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"A COMPREHENSIVE REVIEW ON SOLUBILITY ENHANCEMENT STRATEGIES FOR POORLY WATER-SOLUBLE DRUGS"

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Abstract
The solubility has a direct impact on medication absorption, bioavailability, and therapeutic results, it is essential in assessing the efficacy of pharmaceutical substances. The low water solubility of a large number of recently produced active pharmaceutical ingredients (APIs) presents difficulties for medication formulation and administration. Numerous Solubilization methods have been investigated in an effort to increase systemic absorption and medication dissolving rates. Solubility enhancement strategies are thoroughly examined in this review, including advanced techniques like surfactant-based Solubilization, supercritical fluid processing, and self-emulsifying drug delivery systems, as well as physical modifications like particle size reduction, solid dispersion, and nanotechnology, as well as chemical modifications like salt formation, co-crystallization, and pH adjustment. In order to improve therapeutic performance and commercial feasibility, these methodologies' benefits, drawbacks, and real-world uses in pharmaceutical research are examined. By overcoming solubility challenges, these strategies contribute to the successful formulation of potent and effective therapeutic agents.

Keywords: Solubility, Bioavailability, Drug Delivery, Solubilization Techniques, Formulation

1 INTRODUCTION

Drugs that are poorly water soluble can benefit from a variety of measures to increase solubility and bioavailability. Pharmaceutical Solubilization procedures include solid dispersion, co-solvency, Micronization, nanonization, chemical modification, Hydrotrophy, Complexation, micellar solubility, and pH control. In Novel Chemicals Entities (NCEs) screening research, formulation creation and development, Solubilization of weakly soluble medicines are a common challenge [1, 2]. Solubility refers to the maximum amount of solute that can dissolve fully in a given solvent volume. It possesses both quantitative and qualitative features. Qualitatively, it can be defined as the spontaneous interaction of two or more substances to create a homogeneous dispersion. The concentration of a substance (solute) in a particular volume of solvent at a specific temperature results in a homogeneous solution. Drug solubility can be measured using percentages, parts, molality, molarity, mole fraction, or volume fraction. Solubility equilibrium is extremely significant in medications. The FDA's Biopharmaceutical Classification System (BCS) categorizes medications based on their permeability and solubility (see Table 1). Due to their low solubility, Class II and IV of the system experience dissolution as the rate-limiting stage for medication absorption.[3] Drugs of class II and IV have solubility issues.[4,5] Increasing the solubility of BCS Class II and IV medicines improves their bioavailability. [6]

Table 1: Biopharmaceutical Classification System

Class	Solubility	Permeability	Absorption pattern
1	High	High	Well absorbed
2	Low	High	Variable
3	High	Low	Variable
4	Low	Low	Poorly absorbed

Solubility can be expressed in a variety of ways due to its widespread use. Concentration is typically stated using mass (g of solute per kg of solvent, g per 100 mL of solvent), molarity, molality, mole fraction, or other related terms

Table 2: Solubility Expression [7]

Descriptive terms	Parts of solvent required for one part of solute
Very soluble	Less than 1
Freely soluble	From 1- 10
Soluble	From 10 -30
Sparingly soluble	From 30 – 100
Slightly soluble	From 100 – 1000
Very slightly soluble	From 1000 – 10,000
Insoluble	Greater than 10,000

2 FACTOR AFFECTING SOLUBILITY:

Particle size: Solubility is influenced by particle size. Particle size reduces, leading to an increase in surface area to volume ratio. Increased particle surface area causes more solvent interaction.

Temperature: Solubility varies with temperature. As the temperature rises and the solution process gains energy, the solubility increases. As the temperature rises, the solubility of the solution decreases due to energy release. [8]

Molecular size: The solubility of a material decreases with increasing molecular weight and size, as it becomes more difficult to dissolve larger molecules.

Pressure: Gas solubility varies with pressure, increasing with higher pressure and decreasing with lower pressure. Pressure changes do not affect the solubility of solid or liquid solutes.

Polarity: The polarity of the solute and solvent molecules influences their solubility. Polar solvents typically dissolve polar solutes, while non-polar solvents dissolve non-polar solutes.

Nature of solute and solvent: The concentration of a solute in a solvent at a specific temperature determines its nature. At normal temperature, 200 grams of zinc chloride dissolve in 100 grams of water, but only 1 grams of lead (II) chloride does [9].

