimation rates and uses non-aqueous solvents which increases the dissolution rate and solubility of poorly soluble drugs. While downside of this method includes that it has high risk of drug carrier compatibility and time consuming process with high cost.

Electrospinning Method

It is a process in which solid fibers are produced from polymeric fluid stream solution. Strong electrostatic force is then applied to the conductive capillary which is attached with reservoir containing polymer solution. On increasing electrostatic field, charge species are accumulated

on the surface and form nanofibers by using whipping process for thinning the nanofibers, it may destabilize its shape from hemispherical to conical shape. Beyond critical point, charged polymer jet is ejected from apex of cone. The ejected charged jet is then collected on a screen via electrostatic force. This process is depends on surface tension and electrostatic force used.[17 &27]

It has some benefits compared to drawbacks are Risk of phase separation is minimum through this process, minimal solvent residue, and nanofibers can control the release profile. But, it is a time consuming process and expensive method, and scale up production is also limited for this process.

Polymers used in solid dispersion technique

Before entering the systemic circulation, medications taken orally undergo dissolution and then pass through the epithelial barrier. One of the primary determinants of the drug's bioavailability, in addition to its solubility and permeability, is its rate of dissolution. For the majority of medications, the drug's solubility in the gastrointestinal tract is a serious concern.[36] In oral drug delivery; polymers have been utilized as a crucial tool to regulate the rate of drug release from any formulations. They are also improved when used as stabilizers, taste-masking agents, and protective agents.[37]

By using polymers in the formulation process, we can enhance the permeability through intestine and also enhance the bioavailability of the drug. Some examples of polymers which are used in the solid dispersion formulations of Ibuprofen tablets are:-

- Polyvinylpyrrolidone (PVP),
  - PVP K30, PVP K90
- Hydroxypropyl methylcellulose (HPMC),
  - HPMC E5, HPMC E15
- Eudragit polymer,
  - Eudragit RC, Eudragit RS, Eudragit L100
- Polyethylene glycol (PEG),
  - PEG 4000, PEG 6000
- Poloxamers,
  - Poloxamer 407
- Carboxymethylcellulose (CMC),

- Sodium CMC
- Cyclodextrins,
- Hydroxypropyl-beta-cyclodextrin
- Polyvinyl Alcohol (PVA),
- Methacrylic acid copolymers
- Eudragit S, Eudragit L

But commonly used polymers for Ibuprofen solid dispersion tablets are PEG, HPMC, and Eudragit because of its wetting, solubilizing and surface active properties.

CONCLUSION

The enhancement of solubility and bioavailability of poorly water-soluble drugs remains a major challenge in pharmaceutical development. Among the various approaches explored, solid dispersion has emerged as one of the most promising and widely studied techniques for overcoming solubility limitations. This method involves dispersing the drug in an inert carrier or matrix, which can improve wettability, reduce particle size, and convert the crystalline drug to an amorphous state, thereby significantly enhancing its dissolution rate and bioavailability. This research highlights the key advantages of solid dispersion, including its ability to enhance the dissolution profile without the need for chemical modification of the drug molecule. Various methods such as hot melt extrusion, solvent evaporation, and spray drying have been effectively used to prepare solid dispersions. Additionally, the choice of carrier materials like polyethylene glycol (PEG), polyvinylpyrrolidone (PVP), and hydroxypropyl methylcellulose (HPMC) plays a critical role in determining the stability and efficiency of the final formulation. Despite the promising potential, the technique also faces challenges such as physical and chemical instability, difficulty in scale-up, and recrystallization during storage. However, advancements in formulation technologies and the use of novel polymers and processing techniques are continually addressing these limitations.

In conclusion, solid dispersion remains a powerful and versatile strategy for enhancing the solubility of poorly soluble drugs. It holds significant promise for improving therapeutic efficacy and patient compliance by enabling the development of more effective oral dosage forms. Future research should focus on optimizing formulation parameters, ensuring long-term stability, and exploring novel carriers to further expand the utility of this technique in commercial drug development.

