The term ‘solubility’ is defined as an excess amount of solute that can be incorporated in a given amount of solvent. It can also be defined quantitatively as well as qualitatively. Quantitatively it is the concentration of the solute in a saturated solution at a certain temperature. In qualitative terms, solubility is the spontaneous interaction of two or more substances to form a homogenous molecular dispersion. A saturated solution is one in which the solute is in equilibrium with the solvent. Solubility has a number of concentration expressions like parts, percentage, molarity, molality, volume fraction and mole fraction (1).

In recent years, a large number of drugs have been developed but nearly 70% of new drugs have poor water solubility. Major part of human body is made up of water. Therefore, drugs must be having certain aqueous solubility. The solubility of drugs ultimately has strong impact on their bioavailability (2, 3). Poorly water soluble drugs are eliminated from gastrointestinal tract before their dissolution that results in low bioavailability and reduced clinical effects.

APPLICATION OF VARIOUS POLYMERS AND POLYMERS BASED TECHNIQUES USED TO IMPROVE SOLUBILITY OF POORLY WATER SOLUBLE DRUGS: A REVIEW

RAI MUHAMMAD SARFRAZ1*, SAJID BASHIR1, ASIF MAHMOOD1, HASEEB AHSAN3, HUMAYUN RIAZ1, HINA RAZA1, ZERMINA RASHID1, SYED ATIF RAZA1, MUHAMMAD ASAD ABRAR1, KHAWAR ABBAS7 and TAHIRA YASMEEN8

1Faculty of Pharmacy, University of Sargodha, Sargodha, Pakistan
2Institute of Pharmacy, Physiology and Pharmacology, University of Agriculture, Faisalabad, Pakistan
3Rashid Latif College of Pharmacy, Ferozpur Road, Lahore, Pakistan
4Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan
5Punjab University College of Pharmacy, University of the Punjab, Lahore, Pakistan
6Faculty of Pharmacy, The Islamia University Bahawalpur, Punjab, Pakistan
7University College of Conventional Medicine, The Islamia University Bahawalpur, Pakistan
8The Children’s Hospital and Institute of Child Health, Lahore, Pakistan

Abstract: Solubility is concerned with solute and solvent to form a homogenous mixture. If solubility of a drug is low, then usually it is difficult to achieve desired therapeutic level of drug. Most of the newly developed entities have solubility problems and encounter difficulty in dissolution. Basic aim of solubility enhancement is to achieve desired therapeutic level of drug to produce required pharmacological response. Different techniques are being used to enhance the solubility of water insoluble drugs. These techniques include particle size reduction, spray drying, kneading method, solvent evaporation method, salt formation, microemulsions, co-solvency, hydrosols, prodrug approach, supercritical fluid process, hydrogel micro particles etc. Selection of solubility improving method depends on drug properties, site of absorption, and required dosage form characteristics. Variety of polymers are also used to enhance solubility of these drugs like polyethylene glycol 300, polyvinyl pyrrolidone, chitosan, β-cyclodextrins etc.

Keywords: polymers, solubility, hydrogel microparticles, hydrosols, techniques

* Corresponding author: e-mail: sarfrazra85@yahoo.com; phone: +923338976189
According to Biopharmaceutics Classification (BCS), all the drugs have been divided into four classes: class I - high soluble and high permeable, class II - low soluble and high permeable, class III - low soluble and high permeable and class IV - low soluble and low permeable as shown in Figure 1 (7).

Drugs belonging to Class II under BCS have low and variable oral bioavailability due to their poor aqueous solubility as shown in Table 1.

There are a number of methods for enhancing dissolution rate of poorly water-soluble drugs including: reducing particle size to increase surface area, thus increasing the dissolution rate of drug (8), solubilization in surfactant systems (9, 10) formation of water-soluble complexes (11), drug derivatization such as strong electrolyte salt forms that usually have higher dissolution rate (12-17), producing liquisolid formulations - manipulation of the solid state of a drug substance to enhance drug dissolution e.g., by decreasing crystallinity of the drug substance through formation of solid solutions (18) and solid dispersion formulations (19-22).