3 IMPORTANCE OF SOLUBILITY

Oral drug delivery is the most convenient and widely used route due to easy administration, high patient compliance, and cost-effectiveness. Generic drug companies prefer it for producing bioequivalent formulations efficiently [10].. The main challenge in oral dosage form design is poor bioavailability, influenced by solubility, permeability, dissolution, metabolism, and efflux mechanisms. Low bioavailability is often due to poor solubility and low permeability. Solubility is vital for all dosage forms, including parenteral formulations, as it affects drug absorption, efficacy, and stability. [11] Solubility is crucial for attaining the desired drug concentration in systemic circulation to ensure the required pharmacological response. [12]. poorly water-soluble drugs require high doses to achieve therapeutic levels. Low aqueous solubility is a major challenge in formulation development, as drugs must be in solution at the absorption site. Most drugs, being weak acids or bases, exhibit poor solubility in water, the preferred solvent for liquid formulations. Over 40% of NCEs are poorly water-soluble, leading to low bioavailability, variable absorption, and GI toxicity. Solubility is a key factor in drug formulation, especially for BCS Class II drugs, where enhancing solubility improves bioavailability. Poor solubility also increases development costs, dosing frequency, and patient burden.[13]

4 PROCESS OF SOLUBILIZATION: [14]

- Step 1- Includes breaking intermolecular or ionic connections in the solute and separating contacts between the solvent and the solute molecule/ion.
- Step 2 - A solid molecule separates from the bulk.
- Step 3 - Integrate the solid molecule feed into the solvent hole.

5 METHODS FOR SOLUBILITY ENHANCEMENT

1. Physical modification
   - A. Particle Size Reduction
     - Micronization
     - Nano-suspension
   - B. Crystal Habit Modification
     - Polymorphs Pseudo polymorphs
   - C. Drug Dispersion in Carrier
     - Solid solutions
     - Solid dispersions
   - D. Solubilization by Surfactants
     - Micro emulsion
     - Self-micro emulsifying drug delivery system
   - E. Complexation
2. Chemical Modification
   - Hydrotrophy
   - Co-solvency
   - Nanotechnology
   - Salt formation
   - Co-crystallization
3. pH adjustment
4. Supercritical fluid process
5. Liquisolid methods

1. Physical modification

A. Particle Size Reduction

- **Micronization**

Increasing a drug's surface area reduces particle size and improves solubility.. Micronization, which involves milling drugs using jet mills or colloid mills, improves drug dissolution by reducing particle size and increasing surface area. However, it is not recommended for high-dosage drugs as it does not affect the drug's saturation solubility [15].Micronization and Nano-suspension are two strategies for lowering particle sizes. Drug solubility in Micronization is often inversely related to particle size.

Table 3:Solubility enhancement of poorly water soluble drug by using Particle Size Reduction.

Sr. No.	DRUG	MATERIAL USE
1	Domperidone [16]	Soluplus® or PEG6000 , solvent (acetone and methanol 1:1 v/v), water
2	Fenofibrate [17]	Lactose, polyvinylpyrrolidone or sodium lauryl sulphate
3	Griseofulvin [18]	Trifluoromethane

- **Nano suspension**

This approach is used to dissolve medications that are poorly soluble or insoluble in water and oils. Nano suspension is a biphasic system containing Nano sized particles suspended in water. Surfactants stabilize Nano-sized medicine particles for parenteral, pulmonary, and oral administration. Nano suspension has an average particle size range of 200. And 600 nm, while the particle size distribution of solid particles is frequently smaller than a micron. There are several techniques for Nano crystals, disso cubes, Nano pores, and Nano edges are all examples of Nano suspensions.[19]

Table 4: Solubility enhancement of poorly water soluble drug by using Nano Suspension.

Sr. No.	DRUG	MATERIAL USE
1	Febuxostat [20]	Soluplus, Tween80, pullulan, polyvinyl alcohol (PVA), gelatin, and plasticizers like polyethylene glycol (PEG400) and glycerin
2	Curcumin [21]	PVPK30 , SDS
3	Furosemide [22]	Tween 80
4	Cilostazol [23]	MCC, Isomalt, Crospovidone

B. Crystal Habit Modification

- **Polymorphs**
- **Pseudo Polymorphs**

Polymorphism refers to a solid material's ability to take on several crystalline forms with distinct lattice configurations. Polymorphs refer to different crystalline formations. Solvates refer to the process of incorporating solvent molecules into the crystal lattice of solids. These solvates exist in various Pseudo polymorphs are crystal forms, and this phenomenon is known as pseudo polymorphism. Drugs that exist. Although crystalline forms are chemically similar, they differ physiochemical in terms of melting point, texture, density, Solubility and stability. Likewise, an amorphous form of a medication is more suited than a crystalline form because of its bigger surface area and increased related energy.[24]. The order of several solid forms of medicines is amorphous > metastable.

