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**REVIEW ARTICLE** **OPEN ACCESS**

# Enhancement of Aqueous Solubility of BCS Class II Drug by Solid Dispersion: A Review

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**ABSTRACT**
*Solubility is vital matter to achieve the required systemic or plasma concentration to have the rapeutic response. The majority of drugs are weakly acidic or basic in nature, with low water solubility. For effective absorption of drug in the absorption site they should be available in the solution form. Some drugs have good permeability but lack of water solubility which are said to be BCS class II drugs and solubility of these drugs can be enhanced by various techniques like solid dispersion, co-solvency, salt formation, size reduction and change in pH. In this we study various techniques of formulation by solid dispersion and gauging solid dispersion preparation. Solid dispersion is most promising and reproducible technique.*
***Keywords:*** *BCS class II, solubility, solid dispersion*

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## INTRODUCTION:

The most formulated and advantages over other oral solid dosage forms are tablet which is ease in administration and preparation and most convenient for the patient but some tablet dosage forms are lack in water solubility [1]. There are different types of solid dosage forms like tablets, capsules, pills and sachets. Among them tablet and capsules are more familiar and most convenient. Oral route is most popular and convenient for patients the poor aqueous solubility of drugs becomes the utmost obstruction and which affects the bioavailability of drug in systemic circulation ultimately causing the pharmacological activity [2]. Recently many potential drugs are identifies for different diseases using advanced molecular screening methods. Potential drug bioavailability is affected due to poor water solubility of the drugs which have good permeability.

## BIOPHARMACEUTICAL CLASSIFICATION SYSTEM:

BCS is based on the medicinal substances permeability and water solubility at the absorption site.

**Table 1 All BCS Classes and solubility, permeability**

| S. NO | BCS CLASS | SOLUBILITY | PERMEABILITY |
|---|---|---|---|
| 1 | CLASS – I | HIGH | HIGH |
| 2 | CLASS – II | LOW | HIGH |
| 3 | CLASS – III | HIGH | LOW |
| 4 | CLASS - IV | LOW | LOW |

## SOLUBILITY AND SOLUBILITY EXPRESSIONS:

A drug is considered to be very soluble if a single therapeutic dosage of it dissolves in 250 mL or less of an aqueous solution with a pH range of 1.2 to 6.8 at 37 °C [3].

| DEFINITION | PARTS OF SOLVENT REQUIRED FOR ONE PART OF SOLUTE |
|---|---|
| Very Soluble | > 1 |
| Freely Soluble | 1 – 10 |
| Soluble | 10 – 30 |
| Sparingly Soluble | 30 – 100 |
| Slightly Soluble | 100 - 1000 |
| Very Slightly Soluble | 1000 -10000 |
| Insoluble | <10000 |

**Table 2 Solubility and Solubility expressions**

**PERMEABILITY:**

Drug permeability is the capacity of pharmaceuticals to cross physiological membranes [3]. Many methods are employed to increase the low aqueous soluble drugs are as follows:

- Solid dispersion
- Complexation
- Particle size reduction
- Use of co-solvency
- Salt formation

Among them solid dispersion is most widely used techniques for increasing of aqueous solubility of poorly soluble drugs. Solid dispersion method was first described by Chiou and Reigelman as the solid dispersion of a therapeutic element in an inert carrier produced by any means, including the Fusion method, Solvent evaporation, Lyophilization technique, hot melt extrusion, kneading, etc.

**APPROACHESFOR SOLID DISPERSION:**

- Physical modification
- Chemical modification

**PHYSICAL MODIFICATION:**

- It includes various techniques
- Particle size reduction
- Micronization
- Polymorphs
- Eutectic mixture
- Microemulsions

**CHEMICAL MODIFICATION:**

- Fusion method
- Solvent evaporation method
- Meltextrusion method

**CARRIERS USED:**

For the formulation of solid dispersion, many carriers are used. The nature of the active substance and the solubility of the medication in different carriers influence carrier selection. Different types of carriers used areas follows:

**Table 3 Different Types of Carriers used in Solid Dispersion**

| S.No. | NATURE | CARRIER |
|---|---|---|
| 1. | Acids | Citric acid, tartaric acid, succinic acid, phosphoric acid |
| 2. | Sugars | Dex-trose,mannitol,sorbitol,maltose,galactose,lactose,solublestarch, |
| 3. | Polymeric materials | polyvinylpyrrolidine, peg4000, peg6000, pvpk30, cmc, hydroxy propyl cellulose |
| 4. | Surfactants | polyoxyethylenestearate, poloxamer, deoxycholic acid, tween and spans, sodium |
| 5. | Hydrotropes | Sodium acetate, sodium hydroxy benzoate, sodium hydroxyl benzoate, sodium citrate, resorcional, ascorbic acid |
| 6. | Dendrimers | Pamam, starburst |
| 7. | Others | penta erythritol, urea, urethane, hydroxyalkyl xanthene,skimmed milk |

**SOLVENT USED:**

**Table 4 Different types of solvents and their boiling points**

| S.NO. | SOLVENTS | BOILING POINT |
|---|---|---|
| 1. | Water | 100 |
| 2. | Methanol | 65 |
| 3. | Ethanol | 78.5 |
| 4. | Aceticacid | 118 |
| 5. | 1-Propanol | 97.4 |
| 6. | 2-Propanol | 82.4 |
| 7. | Chloroform | 62 |
| 8. | DMSO | 189 |

**METHODS OF SOLID DISPERSION:**

- Fusion method
- Solvent evaporation
- Lyophillization technique
- Hot melt extrusion
- SCF technology
- Kneading methods

**FUSION METHOD:**

Sekiguchi and obi first reported the melting method. Here the therapeutic ingredient and the carriers are melted thoroughly and allow to cool in the in the room temperature till they become solid (solidification). Solidification can also be done by ice bath agitation and using desiccator. Then the solid mass is crushed and pulverized in mortar and pestle then they are sieved in appropriate mesh sieve. This method can't be employed for the thermolabile drugs [5-6].