Variety of carriers have been used in previously discussed technologies to promote solubility enhancement of poorly water soluble drugs (23-25). These include: polyethylene glycols, polyvinyl pyrrolidone, lactose, chitosan, β-cyclodextrin and hydroxypropyl methylcellulose which are most commonly used enhancers (26-29). Nowadays, poloxamers, a group of block copolymer nonionic surfactants, have also been used for this purpose in various techniques (30, 31). These carriers have strong effect on major parameters of drugs like to enhance solubility, dissolution and bioavailability of many hydrophobic drugs making them suitable chemical moieties (32). Hydrotopes have also been employed to increase aqueous solubility of poorly soluble drugs. In many cases, the aqueous solubility of poorly soluble drugs has been increased by 2-4 orders of magnitude simply by mixing with hydrotopes in water (33, 34). Despite this advantage, application of low molecular weight hydrotopes in drug delivery has not been practical, because it may result in absorption of a significant amount of hydrotopes themselves into the body along with the drug. One approach to prevent absorption of hydrotopes along with drug e.g., from the gastrointestinal tract after oral administration, is to make polymeric hydrotopic agents (hydrotopic polymers). Hydrotopic polymers are

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**Table 1. United States Pharmacopoeia and British Pharmacopoeia solubility criteria.**

<table>
<thead>
<tr>
<th>Descriptive term</th>
<th>Part of solvent required per part of solute</th>
</tr>
</thead>
<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>Practically insoluble</td>
<td>10,000 and over</td>
</tr>
</tbody>
</table>
expected to provide an alternative approach for increasing aqueous solubility of poorly soluble drugs (35-37).

**Techniques used for solubility enhancement**

Different solubility enhancement techniques are used that can be categorized into physical modifications, chemical modifications of the drug substance and other techniques.

*Physical modifications*

Particle size reduction like micronization and nanosuspension, drug dispersion in carriers like eutectic mixtures, solid dispersions, solid solutions and cryogenic techniques.

*Chemical modifications*

Change of pH, use of buffer, derivatization, complexation and salt formation.

*Miscellaneous methods*

Supercritical fluid process, use of adjuvant like surfactant, solubilizes, cosolvency and hydrotrophy.

*Particle size reduction*

Solubility of majority of drugs is linked with particle size. The smaller particle size, the greater surface area will be exposed to solvent resulting in increased solubility. Conventional methods like milling, grinding and spray drying use mechanical forces to break active part of the drugs that mostly results in degradation of the product. Particle size reduction is thus providing an effective, reproducible and economic mean of solubility improvement. Thermo sensitive drugs are also degraded when these are operated through comminution and spray drying. The application of these conventional approaches for poorly water soluble drugs may not be capable to enhance the solubility up to anticipated level (38).

In recent past, large number of studies was conducted in order to improve solubility of drugs through particle size reduction technique. The particle size reduction method for improving bioavailability of danazol in beagle dogs was conducted. Liversidge et al. determined bioavailabilities of three types of formulations like nanosuspension, nanoparticles and cyclodextrin complexes. The solubility of drug was markedly increased as compared to its actual solubility (39).

Another study was conducted on solubility enhancement by size reduction method for norethindrone. Bansal et al. compared their prepared tablets with the market brand of the same drug. Particle size was reduced within range 1-10 microns. It was observed that there was clearly improvement in dissolution and bioavailability in particle size reduced formulation (40). Work was also performed on dissolution enhancement of piroxicam by two micronization methods i.e., solvent change and pH shift. Dissolution was improved 3-4 folds by both of these methods. The studies proved that microcrystallization method is better for modification in crystal habit or structure (41).

Simvastatin nanosuspensions were prepared for enhanced dissolution and solubility. An increase in intrinsic dissolution and surface area was observed in these studies. Studies proved that nanoparticles are a good approach for enhancing solubility (42).

*Spray drying*

In spray drying, drug particles are suspended in air trapped in a chamber and are continuously sprayed by the volatile liquid in order to bring uniformity and enhance dissolution rate of the target product. Studies were conducted to enhance dissolution of fenofibrate by three techniques i.e., micronization, co-grinding and spray drying. Spray drying and co-grinding were found to be powerful techniques for enhancing solubility of fenofibrate oral products (43).