Table 5: Solubility enhancement of poorly water soluble drug by using Polymorphs.

Sr. No.	DRUG	MATERIAL USE
1	Ketoconazole [25]	Glutaric, vanillic, 2,6-dihydroxybenzoic, protocatechuic, and 3,5-dinitrobenzoic acids.

C. Drug Dispersion in Carrier

- **Solid Solutions**

It is the result of combining two crystalline solids to form a new crystalline solid. The two components crystallize concurrently in an uniform one-phase solution, forming a mixed crystal structure. Compared to basic eutectic systems, it is expected to provide faster dissolving rates. [26]

Table 6: Solubility enhancement of poorly water soluble drug by using Solid Solution.

Sr. No.	DRUG	MATERIAL USE
1	Itraconazole [27]	PEG
2	Ibuprofen [28]	HPMC and polyoxyl stearate (POS)

- **Solid Dispersion**

The phrase "solid dispersion" refers to a group of solid products made up of two parts: a hydrophilic matrix and a hydrophobic substance. [29] It is a valuable pharmaceutical method for enhancing the rate of medication absorption, solubility and therapeutic effectiveness. . The most commonly utilized hydrophilic carriers are polyvinyl pyrrolidone, plasdoneS-630, and PEGs.Surfactantsare sometimes used in the process of forming solid dispersions. [30, 31] Examples include Docusate sodium and Myrj-52. Tween 80, Sodium Lauryl Sulphate, and Pluronic F-68. This approach is also used with halofantrine, celecoxib, and ritonavir to increase their solubility. To increase the solid dispersion of hydrophobic medicines.

Table 7: Solubility enhancement of poorly water soluble drug by using Solid Dispersion.

Sr. No.	DRUG	MATERIAL USE
1	Etoricoxib [32]	Poloxamer 407 (PXM 407), poloxamer 188 (PXM 188) and polyethylene glycol 4000 (PEG 4000)
2	Prothionamide [33]	Polyethylene glycol-1500, polyvinylpyrrolidone-10000, and β-cyclodextrin
3	Azithromycin [34]	Mannitol and β-Cyclodextrin
4	Celecoxib [35]	PVPK30

- **Fusion Method**

This approach entails heating the carrier above its melting point and mixing the medication into the matrix. Cooling the mixture helps spread the medication throughout the matrix. [36]

Table 8: Solubility enhancement of poorly water soluble drug by using Fusion Method.

Sr. No.	DRUG	MATERIAL USE
1	Ibuprofen [37]	0.1N Hcl, de ionized water, phosphate buffer
2	Raloxifene [38]	HPMC E5 LV
3	Amiodarone hydrochloride [39]	PEG 1500, 4000 and 6000
4	Aspirin [40]	Aspirin and Polyethylene Glycol 6000

- **Solvent Evaporation Method**

An appropriate organic solvent is used to dissolve both the carrier and the active component. To create a solid residue, the solvent is evaporated at high temperatures in a vacuum. [41] Solvents commonly utilized include ethanol, chloroform, or a dichloromethane-ethanol combination.

Table 9: Solubility enhancement of poorly water soluble drug by using Solvent Evaporation Method.

Sr. No.	DRUG	MATERIAL USE
1	Clotrimazole [42]	Polyethyleneglycol 4000, polyvinyl pyrrolidones

- **Hot-Melt Extrusion**

It is similar to the fusion method, except that the extruder produces intensive component mixing instead. Unlike traditional fusion methods, this technology allows for continuous production, making it suited for large-scale production. Furthermore, since the form can be modified for the following processing stage without grinding at the extruder's output, the product is easier to use. [43]

Table 10: Solubility enhancement of poorly water soluble drug by using Hot Melt Extrusion.

Sr. No.	DRUG	MATERIAL USE
1	Indomethacin-Arginine [44]	Copovidone , phosphate buffer ,water,0.1 N HCL , 100 RPM
2	Tadalafil [45]	Soluplus® , mannitol , lactitol
3	Itraconazole [46]	Soluplus®/βCD and Ac-Di-Sol®

D. Solubilization by Surfactants

- **Micro emulsion**

A pre-concentrate is created by combining a hydrophilic surfactant and solvent to dissolve a medication that is not easily soluble in water. The surfactant should be non-toxic and HLB-compatible. The process results in a translucent emulsion of small, uniform oil droplets containing the solubilized medication. Numerous Drugs that are fully insoluble in water have been rendered more soluble using micro emulsions. The oil-in Water micro emulsion is the ideal formulation because it promotes solubility by enabling molecules with low water content. Solubility is the ability to dissolve into the oil phase. Surfactants can increase oral bioavailability. Permeability changes.

