A Review On Enhancement Solubility Techniques

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Abstract: Solubility is the phenomenon of dissolution of solids in the liquid phase to give a homogeneous system. Solubility is one of the parameters to achieve the desired concentration of drug in systemic circulation for pharmacology response to be shown. Poorly water soluble drugs often require high doses to reach therapeutic plasma concentration after oral administration. Low aqueous solubility is the major problem encountered with formulation development of new chemical entities. The solubility is the most important concept presenting itself as a variable contributor in the formulation of pharmaceuticals. The usable pharmaceuticals with poor solubility means be answered well by solubilization techniques such as chemical modification which involves the use of solubilizer such as physical modification complexation use of surfactant.

The purpose of the review article is to describe the techniques of solubilization for attainment of effective absorption and improved bioavailability.

Keywords: Solubility, Solubility Enhancement, Bioavailability, Co-solvent, PH, emulsion.

Introduction

The term ‘Solubility’ is defined as the maximum amount of solute that can be dissolved in a given amount of solvent to form a homogenous system at specified temperature. The solubility of a drug is represented through various concentration expressions such as parts, percentage, molarity, molality, mole fraction. Drug solubility is the maximum concentration of the drug solute dissolved in the solvent under specific condition of temperature, pH and pressure. The drug solubility in saturated solution is a static property where as the drug dissolution rate is a dynamic property that relates more closely to the bioavailability rate [1]. The solubility of a drug is described in various descriptive terms which is based on the amount of drug dissolved in solvent.

Table 1: Definitions of Solubility

<table>
<thead>
<tr>
<th>Descriptive terms</th>
<th>Approximate volume of solvent in milliliters per gram of solute</th>
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<tbody>
<tr>
<td>Very soluble</td>
<td>Less than 1</td>
</tr>
<tr>
<td>Freely soluble</td>
<td>From 1 to 10</td>
</tr>
<tr>
<td>Soluble</td>
<td>From 10 to 30</td>
</tr>
<tr>
<td>Sparingly soluble</td>
<td>From 30 to 100</td>
</tr>
<tr>
<td>Slightly soluble</td>
<td>From 100 to 1000</td>
</tr>
<tr>
<td>Very slightly soluble</td>
<td>From 1000 to 10,000</td>
</tr>
<tr>
<td>Insoluble</td>
<td>More than 10,000</td>
</tr>
</tbody>
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Need and Objectives of Solubility Enhancement

Drug absorption from the GI tract can be limited by a variety of factors most significant contributor being poor aqueous solubility and poor membrane permeability of the drugmolecule. When administered an active agent orally it must first dissolve in gastric and/or intestinal fluids before it can permeate the membranes of the GIT to reach systemic circulation. Hence, two areas of pharmaceutical research that focus on improving the oral bioavailability of active agents include; enhancing of solubility and dissolution rate of poorly water soluble drugs. The BCS is a scientific framework for classifying a drug substance based on its aqueous solubility and intestinal permeability. As for BCS class II & IV drugs rate limiting step is drugrelease from the dosage form and solubility in gastric fluid and not the absorption, so increasingthe solubility in turn increase the bioavailability for BCS class II & IV drugs [3]. BCS Classification System with examples of different drug is discussed in Table-2

<table>
<thead>
<tr>
<th>BCS Class</th>
<th>Solubility</th>
<th>Permeability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Class II</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Class III</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Class IV</td>
<td>Low</td>
<td>Low</td>
</tr>
</tbody>
</table>

Importance of Solubility

Solubility also has a significant impact on other dosage forms such as parenteral formulations. Solubility is one of the most significant aspects of achieving the required drug concentration in the systemic circulation and the required pharmacological response. After oral administration poorly water-soluble medications sometimes require considerable dosages to attain therapeutic plasma levels. Low water solubility is the fundamental problem with formulating novel chemical entities and developing genetic material liquid medicinal compositions water is the ideal solvent. This is because it allows for the presence of any substance that needs to be absorbed at the absorption site in the form of an aqueous solution [9]. Most medications have poor aqueous solubility and are either weakly basic or mildly acidic.