REFERENCES

1. https://uen.pressbooks.pub/introductorychemistry/chapter/precipitation-reactions/
2. Lachman L, Lieberman H, Kanig JL. The Theory and Practise of Industrial Pharmacy. 3rd ed. Lea & Febiger; 1986.
3. Md. Abdullah, Florida Sharmin, S.M. Ashraful, Md. Selmin. Enhancemrnt of Solubility and Dissolution Characteristics of Ibuprofen by Solid Dispersion Technique. *Manum et al.* 2012.
4. Shivanshi Saini, V.P Bahuguna, Vishal Kumar, Paras Gupta, Anurag Ahlawat, Himanshu Verma. Science of Solubility: Introduction, Importance and Factor of Solubility. ijcrt.org 2023.
5. https://tokaysc6.weebly.com/factors-affecting-solubility.html
6. Himanshi Khatri, Md. Sadique Hussain, Swati Tyagi. Solubility Enhancement Techniques: An Overwiew. Hussain et.al 2022.
7. Dixit V. Bhalani, Bhingaradiya Nutan, Avinash Kumar, and Arvind K. Singh Chandel. Bioavailability Enhancement Techniques for Poorly Aqueous Soluble Drugs and Therapeutics. Biomedicines 2022.
8. Vemula Varun Raj, Venkateshwarlu, Lingala Srikanth. Solubility Enhancement Techniques. IJPSRR 2010.
9. Arun Kumar MS, Rajesh M and Subramanian L. Solubility Enhancement Technique: A Comprehensive Review. WJBPHS 2023.
10. Ashutosh Sharma, Ravi Kumar, Sunil Kumar, Yogesh Sharma, Surbhi Jangir. Solubility Enhancement, Formulation and Evaluation of solid tablets of Tinidazole. Indian Journal of Healthcare, Medical and Pharmacy Practice 2023.
11. Pradeep, Kamal and Beena Kumari. Versatility of nanosuspension formulation in various drug delivery systems: A brief review. Advance pharmaceutical Journal 2020.
12. Ketan T. Savjani, Anuradha K. Gajjar, Jignasa K Savjani. Drug Solubility: Importance and Enhancement Technique. PMC PubMed Central 2012.
13. Illa Narmada, Contemporary review on solubility enhancement techniques. Journal Drug Delivery and Therapeutics, 2023.
14. Jadge, Rajesh Jagtap. Solubility Enhancement Technique: A Review. Sneha Jagtap et al 2018.
15. S.V Kadam, D.M Shinkar, R.B Saudagar. Review on Solubility Enhancement Techniques. S.V Kadam et al 2013.

16. Dhirendra K, Lewis S, Udupan N and Atin K. Solid Dispersion: A Review. Dhirendra K et.al 2009.
17. Kiran Singh Sharma, Jagannath Sahoo, Seema Agarwal, Asha Kumari, Solid dispersion: A technology for improving bioavailability, J Anal Pharm Research. 2019
18. B.A Bhairav, J.K Bachhav, R.B Saudagar. Review on solubility enhancement technique, Asian Journal Pharm Research 2016.
19. Sethia S and Squillanate E. Solid dispersion revival with greater possibilities and application in oral drug delivery. Crt. Review Therapeutic drug carrier system.
20. Mogal S A, Gurjar P N, Yamgar D.S, Kamool A C. Solid dispersion technique for improving solubility of some poorly soluble drug. Scholars research liberary/ 2121
21. Sasmit Nagappa Mali, Dr. Kailas Madhukar Karande. A review on: Biopharmaceutics classification System. International journal of creative research Thoughts. 2021
22. A.S Hussain, L.J Lesko, K.Y Lo, V.P Shah, D Volpe, R.L William. The Biopharmaceutics Classification System: Highlights of FDA draft guidance, 1999
23. P.S Argade, D.D Magar, R.B Saudagar. Solid Dispersion: Solubility enhancement Technique for poorly water soluble drugs. Journal of Advanced Pharmacy Education and Research 2013.
24. R.B Desi Reddy, P. Sivanarayana, T Madhu Mounica, N Prathibha, G Sandhya, P.A Lekhya. Solid Dispersion - An approach to enhance. The dissolution rate of Amlodipine, International journal of Pharmacy 2013.
25. Sneha Jagtap, Chandrakant Magdum, Dhanraj Jadge, Rajesh Jagtap. Solubility Enhancement Technique: A Review. Journal of Pharmaceutical Science and Research 2018.
26. Laxmikant B Dhande, Madhuri T Deshmukh, Abhijit N Khopade, Rajkumar V Shete, Vaibhav V Kunjir. A review on solubility enhancement by Solid dispersion Method. Journal of Drug Delivery and Therapeutics 2021.
27. Swati Sareen, George Mathew, Lincy Joseph, Improvement in solubility of poorly soluble Drugs by solid Dispersion. PubMed central 2012.
28. Mohamed Salah Attia, Azza Ali Hasan, Fakhr-Eldin, Sdiman Ghazy, Eman Gomaa. Solid Dispersion as Technical solution to boost the dissolution rate and bioavailability of poorly soluble drugs. Indian Journal of Pharmaceutical Education and Research 2021.
29. Radu M Nanau, Manuela G Neuman. Ibuprofen induced hypersensitivity syndrome. Translational Research 2010.