Advantages of Micro emulsions

-Advantages include ease of production, clarity, filterability, and compatibility with various drug solubility levels. [47]

Table 11: Solubility enhancement of poorly water soluble drug by using Micro Emulsion.

Sr. No.	DRUG	MATERIAL USE
1	Chloramphenicol [48]	Oleic acid, tween 20/60, 1-propanol and phosphate buffer.
2	Itraconazole [49]	Isopropyl myristate (IPM) and oleic acid (1:1) as oil, Tween-80, Transcutol P
3	Sertaconazole [50]	Oleic acid, Tween 80, propylene glycol and water.

- **Self-Micro Emulsifying Drug Delivery System (SMEDDS)**

The self-emulsifying drug delivery system consists of a transparent isotropic solution containing oil, surfactant, co-surfactant, hydrophilic solvents, and a co-solvent. Oil-in-water micro emulsions are created using SEDDS and SMEDDS. These are isotropic oil-surfactant solutions. When administered orally, these new colloidal compositions act as Micro emulsions of oil in water.

Table 12: Solubility enhancement of poorly water soluble drug by using SMEDDS

Sr. No.	DRUG	MATERIAL USE
1	Phyllanthin [51]	Phyllanthin/Capryol 90/Cremophor RH 40/Transcutol P (1.38:39.45:44.38:14.79) in % w/w.
2	Acyclovir [52]	Acyclovir (50 mg), Tween 60 (60%), glycerol (30%) and sunflower oil (9%)

E. Complexation

Cyclodextrins (CDs) have been used with medications to improve their water solubility and stability. Pharmaceutical formulations typically use water-soluble Cyclodextrins derivatives. Cyclodextrins having molecular weights larger than 1000 Da are big and unlikely to pass through the skin. It has. Cyclodextrins Complexation has been reported to increase and decrease skin penetration. In addition to their use. CDs can also be employed to stabilize and improve membrane permeability in addition to increasing solubility. Cyclodextrins Significantly increase permeability across biological membranes. [53]

Table 13: Solubility enhancement of poorly water soluble drug by using Complexation.

Sr. No.	DRUG	MATERIAL USE
1	Cyclodextrins [54]	Chrysin,apigenin,luteolin
2	Albendazole [55]	Beta-cyclodextrin , acetic acid solutions

2. Chemical modification

- **Hydrotrophy**

Solubilization happens when a large amount of a second solute is introduced to increase the solubility of the first in water. Complexation promotes solubility by weakly interacting with hydrotropic compounds such sodium benzoate, sodium acetate, sodium alginate, and urea. Drugs that are poorly soluble. Hydrotropic agents are ionic organic salts. [56] Many salts have massive anions or cations that are also particularly soluble in water, a phenomenon known as "hydrotropism," which causes the "salting in" of non-electrolytes. Specifically, "hydrotropic salts." In hydrotropic solutions, the hydrotropic agent and solute make a weak contact. Which are not colloidal.[57,58]

Advantages

-The solvent nature of Hydrotrophy is pH independent, very selective, and does not require emulsification.

-It does not involve the creation of an emulsion or the use of organic solvents.[59]

Table 14: Solubility enhancement of poorly water soluble drug by using Chemical Modification.

Sr. No.	DRUG	MATERIAL USE
1	Furosemide [60]	Urea, sodium acetate, sodium benzoate, sodium citrate
2	Meloxicam [61]	Sodium benzoate
3	Glipizide [62]	Sodium Benzoate, Sodium acetate, Sodium salicylate
4	Chartreusin [63]	Sodium Benzoate, Sodium trihydroxy Benzoate

- **Co-Solvency**

Co-solvents, which are water-miscible solvents with high solubility, can boost the solubility of a medication with low solubility in water. Co-solvents are liquid solutions that combine water-miscible solvents to increase the solubility of insoluble compounds. Cosolvent methods might be appropriate for weakly Lipophilic or extremely crystalline soluble substances with high solubility in solvent mixtures. Cosolvents can improve the solubility of weakly soluble molecules by thousands oft imes when compared to the drug solubility in water alone. Dimethyl sulfoxide (DMSO) and dimethyl acetamide (DMA) are commonly utilized as cosolvents due to their high solubility capacity for difficult-to-dissolve medicines and low toxicity. [64] Weak electrolytes and nonpolar compounds often have low water solubility. These solutes are more soluble in a mixture of solvents rather than a single solvent. This phenomenon is known as co-solvency. The solvents that, in Co-solvents are substances that when combined increase the solubility of a solute.