Review Literature

1) S. K. Leticia et al.108 compared carbamazepine (CBZ) solid dispersions prepared by spray drying of aqueous dispersions with the corresponding physical mixtures. The influence of the association of p-CD and HPMC on the CBZ dissolution profile of the preparations was investigated. Results demonstrated that CBZ release from solid dispersions is dependent on theratio of p-CD and HPMC. The spray-drying process

2) M. S. Nagasaki et al.110 described the formulation of solid dispersions of ketorolac using HP (3-CD and P-CD as carriers, to improve the aqueous solubility of the drug, thus enhancing its bioavailability. DSC and XRD studies indicated loss of crystalline nature of the drug, in the dispersions prepared with HP P-CD, NMR studies revealed a strong interaction between drug and HP P-CD. Solid dispersions of the drug with P-CD retained the crystalline nature of the drug. HP P-CD proved to be BCS-IV, as a carrier in the kneaded dispersion prepared using 1:1 alcohol water mixture.

3) I. Corrigan et al.109 prepared successfully hydrocortisone-PVP composites using the supercritical fluid gas anti solvent method (GAS). Analysis by DSC and powder XRD indicated that these systems were more crystalline than corresponding systems prepared by spray drying. These composites prepared by the GAS method were more similar in physicochemical properties to co-precipitates prepared by conventional solvent evaporation. However, they have dissolution rates lower than those of corresponding systems prepared by the other processing methods but equivalent to those of corresponding physical mixtures.

4) H. H. Yoshii et al.107 prepared inclusion complexes of d-limonene, phenyl ethanol, aceto phenone, or methanol in a slurry form a-, p- and y-cyclohexatriene in organic solvents or alcohol under anhydrous conditions. Ethanol and methanol were found to be good solvents forthis method. There existed an optimal amount of ethanol for the maximum inclusion of d- limonene as a guest compound. However, an excess ethanol inhibited the inclusion. An adsorption model of alcohol on cyclohexatriene, analogous to the substrate inhibition model of enzymes kinetics to correct the inclusion ratio with the amount of alcohol added to cyclohexatriene.

5) E. Alvarez-parrilla et al.105 studied the effect of electrostatic interactions on the complexation of ionic guests by charged P-cyclodextrin derivative. Special attention is paid to the numerous studies concerning the effect of electrostatic interactions on the complexation offluorescent and UV probes; the catalytic and chiral recognition properties of P-cyclodextrin derivatives; the complexation of two bile salts (sodium cholate, NaC, and sodium deoxycholate, NaDC). The formation of three in one complexes between NaC and Alkyl diamino P-cyclodextrin derivatives is also presented.

6) V. R. Sinha et al.104 prepared inclusion complexes of celecoxib with -cycloextrin in solution and solid state. Complexes were prepared by spray drying while physical mixtures were obtained by simple blending and characterized by IR, X-ray diffraction and NMR spectroscopy, SEM, DSC and polarimetry. Dissolution study showed that celecoxib entrapped in spray dried complexes dissolved much faster than pure drug and physical mixtures.
7) A. H. Al-marzouqi et al.103 studied the complex formation of Itraconazole (ITR), an antifungal agent with P-Cyclohexatriene (P-CD) which showed an improvement in the tet solubility of drug in aqueous solution. Drug formulations of Itraconazole were prepared by complexation of drug into P-cyclodextrin using super critical carbon dioxide (SCCO2). The formation of an inclusion complex in SCCO2 method was verified by UV spectroscopy, P- XRD and SEM analysis and compared to those obtained by physical mixing and co-precipitation method.

8) K. Uekama et al.102 studied the complex formation of diltiazem, which is freely soluble in water and having a short half-life with P-Cyclodextrin derivatives such as Diethyl- P- Cyclohexatriene, Triethyl P-Cyclodextrin. The solid complexes of diltiazem with diethyl-and triethyl- P-Cyclodextrin in (1:1 M) were prepared by kneading method. Pharmacokinetic parameters CEMEX, Tmax, AUC, MRT, VRT were measured following oral administration of tablets of drug alone and its ethylated P-Cyclodextrin complexes to five rats. It was concluded that diethyl- P-Cyclodextrin complex may be a candidate for the sustained release of diltiazem.

9) T. Ikeda et al.96 investigated the inclusion complex formation between cyclodextrin and autoinducer of bacteria in aqueous solution by ID 1H-NMR and ROESY spectra. An inhibition effect was observed on autoinducer activities of quorum sensing in Pseudomonas aeruginosa by adding cyclodextrin to the bacterial culture medium.