PVP-K30 and PVP-VA64 polymers were used to prepare solid dispersions of loperamide by spray drying. Phase behavior analysis of solid dispersions has been studied. There was an increase in solubility of drug through solid dispersions prepared by spray drying technique (44). Itraconazole and polyvidone-vinyl acetate 64 (PVPVA 64) were used as model drug to improve dissolution through spray drying. Due to good solubilizing and wetting properties, polyethylene glycol 6000 (PEG 6000) was added. Forty percent rise in dissolution was observed in this study (45). Nanocrystals of nifedipine were prepared by spray drying technique. Marked increase in solubility of nanocrystals was seen when compared to the marketed brand (46). Inclusion complexes of acetaminophen, indomethacin, piroxicam and warfarin were prepared with β-cyclodextrin to see solubility patterns by spray drying. Dissolution rates of drugs prepared by spray drying were faster as compared to physical mixtures of the drugs and polymers (47).

*Inclusion complexes*

*Kneading method*

In kneading method, drug and polymers are triturated in pestle and mortar by the dropwise addi-
tion of liquid which may be water or hydro alcoholic mixture, resulting in formation of slurry and reduction of particle size resulting in enhanced bioavailability due to kneading. Then, kneaded mixture is dried and passed through mesh, if required, to bring uniformity in contents (48).

Satranidazole β-cyclodextrin inclusion complexes were prepared by kneading method. After the detailed study of this complexation, it was observed that marked increase in solubility was seen (49). Nikhil et al. prepared inclusion complexes of acyclovir by kneading method in distilled water. PEG 6000 and PVP K30 were used as polymers. They also compared inclusion complexes prepared by kneading method as well as solid dispersion method. Inclusion complexes prepared by kneading technique were found good in all aspects (50).

In other study, inclusion complexes of olmesartan medoxomil were prepared by kneading method and incorporated into mouth dissolving tablets. Complexation resulted in improved dissolution and solubility and improved mechanical stability of tablets was seen (51). Alves et al. prepared solid dispersions of efavirenz in PVP K-30 by two methods i.e., kneading and conventional solvent method. These were characterized by DSC, FT-IR, SEM, XRD and dissolution. Solid dispersions prepared by kneading method have shown higher dissolution rates (52). Patel prepared etoricoxib-β-cyclodextrin complexes by kneading method. Phase solubility studies were performed for each substance to build phase solubility diagram. Marked increase in solubility was observed by inclusion complexes from this method (53). Nimesulide dissolution can be enhanced by using complexation through kneading method (54).

Solid dispersions

Solvent evaporation method

In this technique, drug and carrier are dissolved in separate miscible solvents and then evaporation is done under vacuum to yield a solid solution. Many researchers have studied solid dispersion of meloxicam, naproxen and nimesulide using solvent evaporation technique. Dissolution study revealed that the modified solvent evaporation is the most convenient and effective method for solubility enhancement of poorly water soluble drugs, among various methods of preparation of solid dispersions (55).

PEG 6000 was used as hydrophilic carrier and solvent evaporation as method of preparation of solid dispersions of atenolol. Dissolution studies have been carried to determine drug concentration against time. The study revealed that dissolution was greatly increased (56). Islam et al. made solid dispersions of gliclazide by solvent evaporation technique. They observed solid dis-

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand Name</th>
<th>Company Name</th>
<th>Polymer Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Griseofulvin</td>
<td>Griseofulvin tablet</td>
<td>Novartis</td>
<td>PEG</td>
</tr>
<tr>
<td>Nabilone</td>
<td>Cesamet</td>
<td>Eli-Lilly and Co.</td>
<td>PVP</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>Kaletra</td>
<td>Abbott Laboratories</td>
<td>PVP-vinyl acetate</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>Spironox</td>
<td>Janssen Pharmaceuticals</td>
<td>Hypromellose</td>
</tr>
<tr>
<td>Etravirine</td>
<td>Intence</td>
<td>Yardley</td>
<td>Microcrystalline cellulose</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug</th>
<th>Polymer</th>
<th>Method</th>
<th>Solvent used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fenofibrate</td>
<td>PEG6000, Poloxamer 407</td>
<td>Melt evaporation, Lyophilization</td>
<td>Chloroform</td>
</tr>
<tr>
<td>Glipizide</td>
<td>PEG6000, mannitol, PVPK30</td>
<td>Fusion (melt) method</td>
<td>Dichloromethane</td>
</tr>
<tr>
<td>Acyclovir</td>
<td>PEG6000, PVPK30</td>
<td>Solvent evaporation method</td>
<td>Methanol</td>
</tr>
<tr>
<td>Valdecoxib</td>
<td>PVP</td>
<td>Kneading</td>
<td>Water</td>
</tr>
<tr>
<td>Flurbiprofen</td>
<td>HPC</td>
<td>Solvent evaporation method</td>
<td>Ethanol</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>PEG6000</td>
<td>Solvent evaporation method</td>
<td>Acetone</td>
</tr>
<tr>
<td>Chlordiazepoxide</td>
<td>PVPK30, mannitol</td>
<td>Co-precipitation method</td>
<td>Ethanol</td>
</tr>
</tbody>
</table>
The solubility of drug was increased (57). Dependent and independent techniques were applied. Poloxamers 407 in their studies. Both model and independent techniques were applied. The solubility of drug was increased (57).