For example, phenobarbitone is insoluble in water. To obtain a transparent solution, dissolve in a mixture of alcohol, glycerine, and propylene glycol. Co-solvency refers to the process of increasing the solubility of a solute through the use of a combination of solvents. The solvents utilized are referred to as co-solvents. Examples of regularly used co-solvents are ethanol, sorbitol, Glycerine, propylene glycol, polyethylene glycol, and so on.

Advantages

-It has strong Solubilization ability for poorly soluble medicines and is easy to manufacture, produce, and assess.

Disadvantages

-Insoluble materials, like other solubilized forms, have lower chemical stability than crystalline states. [65]

Table 15: Solubility enhancement of poorly water soluble drug by using Co-Solvency

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Sr. No.	DRUG	HYDROTROPES USE
1	Etoricoxib [66]	PEG 400, PG, and glycerin
2	Griseofulvin [67]	DMF, water , methanol + water , ethanol + water , acetonitrile + water and *N*-methylpyrrolidone (NMP)

- **Nanotechnology**

Nanotechnology involves studying and using materials and structures at the Nano scale (100 nm or less). Micronized products have a small effective surface area for dissolving, leading to the need for nanonization. Micronization alone does not provide sufficient oral bioavailability

for many novel products. Chemical entities (NCEs) with restricted solubility. Preparatory techniques include sonication and high Pressure homogenization, vacuum deposition, and high-temperature evaporation. [68]

Advantages

-The production of spherical particles with smooth surfaces, narrow particle size distributions, and large specific surface areas improves solubility and dissolving rate. [69]

Table 16: Solubility enhancement of poorly water soluble drug by using Nanotechnology

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Sr. No.	DRUG	MATERIAL USE
1	Nab-paclitaxel [70]	Protein albumin

- **Salt formation**

Due to various instability issues, it is frequently impossible to develop an API in its purest form. This reaction produces salts, co-crystals, solvates, hydrates, and polymorphs. Salt production has enhanced medication candidates that are poorly soluble due to weak acid and basic properties. Salts form when a material ionizes in solution. It works well in both solid and liquid dose forms. When acidic or basic a salt is created when medication is transformed into a salt that is more soluble than the base medicament. For example, diclofenac is Diclofenac sodium, on the other hand, is water soluble. [71,72]

Table 17: Solubility enhancement of poorly water soluble drug by using Salt formation

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Sr. No.	DRUG	MATERIAL USE
1	Ketoconazole [73]	Oxalic acid (OXA) and fumaric acid (FUMA)
2	Olanzapine [74]	Coformers (Phol, Res) and salt-formers (SA, AA, 3HBA, 2ATPA)
3	Acetazolamide [75]	Piperazine, theophylline
4	Isoniazid [76]	Oxalic, maleic and methanesulfonic acids

- **Co-Crystallization**

Co-crystallization alters molecular interactions, which can be employed to improve therapeutic efficacy. A co-crystal is a solid crystal made up of multiple components, at least one of which is an acceptable ion or molecule, at ambient temperatures. To choose the best co-crystal, analytical methodologies and a rational physicochemical approach could be used. Solvates and co-crystals are only physically different from one another. Solvents are generated when one of the components is liquid and the other solid. When both parts are solid, Co-crystals are formed. Several co-crystallization processes include: 1) solvent evaporation. 2) Grinding. 3) Slurry Co. crystallization 4) Solvent drop grinding 5) High-throughput co-crystallisation. 6) Hot melt extrusion (7) Sonocrystallization technique.

Table 18: Solubility enhancement of poorly water soluble drug by using Co-Crystallization

Sr. No.	DRUG	MATERIAL USE
1	Atorvastatin calcium [77]	Citric acid,nicotinamide
2	Carvedilol [78]	Hydrochlorothiazide (HCT), a diuretic drug, as coformer.