10) A. Usayapant et al.95 studied the effects of 2-hydroxypropyl-P-cyclodextrin (HPCD) on drug solubility and drug release from suppository bases for dexamethasone (DX), dexamethasone acetate (DXA), hydrocortisone (HC), hydrocortisone acetate (HCA), and prednisolone acetate (PNA). It was found that HPCD significantly increased the aqueous solubility of all five steroids, and the increased drug solubility significantly influenced the drug release from the polyethylene glycol (PEG) base but not from the cocoa butter base.

Techniques for Solubility Enhancement
When the solubility of substances in aqueous media is limited, formulation strategies are required early on in the drug discovery and they remain of critical importance for lead substance selection and commercial drug product development.

Various techniques have been used in attempt to improve solubility and dissolution rates of poorly water soluble drugs which include as following:

a) Particle Size Reduction
   - Micronization
   - Nanonization

b) Cosolvency

c) Hydrotropy

d) pH Adjustment

e) Sonocrystallization

f) Supercritical Fluid (SCF) Process

g) Solid Dispersion
   - Fusion Method
   - Solvent Method
   - Fusion Solvent Method
   - Spray Drying
   - Lyophilization (Spray Freeze Drying Method)
   - Dropping Method

h) Inclusion Complexation

i) Self-Emulsifying or Self-Micro Emulsifying Systems

j) Liquisolid Methods

In these techniques carrier plays an important role in improving solubility and dissolution rate. Polymers, super disintegrants, surfactants are extensively studied in recent years for dissolution enhancement in drugs. This part of this I review discusses technological overview and effect of polymers, super disintegrants and surfactants on dissolution enhancement of drugs while describes the role and applications of cyclodextrins, carbohydrates, hydrotropes, dendrimers, acids and miscellaneous carriers in enhancing dissolution of drug

a) Particle Size Reduction

The drug solubility depends on its particle size. Large particles provide a low surface area, which results in less interaction of particles with the solvent. One of the methods to increase the drug’s surface area is to reduce its particle size, which improves its dissolution property. Conventional methods of particle size reduction, such as comminution and spray drying, rely upon mechanical stress to disaggregate the active compound. Particle size reduction is thus
permitting an efficient, reproducible, and economic means of solubility enhancement. However, the mechanical forces inherent to comminution, such as milling and grinding, often impart significant amounts of physical stress upon the drug product which may induce degradation. The thermal stress which may occur during comminution and spray drying is also a concern when processing thermo-sensitive or unstable active compounds. Using traditional approaches for nearly insoluble drugs may not be able to enhance the solubility up to desired levels. To increase the therapeutic efficacy of medications in dose form, solid dispersion is a fully pharmaceutical approach.

- **Micronization**

  **Fig 1**

  Micronization is another conventional technique for particle size reduction. Micronization increases the dissolution rate of drugs through increased surface area, but does not increase equilibrium solubility. Decreasing the particle size of these drugs, which cause increase in surface area, improves their rate of dissolution. Micronization of drugs is done by milling techniques using jet mill, rotor stator colloid mills and so forth. Micronization is not suitable for drugs having a high dose number because it does not change the saturation solubility of the drug. These processes were applied to griseofulvin, progesterone, spironolactone diosmin, and fenofibrate. For each drug, micronization improved their digestive absorption, and consequently their bioavailability and clinical efficacy. Micronized fenofibrate exhibited more than 10-fold (1.3% to 20%) increase in dissolution in at 30 minutes biorelevant media.

- **Nanonization**

  Recently, various nanonization strategies have emerged to increase the dissolution rates and bioavailability of numerous drugs that are poorly soluble in water. Nanonization broadly refers to the study and use of materials and structures at the nanoscale level of approximately 100 nm or less. Nanonization can result in improved drug solubility and pharmacokinetics, and it might also decrease systemic side-effects. For many new chemical entities with very low solubility, oral bioavailability enhancement by micronization is not sufficient because the micronized product has the tendency to agglomerate, which leads to a decrease in effective surface area for dissolution. The next step is nanonization. There are different techniques used for nanonization of drug including wet milling, homogenization, emulsification-solvent evaporation technique, Pear milling, Spray drying etc. There are many examples of nanonization of drugs.
b) Cosolvency

Fig no 1.1
The solubility of poorly soluble drugs in water can be increased by mixing it with some water miscible solvent in which the drug is readily soluble. This process is known as co-solvency and the solvent used in combination are known as cosolvent. Co-solvent system works by reducing the interfacial tension between the aqueous solution and hydrophobic solute. The cosolvents are having hydrogen acceptor or donor groups with a small hydrocarbon region. The hydrophobic hydrocarbon region usually interferes with the hydrogen bonding network of water which consequently reduces the intermolecular attraction of water while the hydrophilic hydrogen bonds ensures water solubility.