**SOLVENT EVAPORATION METHOD:**

In certain solvents, the carrier and drug are solubilized, and the solvent is then evaporated at lower pressure. To get clear of any remaining solvent residue, the resulting mixture is left to dry off and maintained at room temperature in a desiccator. Then the solvent mass is crushed and sieved [7].

**LYOPHILIZATIONTECHNIQUE:**

It is an alternative methodology to the one described above. The carrier and drug are dissolved in general solvent. Then they are frozen (about -50ºC). Then this frozen is directly sublimated(sublimation) to form lyophilized molecular dispersion [8].

a) Vial freeze drying
b) Spray freeze drying

**a) Vial Freeze Drying:**

Individually solubilized in the specified solvent, the carrier and drug are then mixed at a concentration of 40/60 v/v and immersed in liquid nitrogen until completely frozen. Various solvent dispersion are prepared by keep the drug ratio constant and changing the carrier ratio in increasing order. Then lyophilize them in the lyophilizer then they are dried in the freeze dryer.

**b) SPRAYFREEZEDRYING:**

Separately, the carrier and drug are solubilized in particular solvent before being combined in a 40/60 v/v ratio. A nozzle sprays the mixture into liquid nitrogen. While spraying the solution into the liquid nitrogen liquid feed rate and atomizing air flow should be considered and the liquid feed should be 10cm above the liquid nitrogen. Resultant solution is transferred to the lyophilizer and Lyophilization procedure is begin as soon as the liquid nitrogen vaporizes [11].

**EVALUATION OF THE SOLID DISPERSION:**[1]

The solid dispersion can be evaluated by

- Evaluation of blend before compression
- Evaluation of tablet after compression

**EVALUATION OF BLEND BEFORE COMPRESSION:**

- ANGLE OF REPOSE
- BULK DENSITY
- TAPPED DENSITY
- COMPRESSIBILITY INDEX
- HAUSNER'S RATIO
- VOID VOLUME
- POROSITY

**EVALUATIONOFTABLETAFTERCOMPRESSION:**

- WEIGHT VARIATION
- HARDNESS
- FRIABILITY TEST
- MECHANICAL STRENGTH
- UNIFORMITY OF DISPERSION
- WETTING TIME
- IN VITRO DISSOLUTION STUDIES

**EVALUATION OF BLEND BEFORE COMPRESSION:**

**ANGLE OF REPOSE:**

It should be analyzed for determining the flow property of the blend. It is done by fixed funnel method. A funnel with orifice of 20mm diameter is taken. The funnel is fitted in the burette stand and a paper is kept below the funnel at the distance of 2cm. A cotton plug is placed in the end the funnel and the weighed quantity of the blend is filled in the funnel. Then the cotton plug is removed from the funnel and allowed for free flowing of the powder on the paper.

**STANDARD VALUE OF ANGLE OF REPOSE**

**BULK DENSITY:**

It was calculated by accurately filling the graduated cylinder with the blend and measuring its weight and volume. The following formula is used to calculate bulk density:

Bulk density=Weight of the Powder/ Volume of the Packing

**COMPRESSIBILITY INDEX:**

The following equation may be used to determine a material's size, morphology, surface area, moisture content, and cohesiveness using the compressibility index:

Compressibility index(%) = [(TD-BD) ×100]/TD

**HAUSNER'S RATIO:**

It was used to explain how the powder flowed. To calculate this, use the equation below:

Hausner's ratio=(Tapped density×100)/ (Poured density)

| S. NO | FLOWABILITY | HAUSNER'S RATIO |
|---|---|---|
| 1. | EXCELLENT | 1.00-1.11 |
| 2. | GOOD | 1.12-1.18 |
| 3. | FAIR | 1.19-1.25 |
| 4. | POSSIBLE/PASSABLE | 1.26-1.34 |
| 5. | POOR | 1.35-1.45 |

**Table 5 Flowability and Hausner's ratio**

**SPECIFICATION OF HAUSNER'S RATIO**

**VOID VOLUME:**

The void volume is the amount of empty space between the particles. The formula with the letter "v" serves as an indicator:

($V_b$ –Bulk Volume and $V_p$– True Volume)

$$V = V_b - V_p$$

**Porosity:**

The porosity of a packing is defined as its void volume to bulk volume ratio. It was denoted by €. The following formula can be used to calculate porosity:

$$€ = V_b - V_p/V_p = 1 - V_p/V_b$$

It can be computed using the formulas below and is commonly stated as a proportion:

$$\%€ = (1 - V_p/V_b) \times 100$$

**CONCLUSION:**

Most of the oral tablets are having poor aqueous solubility and which ultimately affects the bioavailability and pharmacological activity. As oral tablets are most convenience dosage form which have a drawback of low dissolution which can be maximized through solid dispersion method which a most challenging method for maximizing the dissolution rate of the drugs because of its simple and reproducible methods. They produce solid dispersion of uniform drug content and has good flow property.

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