3. pH adjustment

Adjusting the pH can make water-insoluble drugs water-soluble. To obtain solubility with this approach, it's important to consider the buffer capacity and pH tolerance. Alkalizing excipients can enhance the solubility of weakly acidic medications, whereas weakly basic pharmaceutical scan benefit from them. Decrease the pH. [79] It can also be applied to lipophilic and crystalline substances that are poorly soluble [80]. In theory, pH changes can be used to both parenteral and oral delivery systems. The poorly soluble medication because blood is a strong buffer with a pH ranging from 7.2 to 7.4, it may precipitate following an intravenous infusion.

Advantages

-Analysed and formulated easily.

-Easy to expedite and create.

-Its low chemical usage makes it ideal for high-throughput testing. [81]

Disadvantages

-Non-physiological pH and high pH have been linked to tolerance and toxicity (both local and systemic). [82]

4. Supercritical fluid process

Carbon dioxide serves as the critical point for supercritical fluids (SCFs), which can dissolve non-volatile solvents. A SCF exists in a single phase above its critical temperature and pressure. SCFs are useful for product processing due to their intermediate qualities between liquids and gases. Furthermore, near the crucial spots, even in modest Changes in operating temperature, pressure, or both have a major impact on

density, transport properties such as viscosity, diffusivity, and other physical qualities include dielectric constant and polarity. The most commonly used Water, ethanol, ammonia, nitrous oxide, ethylene, propylene, and n-pentane are examples of supercritical solvents. Compressed fluid anti solvents can be used to expand supercritical solutions quickly, infuse bioactive ingredients into polymers, precipitate using compressed anti solvents (PCA), recrystallize gases, and improve solutions. Dispersion by supercritical fluid (SEDS) and aerosol-based SCF processing have all been developed to address various some facets of these difficulties. [83]

Advantages

-SCF techniques enable precise Micronization of medicinal particles to sub-micron levels.
-After Solubilization in the SCF, drug particles can be recrystallized into smaller sizes.
-Current SCF methods have been used to make Nano suspensions with diameters ranging from 10 to 100 nm. [84]

Table 19: Solubility enhancement of poorly water soluble drug by using Supercritical fluid process.

Sr. No.	DRUG	MATERIAL USE
1	Griseofulvin [85]	Menthol solid Cosolvent.

5. Liquisolid methods

Drug absorption and adsorption occur when a liquid is supplied to a porous carrier material having fibers, such as cellulose. The liquid first absorbs into the particles and is captured by their internal structure. Once saturated, the liquid is adsorbed onto the internal surfaces. Exterior surfaces of the porous carrier particles. A liquid medicine can be turned into a dry, non-adherent and free Flowing, compressible powder is created by combining it with particular powder excipients such as the carrier and coating substance. Coating materials include both microcrystalline and amorphous cellulose, as well as silica particles. [86,87]

Advantages

-Used in the manufacture of liquid and oil-based medicines.
-Drug release can be modified using several carriers and additives, including PVP, PEG 6000, hydroxypropyl methylcellulose
-It enhances the bioavailability and solubility of water-insoluble drugs when taken orally.
-This technology is specifically developed to handle powdered liquid medicines. [88]

Disadvantages

-It is not suited to big doses of insoluble medicines (more than 100 mg).
-It requires recipients with strong adsorption and specific surface area characteristics. [89].

Table 20: Solubility enhancement of poorly water soluble drug by using Liquisolid methods.

Sr. No.	DRUG	MATERIAL USE
2	Rifampicin [90]	Vicel PH 102 as carrier material and Aerosil 200 as coating material. PEG 400, PG and Polysorbate 80
3	Ritonavir [91]	Transcutol HP,labrasol,labrafil

6 CONCLUSION

Drug dissolution determines the rate of oral absorption of weakly water-soluble drugs, as solubility is required for absorption from the GI tract. Formulation scientists must address the challenge of solubility. To improve the solubility of drugs, the different approaches outlined above can be employed either alone or in combination. Choosing the best solubility enhancement strategy is vital for meeting the goals of a successful formulation, having good oral bioavailability, decreased dose frequency, and enhanced patient compliance, maintaining a low production cost. Inclusion complex creation, supercritical fluid, cryogenics, and Nano-suspension .The most appealing approaches to choose from the different solubility choices when it comes to conquer the solubility Problem with hydrophobic medicines. Solubility enhancement methods are heavily influenced by drug properties such as solubility, chemical nature, melting point, absorption site, physical nature, and pharmacokinetic behaviour. Additionally, dosage form requirements such as tablet or capsule formulation, strength, and immediate or modified release also play a significant role. This Overall, the analysis concludes that the solubility of each molecule is critical and has a significant impact on the development of Pharmaceutical formulation.

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