Fig no 2
c) **Hydrography**

This is a solubility sensation; using it, the water solubility of the solute can be enhanced by the excess addition of a second solute. The term hydrotrophy was used in earlier reports to describe non-micelle-forming materials, either solids or liquids, organic or inorganic, which are proficient in improving solubility of insoluble substances.

d) **pH Adjustment**

Poor water soluble drug may potentially dissolve in water by applying a pH change. To access the solubility of this approach, the buffer capacity and tolerability of the selected pH are important to consider. Solubilized excipients that increase environmental pH within the dosage form to a range higher than pKa of weekly acidic drugs increase the solubility of that drug; those excipients that act as alkalinizing agents may increase the solubility of weekly basic drugs.

e) **Sonocrystallization**

Recrystallization of poorly soluble materials using liquid solvents and antisolvents has also been employed successfully to reduce particle size. The novel approach for particle size reduction on the basis of crystallization by using ultrasound is Sonocrystallisation. Sonocrystallisation utilizes ultrasound power characterized by a frequency range of 20-100kHz for inducing crystallization. It’s not only enhances the nucleation rate but also an effective means of size reduction and controlling size distribution of the active pharmaceutical ingredients. Most applications use ultrasound in the range 20 kHz-5 MHz.

![Fig no.3](image-url)
### f) Supercritical fluid (ScF) Process

Supercritical fluid technology was employed for the first time industrially in the early 1980s in the pharmaceutical sector. During that period, SCF technology was used by pharmaceutical industries for developing pharmaceutical materials through crystallization and precipitation. The SCF method is safe, eco-friendly, and cost-effective. The low operational parameters (pressure and temperature) make SCFs attractive for pharma research. An SCF survives as a single phase above its critical pressure (Pc) and temperature (Tc). SCFs have properties useful to product processing because they are intermediate between those of pure liquid and gas (i.e., liquid-like density, gas-like compressibility and viscosity and higher diffusivity than liquids). Moreover, the density, transport properties (such as viscosity and diffusivity), and other physical properties (such as dielectric constant and polarity) vary considerably with small changes in operating temperature, pressure, or both around the critical points. Hence, it is possible to fine-tune a unique combination of properties necessary for a desired application.

These unique processing capabilities of SCFs, long recognized and applied in the food industry, have recently been adapted to pharmaceutical processes. Commonly used supercritical solvents include carbon dioxide, nitrous oxide, ethylene, propylene, propane, n-pentane, ethanol, ammonia, and water. Once the drug particles are solubilized within SCF, they may be recrystallized at greatly reduced particle sizes. The flexibility and precision offered by SCF processes allows micronization of drug particles within narrow ranges of particle size, often to sub-micron levels. Current SCF processes have demonstrated the ability to create nano suspensions of particles 5-2,000 nm in diameter. Several pharmaceutical companies, such as Nectar Therapeutics and Lavisher, are specializing in particle engineering via SCF technologies for particle size reduction and solubility enhancement [18, 19]. Several methods of SCF processing have been developed to address individual aspects of these shortcomings, such as precipitation with compressed antisolvent processes (PCA). Rapid Expansion of Supercritical Solutions, Gas Antisolvent Recrystallization, Precipitation with Compressed Fluid Antisolvent, Impregnation or infusion of polymers with bioactive materials, Solution enhanced Dispersion by Supercritical Fluid, solution enhanced dispersion SCF (SEDS), supercritical AntisolventSolid Dispersion Solid dispersion is defined as a dispersion of one or more active ingredients in an inert carrier or matrix at solid state. In solid dispersion technique poorly water soluble drugs is dispersed in highly soluble solid hydrophilic matrix which enhance the dissolution of the drug and can yield molecular level mixing (solid solution) and non-molecular level mixing(eutectic product). eg. PEG 4000 increases the rate of dissolution. Concept of SD was originally proposed by Sekiguchi and Obi who investigate the generation and dissolution performance of eutectic melts of sulfonamide drugs and water soluble carrier in early 1960. SD is most promising aspects and simplicity of concept it has failed to get the popularity due to manufacturing, stability and scale up issues Solubility of the Griseofulvin, Keto profen, aceclofenac, oxacarbazepine, Albendazole, Biforanazole, is induced by SD technique. Various techniques to prepare the solid dispersion of hydrophobic drugs with an aim to improve their aqueous solubility are listed here.