Solid dispersions of allopurinol were prepared by solvent evaporation technique. Polyvinyl pyrrolidone was the polymer applied. Increase in wettability and dissolution rate was observed in the studies along with solubilizing effect of PEG 6000. The formulation prepared by solvent evaporation technique had greater dissolution (58). Frizon et al. prepared solid dispersions of loratadine by solvent evaporation technique. They have used PVP-K13 as carrier. Results have shown an increase in solubility, especially in acid medium, where the drug was protonated, and an enhancement in dissolution profiles was seen (59). Various brands prepared by solid dispersion method are shown in Table 2 and solid dispersions prepared by different methods are shown in Table 3.

Salt formation

The solubility of poorly water soluble drugs has been improved from several years by using salt formation technique. The solubility is also considered as a function of pH. The pH-solubility interrelationships also show which counter ions would be necessary to form salts, how simply the salts may dissociate into their free acid or base forms, what their dissolution behavior would be under different gastrointestinal tract pH conditions, and whether solubility and dissolution rate of salts would be influenced by common ions (60, 61).

Drugs should have specific characteristics for the selection of salt formation technique. The drug for salt formation should have ionizable groups that will assist salt formation. For the selection of counter ion the following criteria are used:

1. The drug and the counter ion should have minimum difference of 2-3 pKa units.
2. Counter ion should decrease crystal lattice forces.
3. It should be FDA approved.

Cheong and Choi prepared piroxicam-ethanolamine salts (PX-EAs) with improved physicochemical properties for transdermal application. Three types of salts were prepared i.e., piroxicam monoethanolamine salt (PX-MEA), piroxicam diethanolamine salt (PX-DEA) and piroxicam triethanolamine salt (PX-TEA). The solubility and permeability of first two salts were higher than the third one (62). Nielsen et al. prepared amorphous sodium salt from a sodium hydroxide-containing aqueous solvent in equimolar amounts of NaOH and furosemide. The structure was confirmed by Fourier transform infrared spectroscopy (FTIR). High solubility was seen in case of amorphous salt form i.e., an 8- and 20-fold higher intrinsic dissolution rate (IDR) when compared to amorphous and crystalline free acid, respectively (63).

Microemulsions

Microemulsions have been used to increase the solubility of many drugs that are poorly soluble in water (64, 65). Microemulsion is an optically clear pre-concentrate containing a mixture of oil, hydrophilic surfactant and hydrophilic solvent which dissolves a poorly water soluble drug. Microemulsions have small and uniform oil droplets containing such drug. Microemulsion is a system containing oil, water and surfactant, frequently in combination with a co-surfactant used in various ratios, with a droplet size usually in the range of 20-200 nm and it is isotropic, thermodynamically stable transparent system. There is another system that is called self microemulsifying drug delivery system (SMEDDS). It is an anhydrous system of microemulsions. It is composed of oil, surfactant and co-surfactant and has the ability to form o/w microemulsion when dispersed in aqueous phase under gentle agitation. The agitation required for the self-emulsification comes from stomach and intestinal motility (66-68). Different nonionic surfactants are used in microemulsions, such as sugar esters like sorbitan monooleate (Span 80), cationic or anionic like alkyltrimethylammonium bromide and sodium dodecyl sulfate, or zwitterion such as phospholipids like lecithin etc. Combinations of ionic and non-ionic surfactants were also found to be effective (69).

Lee et al. prepared o/w microemulsion of aceclofenac to enhance permeability across skin barrier. They have used Labrafil® M 1944 CS as an oil phase and constructed pseudo-ternary phase diagrams. Aceclofenac permeability was enhanced 5 times when incorporated into microemulsion containing ethanol as vehicle (70).

