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# An Exhaustive Review on Solubility for Enhancement Techniquies

Kavipriya.R*,Dinesh K, Hariharan S, Kaviarasan K & Dharshini J

*RVS padmavathi Ammal College of Pharmacy, Coimbatore,india*

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**ABSTRACT**
The solubility of drugs is an important factor for pharmaceutical formulations. The solubility of the drug is more important for the success for the drug should reach the site of action. The bioavailability and the solubility of drug are also important for pharmacological effect of any formulations , especially in the case of oral dosage form. Absorption and dissociation rate may decrease in poorly soluble drugs, so the solubility of drugs is important to improve the methods of salts formulation, solid dispersion, co solvency, the addition of solubilizing agent, to enhance the dissociation rate of the drug all these approaches are mostly used.

**KEYWORDS:** Solubility enhancement, physical methods, chemical methods, othermethods

## I. INTRODUCTION

For the enhancement of the process of solubilization of poorly soluble drugs and further enhance the bioavailability of the drugs, a variety of methodologies can be adapted. Micronization, chemical methods , PH change , solid dispersion, covalency , complexation, hydrotropy are commonly used in solubilization process.

**TECHNIQUES INVOLVED IN SOLUBILITY ENHANCEMENT**

**PHYSICAL METHODS PARTICLE SIZE REDUCTION**

1) Micronization
2) Nanosuspension

**MODIFICATION OF CRYSTAL HABITS**

1) Polymorphs
2) Pseudopolymorph

**DRUG DISPERSION IN CARRIERS**

1) Solid dispersion
2) Solid solution

**COMPLEXATION**

1). Use of complexing agent

**SOLUBILIZATION BY SURFACTANT**

1) Microemulsion

**CHEMICAL METHODS**

**1) Change in PH**
**2) Use of buffer**
**3) Derivatization**

**OTHER METHODS**

**1) Co crystallization**
**2) Co solvency**
**3) Hydrotrophy**
**4) Solvent deposition**
**5) Nanotechnology approaches**

**PHYSICAL METHODS PARTICLE SIZE REDUCTION**

**1) MICRONIZATION**

It is the process of reducing the average diameter of solid material's particles. Traditional techniques for micronization focus on mechanical means, such as milling and grinding. Modern techniques makeuse of the properties of superficial fluids and manipulate the principle of solubility.

**2) NANOSUSPENSIONS**

This technology is applied to poorly soluble drugs that is insoluble in both water and oils. A pharmaceutical nanosuspension is a biphasic system consisting of nanosized drug particles in aqueous vehiclestabilized by surfactants for either oral and topical use or parental and pulmonary administration. The particle size distribution of the solid particles in nanosuspension

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is usually less than one micron with an average particle size ranging between 200 and 600 nm.

**MODIFICATION OF CRYSTAL HABIT**

**1) POLYMORPHS**

**2) PSEUDOPOLYMORPHS**

It is the ability of an element or compound to crystallize in more than one crystalline form. Different polymorphs of drugs are chemically identical, but they exhibit different physiochemical properties include solubility, melting point , density, texture, stability. Similar amorphous form of drug is always more suited than crystalline form due to higher energy associated and increased in surface area. Order for dissolution of different solid form of drug amorphous > metastable polymorph > stable polymorph.

**DRUG DISPERSION IN CARRIERS**

**1) SOLID SOLUTION**

It is blend of two crystalline solids that exists as a crystalline solid. A mixture of crystal is formed because the two components crustalline together in homogenous one phase system. Hence, it is expected to yield much higher rates of dissolution than simple eutectic system.

**2) SOLID DISPERSION**

It is generally prepared with drug which having poor aqueous solubility and hydrophilic carriers. It is widely used to improve the dissociation rate , solubility and oral absorption of poorly water soluble drugs. It is first introduced to overcome low bioavailability of lipophilic drug by forming eutectic mixture of drugs with water soluble carriers.

**COMPLEXATION**

**1) USE OF COMPLEXING AGENT**

It is an extensively used technique in the pharmaceutical field to improve solubility of several pharmaceutical ingredients and subsequently the bioavailability of poorly water soluble drugs. All complexing process have their importance and helps in their importance and helps in delivery of pharmaceutical drugs with improved bioavailability. Finally , based on the widespread use of complexation in cancer and other therapeutic fields . It can beconducted that complexation can be included in drug delivery application for the improvement of bioavailability with reduced toxicity.

**SOLUBILIZATION BY SURFACTANT**

1) **MICROEMULSION**

It is an optically clear pre concentrate, isotropic, thermodynamically stable transparent, translucent system containing the mixture of oil, hydrophilic surfactant and hydrophilic solvent , which dissolves poorly water soluble drugs. The criteria for the selection of surfactant are HLB and non toxicity.Microemulsion have been employed to increase the solubility of many drug that are practically insoluble in water, along with incorporation of protein for oral parenteral.

**CHEMICAL METHODS**

**1) CHANGE IN PH**

Poorly soluble drugs with the part of the molecule that can be protonated or deprotonated may potentially be dissolved in water by applying the PH change. PH adjustment can in principle be used for both oral and parental administration . Upon intravenous administration the poorly soluble drug may be precipitate because the blood is a strong buffer with PH between 7.2 – 7.4.Ionizable compound are stable and soluble after PH adjustment are best suited . The compound types may be acids or bases or zwitter ionic, It can also be applied to crystalline as well ass lipophilic poorly soluble compound.