#### Fusion method:
- Traditional methods
  - solution
  - suspension
- Optimized methods
  - hot stage extrusion
  - melt agglomeration
- Solvent evaporation method-co-precipitation
  - N2 steam
- Freeze drying
- SCF

Methods of preparation of solid dispersion

Solvent evaporation method

![Diagram of Solvent evaporation method]

- **Fusion Method**
  
  In the fusion method of preparation, the carrier is heated to a temperature just above its melting point and the drug is incorporated into the matrix. The mixture is cooled with constant stirring to homogeneously disperse the drug throughout the matrix. Several mechanisms could operate during the process of dispersion. If the drug has a high degree of solubility in the carrier, the drug could remain “dissolved” in the solid state, yielding what is known as a solid solution. Particle size reduction under these conditions proceeds to the ultimate level leading to molecular dispersion of the drug in the carrier matrix. These systems show very high drug dissolution rates compared to control samples. If, on the other hand, the solubility of the drug in solid state is not so high, crystallites of the drug become dispersed in the matrix. Such systems show only moderate increases in dissolution rates. A third mechanism is the conversion of a drug to an amorphous form in the presence of the matrix, again exhibiting different dissolution rates and solubility. Other factors that may play a role include solubilizing effect conferred by the carrier itself, improved wetting decreased surface hydrophobicity, complexation, and crystallization of the drug in a metastable polymorphic form of alter thermodynamic properties.
Solvent Method

In this method first dissolve both the active drug and the carrier in a common solvent and then evaporate the solvent under vacuum to produce a solid solution. This enabled them to produce a solid solution of the highly lipophilic R-carotene in the highly water soluble carrier polyvinyl pyrrolidone. Many investigators studied solid dispersion of meloxicam, naproxen and nimesulide using solvent evaporation technique. [39] This technique increases solubility and stability of solid dispersions of hydrophobic drugs. The main advantage of the solvent method is that thermal decomposition of drugs or carriers can be prevented because of the low temperature required for the evaporation of organic solvents.
Fusion-Solvent Method
In the fusion methods, a carrier(s) is/are melted and the drug(s) is / are incorporated in the form of a solution. If the carrier is capable of holding a certain proportion of liquid yet maintaining its solid properties, and if the liquid is innocuous, the need for solvent removal is eliminated. Otherwise, this method faces the same criticism of solvent retention described before. This method is particularly useful for drugs that have high melting points or that are thermolabile. The feasibility of the method has been demonstrated for spironolactone and griseofulvin dispersions in polyethylene glycol 6000.

Spray Drying
In this type of preparation, the carrier and the active ingredient are dissolved or suspended in a suitable solvent. This solvent is evaporated by drying it to apply a stream of heated air to remove the solvent. Due to the large surface area of the droplets, the solvent rapidly evaporates and solid dispersion is formed quickly.

Lyophilization (Spray Freeze Drying Method)
This method is used to avoid the heating during the preparation of thermosensitive drugs; spray freeze drying (SFD) has been successfully developed to prepare solid dispersions at ambient temperature, which was made significant development by the research work of William III. SFD technology involves the atomization of a feed liquid containing poorly water-soluble or insoluble APIs and excipients directly into a cryogenic liquid at ambient temperature to produce a frozen micronized powder that is subsequently dried. This process offers a variety of advantages compared to traditional technologies for solid dispersions, including amorphous structure and high surface area.

Dropping Method
A solid dispersion of a melted drug carrier mixture is pipetted then dropped onto a plate, where it solidifies into round particles. The size, shape of the particles can be influenced by factors such as the viscosity of the melt and the size of the pipette. As viscosity is highly temperature dependent, it is very important to adjust the temperature so that when the melt is dropped on the plate it solidifies to a spherical shape.

g) Inclusion Complexation
The aqueous solubility, dissolution rate, and bioavailability of medications that are only mildly water-soluble have been improved more successfully than any other solubility augmentation techniques. These are created when nonpolar molecules cannot dissolve into the area of another molecule, most frequently Cyclodextrin. Cyclodextrins are the host molecules that are used most frequently. Inclusion complexes are created when a nonpolar molecule, or a nonpolar component of a molecule is incorporated into the cavity of a different molecule or group of molecules, known as the host. Various techniques are used to prepare for making inclusion complexes of very soluble drugs with an aim to improve their aqueous solubility are listed here.
Fig no 8

a) Kneading
The method involves the formation of paste of cyclodextrin with guest molecules by using a small quantity of either water or ethanol to form kneaded mass. Kneaded mass can be dried at 45 °C and pulverized.