Shakeel et al. prepared nanoemulsions of indomethacin. They characterized various parameters and declared nanoemulsion as a good source for delivery of drugs across skin (71). Analgesic effect of microemulsion of naproxen, was confirmed by hot plate and tail-flick tests. Enhanced permeability was observed across the skin (72). Li et al. have prepared w/o microemulsion of metformin hydrochloride. Intestinal perfusion test was performed and this microemulsion was found to enhance oral bioavailability of BCS class III drug by promoting lymphatic absorption (73).
**Cosolvency**

The solubility of a poorly water soluble drug can be improved frequently by the addition of water miscible solvent known as cosolvent in which the drug has good solubility. Previously, this was one of the most widely used technique because it is simple to produce and evaluate (74). Cosolvents are combination of water with one or more water miscible solvents to form solution in order to enhance the solubility of poorly water soluble drugs. Different solvents are used to form cosolvents mixtures such as PEG 300, propylene glycol or ethanol. The formulations prepared by the use of cosolvents can be administered orally and parenterally. The drugs that have poor water solubility but are lipophilic in nature and exist in crystalline form are best candidates for cosolvency technique to enhance solubility. This technique can also be used to enhance the solubility in combination with other solubilization techniques and pH adjustment (75, 76).

The most commonly used low toxicity cosolvents for parenteral use are propylene glycol, ethanol, glycerin, and polyethylene glycol. Dimethyl sulfoxide and dimethylacetamide (DMA) have been widely used as cosolvents because of their large solubilization capacity for poorly soluble drugs and comparatively their low toxicity. Cosolvents can increase the solubility of poorly soluble compounds several thousand times compared to the aqueous solubility of the drug alone (77).

**Prodrug approach**

From last few decades, prodrug approach has been most commonly used to enhance the solubility of poorly water soluble drugs as well as to improve the other pharmaceutical properties such as taste, odor, stability etc. Prodrug formation can be utilized to improve the physicochemical properties such as compound lipophilicity and solubility to overcome the problems associated with the pharmacokinetics of drugs moieties. This technique is also useful because it prevents presystemic metabolism of the drugs as well as chemical decomposition. This technique is based upon the principle to cover up the functional group that is unwanted with another functional group, which is referred as promoiety. Prodrug formation is usually associated with protein and peptide molecules. Cyclic prodrug can be formulated by using C and N terminal ends reduced the metabolic degradation caused by exopeptidase. Recent studies shown that there was marked increase in permeability and solubility of hexapeptide by the application of cyclic prodrug (78). Derivatization is another lucrative approach for synthesis of prodrug to enhance bioavailability of drug molecules particularly for peptide molecules. Derivatization could be possible in C terminal amide group, N terminal amide group and phenol group in different peptide molecule (79).

**Supercritical fluid process**

Supercritical fluid (SCF) process is another novel technique that is widely used to enhance solubility of different poorly water soluble drugs. Supercritical fluids are fluids whose temperature and pressure are greater than its critical temperature (Tc) and critical pressure (Tp), allowing it to assume the properties of both a liquid and a gas. SCF near to its critical temperature are highly compressible that allows great changes in the density and mass transport properties of fluid that largely determine its solvent power when there is slight change in pressure. Once the drug particles are solubilized within the SCF such as carbon dioxide, they may be recrystallized at greatly reduced particle sizes. Particles formed in the SCF are usually of micron size or even smaller. Recently available processes provide nanoparticulate suspensions of particles 5-2,000 nm in diameter. Most of the pharmaceutical companies such as Nektar Therapeutics and Lavipharm are working on the solubility enhancement of different water insoluble drugs. Different methods of SCF processing have been developed such as precipitation with compressed anti-solvent process (PCA), solution enhanced dispersion by SCF (SEDS), supercritical anti-solvent processes (SAS), rapid expansion of supercritical solutions (RESS), gas anti solvent recrystallization (GAS) and aerosol supercritical extraction system (ASES) (80, 81).