30. Sagar Bashyal. Ibuprofen and its different analytical manufacturing method: A review. Asian Journal of Pharmaceutical and clinical research 2018.
31. Rabia Bushra, Nausheen Aslam. An overview of clinical pharmacology of Ibuprofen. Omen Medical Journal 2010.
32. Dawn Connelly. A brief history of Ibuprofen. The Pharmaceutical journal 2017.
33. Isha Gargya, Baljeet Singh, Sanjay Talnia. NSAIDS: Their effects and side effects in Orthodontic Therapy- A Review. Dental Journal of Advanced Studies 2017.
34. Rainsford KD: Ibuprofen: pharmacology, efficacy and safety. Inflammopharmacology. Epub 2009.
35. https://pubchem.ncbi.nlm.nih.gov/compound/Ibuprofen.
36. Sreejan Manna, Jyoshna Kollabathula. Formulation and Evaluation of Ibuprofen controlled releases matrix tablet using solid dispersion. International Journal of Applied Pharmaceutics 2019.
37. Ravinder Kaur, Mrs. Sukhvir Kaur. Role of Polymers in Drug delivery. Journal of Drug Delivery and Therapeutics 2014.
38. Abhik Kar, Abdul Baquee Ahmed. Enhancement of solubility and dissolution of Ibuprofen by Solid Dispersion Technique and formulation of Sustained Release Tablet containing the optimized batch of Solid Dispersion. International research of Current Pharmaceutical Research 2017.
39. Ain.S, Philip.B. Pathak.K. Preformulative assessment of preformed complexes of gemfibrozil with cyclodextrins, PDA Journal of Pharmaceutical Science & Technology, Vol.62, No. 2, July-August 2008, pp.300-308.
40. Khushboo, Shabnam Ain, Babita Kumar, Qurratul Ain, Formulation and characterization of antifungal nanoemulsion of Ketoconazole, Indo American Journal of Pharmaceutical Sciences, 2023, 10 (09), 1-11.
41. Shabnam Ain, Gaurav Mishra, Babita Kumar, Qurratul Ain and Raj Kumar Garg, “Antidiabetic Potential of Developed Solid Lipid Nanoparticles Loaded with Quercetin: in-vitro and in-silico Studies” Annals of Phytomedicine 11(2): 1-11, 2022.
42. Vikas Yadav, Shabnam Ain, Babita Kumar, Qurratul Ain, Formulation and evaluation of Niosomes of ketoconazole, Indo Am. J. P.Sci., 2023, 10 (10), 39-53.
43. Pandey, S., Kumar, V., Ain, S., Ain, Q., Kumar, B., Ruhela, N., Bhuvnesh,(2025). Alzheimer’s Disease: An Overview, International Journal of Research in Pharmacy and Allied Science. 4(2),13-32.DOI: https://doi.org/10.71431/IJRPAS.2025.4202 .

44. Pandey, S., Kumar, V., Ain, S., Ain, Q., Bhuvnesh, Ruhela, N., Nagar, C., Kumar, B. (2025). Impact of Heavy Metals on Respiratory Disease, International Journal of Research in Pharmacy and Allied Science. 4(3),1-12. DOI: https://doi.org/10.71431/IJRPAS.2025.4301.
45. Shabnam Ain, Qurratul Ain, Sneha Pandey, Vishakha Tyagi, Yashvardhan Vats, Nidhi Ruhela and Babita Kumar, Assessment of ground water quality in different areas of Uttar Pradesh and Haryana, Cuestiones de Fisioterapia., 2025, 54 (2), 3557-3575.