**2) USE OF BUFFER**

It maintains the PH of the solution overtime and it reduces are eliminate the potential for precipitation upon dilution. On dilution PH alternation occurs that decrease solubility. Change of PH by 1 fold increase solubility by 10 folds if it changes by 1 PH unit , that decrease solubility by 10folds.

**3) DERIVATIZATION**

It is a technique used in chemistry which transforms a chemical compound into a product similar chemical structure called derivative . Derivative have different solubility as that of adduct. It is used for quantification of adduct formation of esters and amides via acyl chlorides.

**OTHER METHODS**

**1) CO CRYSTALLIZATION**

The most common state of delivering dosage form is solid such as tablets, capsules, etc.., Various other states exist which allow delivering the API faster than the solid state. But this state provide API in the most convenient, compact and stable format to store. Thus , an important part of drug development becomes the understanding and controlling of the solid- state chemistry. Many times an API cannot be formulated in its pure form

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due tovarious issues of instability.

## 2) CO SOLVENCY

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 the combination are known as co solvent. Co solvent system works by reducing the interfacial tension between aqueous solution and hydrophobic solute. It is also known as solvent blending. There is a dramatic change in the solubility of drugs by the addition of organic co solvent into the water.

## 3) HYDROTROPY

It is a solubilization phenomenon whereby addition of large amount of asecond solute result in an increase in the aqueous solubility of existing solute. Concentrated aqueous hydrotropic solutions of sodium benzoate, sodium salicylate, urea, nicotinamide, sodium citrate and sodium acetate have been observed to enhance the aqueous solubilities of many poorly water soluble drugs.

## 4) SOLVENT DEPOSITION TECHNIQUE

Reduction of particle size remains the accepted method for increasing dissolution rates. However , upon micronization, hydrophobic drugs have a tendency to clump when exposed to dissociation medium. The term 'minuscular form' on the surface of an absorbent. This technique was termed as solvent deposition . The term " minuscular form" implies that drug has undergo molecular micronization when it is dispersed on the extensive surface of the micro particulate absorbent . It is an approach used for increasing the dissociation rates of relatively insoluble powders.

## 5) NANOTECHNOLOGY APPROACHES

Drugs with poorly solubility possess difficulties in formulations by applying conventional approaches as they present problems such as slow onset of action, poor oral bioavailability, lack of dose proportionally, failure to achieve steady state plasma concentration, and undesirable side effects..Nanotechnology is a promising strategy in the development of drug delivery system especially for those potent drugs whose clinical development failed due to poor solubility, low permeability, inadequate bioavailability and other poor biopharmaceutical properties.

## II. CONCLUSION

By this article we conclude that, solubility of the drug is the most important factor that controls the formulation of the drug as well as therapeutic efficacy of the drug, hence the most critical factor in the formulation development. Dissolution of drug 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 form of different drugs.

The various techniques described above alone or in combination can be used toenhance the solubility of the drug. Solubility can be enhanced by many techniques and number of folds increase in solubility. Because of solubility problem of many drugs the bioavailability of them gets affected and hence solubility enhancement becomes necessary.

## REFERENCE

[1]. Danielsson I, Lindman B, The definition of Microemulsion, ColloidsSurfaces, 1981; 3, 391-392.
[2]. Holm R, Porter CJH, Edward GA, Mullertz, A, Kristensen HG,Charman WN, Examination of oral
[3]. Absorption and lymphatic transport of halofantrine
[4]. In a triple cannulated canine model after Administration in self-microemulsifying drug
[5]. Delivery systems (SMEDDS) containing structured Triglycerides. European Journal of Pharmaceutical Sciences 2003; 20, 91-97. Pouton CW.
[6]. Lipid formulation for oral Administration of drugs, non- emulsifying, self-Emulsifying drug delivery systems. European Journal of Pharmaceutical Sciences 2000; 11, S93- S98.
[7]. Pouton CW. Formulation of self-microemulsifying Delivery system. Advance Drug Delivery Reviews, 1997; 25, 47-58.
[8]. Ogino K, Abe M. Microemulsion formation with Some typical surfactants, Surface and Colloid Science, Matijevic E, New York: PlenumPress, 1993, 85-95.
[9]. Lieberman H.A, Rieger M.M, Banker G.S. Pharmaceutical dosageforms, Disperse systems.New York, Marcel Dekker, Inc, 1998. 149 -181.
[10]. Paul B.K, Moulik S.P. Microemulsions, an

overview, Journal ofDispersion Science and Technology 1997; 18(4), 301-304.

[11]. Attwood D. Microemulsions. In Colloidal Drug Delivery Systems,Kreuter H. (ed.) New York Marcel Decker Inc, 1994; 31-40.

[12]. Tenjarla S.N. Microemulsions: an overview and Pharmaceuticalapplications. Therapeutic Drug Carrier Systems. 1999; 16, 461–521.

[13]. Kalaiarasi K, Shah D.O. Microemulsions: evolvingTechnologies forcosmetic application, Journal of The Society of Cosmetic Chemistry,