**Hydrogel micro particles**

Hydrogels are three dimensional particles having capability of absorbing large amount of water maintaining insolubility behavior due to crosslinking agents. Microparticles are suitable for delivery of drugs because of their large surface area and ability to modify their size and hydrophobicity. Ibrahim et al. prepared biodegradable pH-responsive alginate-poly(lactic-co-glycolic acid) nano/micro hydrogel matrices for oral delivery of silymarin. They used freeze dried and air dried techniques for preparation of hydrogel microparticles. They declared this grafting technique suitable for both sustained release and for enhancing dissolution and bioavailability (82). Efforts are being made to utilize these emerging tools in solubility enhancement of hydrophobic drugs.

Lee and Kim prepared pH sensitive hydrogel microparticles using methacrylic acid (MAA) and ethylene glycol (EG) contents by dispersion photo
polymerization. Poly(ethylene glycol)dimethacrylate (PEGDMA) was used as crosslinking agent. They have checked release behavior at various pH values (83). Sajeesh et al. prepared cyclodextrin complexed insulin hydrogel microparticles by using ionic gelation method to enhance the solubility (84). Cavalier et al. prepared hydrogel microparticles of doxorubicin (85).

**Nanosuspensions**

These are solid colloidal dispersions of particle size in nano size range (200 to 500 nm). Size reduction enhances dissolution and bioavailability profile of water insoluble or poorly soluble drugs. Particle size reduction according to Noyes Whitney equation proportionally increases dissolution profile of drugs to surface area. Similarly, according to Ostwald Freundlich equation, solubility profile of poorly soluble drugs increases as particle size is switched to nano-scale. Moreover, according to Kelvin’s equation, saturation solubility increases as particle size moves down from 1 µm. As particle size decreases, dissolution rate remarkably increases (85).

Kocbek et al. prepared nanosuspensions of ibuprofen by two different approaches i.e., solvent diffusion method and melt emulsification. Nanoparticles were lyophilized by using poloxamer 188. Melt emulsification method was found much better as compared to solvent diffusion method as there was complete lack of exposure of formulation to organic liquids while preparing nanosuspension. More improvement in dissolution profile and less gastric irritability was also seen with this method (86).

Mou et al. developed itraconazole nanosuspensions by spray drying technique by using hydroxypropyl methylcellulose (HPMC) and poloxamer 407. Nanoparticles were characterized by particle size analysis, scanning electron microscopy (SEM), transmission electron microscopy (TEM), X-ray powder diffraction (XRD), X-ray photoelectron microscopy and pharmacokinetic analyses were also performed. Mannitol was included in formulations as matrix yielder. AUC after administering to rats was enhanced with nanosuspensions (87).

**Cryogenic technologies**

Cryogenic techniques are being utilized in pharmaceutical sector in order to enhance dissolution ability of hydrophobic drugs due to knitting of their nano-sized amorphous particles that present higher porosity and surface areas at lower temperature. Various techniques has been reported in literature under this category like spray freezing onto cryogenic fluids (SFF), spray freezing into cryogenic liquids (SFL), spray freezing into liquid (SFV/L) and ultra-rapid freezing (URF). Schematic presentation of cryogenic technology has been described as shown in Figure 2 (88).

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**Figure 2. Schematic presentation of cryogenic technology**
Vaughn et al. prepared and compared micronized danazol powder by spray freezing into liquid technique and evaporation precipitation into aqueous solution. X-ray diffraction patterns (XRD) proved a marked decrease in crystallinity of danazol seen in SFL micronized powder. Scanning electron microscopy (SEM) images confirmed high porosity of micronized product. They have conducted release studies for 60 min and almost 100% drug release was observed within two minutes in case of SFL product (89).

CONCLUSION

From this article, we clearly conclude that solubility is one of the most important parameters to produce desired therapeutic level of drug at the site of action. So, it is very critical for formulation development. The rate determining step for the oral absorption of poorly water soluble drugs is dissolution and the absorption of drug from the gastrointestinal tract is based on the solubility of drugs. As described above, various techniques are used to enhance solubility of the drugs alone or in combination. The proper selection of solubility enhancement method is important in order to obtain desired outcomes. Choice of method for solubility improvement is based upon drug properties like solubility, chemical nature, melting point, absorption site, physical nature, pharmacokinetic behavior etc. Dosage form requirement like tablet or capsule formulation, strength, immediate or modified release are also considered. Thus, by using proper methods, we can enhance the solubility of poorly soluble drugs many folds.

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Application of various polymers and polymers based techniques used to... 355


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