b) Melting
Excess quantity of guest is melted, mixed with powdered Cyclodextrin, after cooling excess quantity of guest is removed by washing with weak complex forming solvent. The method is restricted to sublimable guest like menthol.

c) Co-evaporation/Solvent evaporation method
To the alcoholic solution of guest, aqueous solution of host is added and stirred for sometimes and evaporated at room temp until dry. The final mass obtained is pulverized and sieved and fraction is collected.

d) Microwave Irradiation
This method is developed for rapid organic synthesis and reactions, which require shorter reaction time and higher aim product.

e) Freeze Drying/Lyophilization technique
The required stoichiometric quantity of host and guest were added to aqueous solution of cyclodextrin and this suspension stirred magnetically for 24 hours, and resulting mixture is freeze dried at 60 °C for 24 hours.

f) Spray drying/Atomization
In this method, host solution prepared generally in ethanol: water 50% v/v. To this guest is added and resulting mixture is stirred for 24 hr. at room temperature and solution is spray dried by observing following conditions-air flow rate, atomizing air pressure, inlet temperature, outlet temperature, flow rate of solution etc. Product obtained by passing through 63-160 micrometer granulomere sieve.

g) Self-Emulsifying or Self-Micro Emulsifying System
Self-emulsifying or self-micro emulsifying systems use the concept of in situ formations of emulsion in the Gastrointestinal tract. The mixture of oil, surfactant, co-surfactant, one or more hydrophilic Solvents, and co-solvent forms a transparent isotropic solution that is known as the self-emulsifying drug delivery system (SEDDS). The absence of external phase (water) and forms fine o/w emulsions or micro-emulsions spontaneously upon dilution by the aqueous phase in the GIT and is used for improving Lipophilic drug dissolution and absorption. The ease of emulsification could be associated with the ease of water penetrating the various liquids crystalline or gel phases formed on the surface of the droplet. One of the advantages of SEDDS about scale-up and manufacture is that they form spontaneously upon mixing their components under mild agitation and they are thermodynamically stable. The drawbacks of this system include chemical instabilities of Drugs and high surfactant concentration. The large quantity of surfactant in self-emulsifying formulations (30-60%) irritates GIT. Most self-emulsifying systems are limited to Administration in lipid-filled soft or hard-shelled gelatin capsules due to the liquid nature of the product. Interaction between the capsule shell and the emulsion should be considered to prevent the hygroscopic
contents from dehydrating or migrating into the capsule shell.

h) **Liquisolid Methods**

When the drug dissolved in the liquid vehicle is incorporated into a carrier material which has a porous surface and closely Matt fiber in its interior as cellulose, both absorption and Adsorption take place; i.e., the liquid initially absorbed in the Interior of the particles is captured by its internal structure, and after the saturation of this process, adsorption of the liquid Onto the internal and external surfaces of the porous carrier particles occur. Then, the coating agent having high Adsorptive properties and large specific surface area gives the Liquisolid system the desirable flow characteristics. Liquisolid Solid system is acceptably flowing and compressible powdered forms of liquid medications. In the concept of Liquisolid System, liquid drugs having low aqueous solubility dissolved in suitable non-volatile solvents, converted into radially compressible powder by simple admixture with selected powdered excipients referred as carrier and coating materials. Microcrystalline and amorphous cellulose and silica powders may be used as coating materials.
Conclusion
Solubility is the most important physical characteristic of a drug for its oral bioavailability. Formulation, development of different dosage forms of different drugs, the therapeutic efficacy of the drug, and for quantitative analysis. Dissolution of drugs is the rate determining step for oral absorption of the poorly water-soluble drugs and solubility is also the basic requirement for the formulation and development of different dosage forms of different drugs. The various techniques described above alone or in combination can be used to enhance the solubility of the drug. Solubility can be enhanced by many techniques and the number of folds increase insolubility. Because of the solubility problem of many drugs, the bioavailability of them gets affected and hence solubility enhancement becomes necessary. It is now possible to increase the solubility of poorly soluble drugs with the help of various techniques as mentioned above.

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