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Review Article

A review on solid dispersion and latest approaches used to improve solubility of poorly water soluble drugs

Ramanpreet Kaur* and Sandeep Kumar

Department of pharmaceutics, ASBASJSM College of Pharmacy, BELA, Ropar, Punjab, India

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ABSTRACT

In the present day solubility of drugs in GIT fluids becomes necessary for the preparation of solid unit dosage forms of drugs. Otherwise if the drug has poor solubility then the drug does not show its effect properly in the body. So, solubility is a main aspect in the formulation of unit doses. Various methods like Lyophilization (Freeze drying process), Super critical fluid technology, Nanotechnology, Liquisolid compact technology, Self-emulsifying agents (SMEDDS) etc. are used to improve the solubility and dissolution rate of poorly water soluble drugs.

Keywords: Solubility, Diverse, unit doses, Liquisolid, dehydration, availability.

INTRODUCTION

Solubility: Solubility is the quality of being soluble and easily dissolved in liquid.

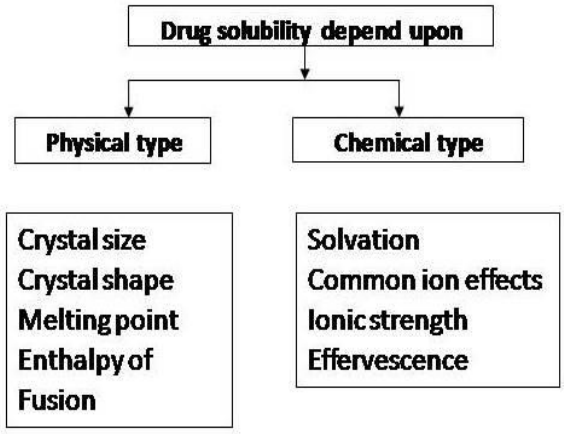

Fig.1

Possible causes of poorly water soluble drugs:

- ❖ Water Solubility >100 µg/ml
- ❖ Melting point >200 °C
- ❖ Highly hydrophobic (log p>3)
- ❖ Low intrinsic dissolution rate > 0.1 mg/cm²/m
- ❖ Atomic weight (>500 Unit)

Dissolution: Drug dissolution is the process by which drug molecules or ions transfer from a solid state into solution. In essence when drug dissolves, solid particles separate and mix molecules with the liquid and appear to become a part of that liquid.

A diverse pathway for improving drug solubility:

- Decrease particle size of drug.
- Decreased contact angle between two immiscible layers.
- To decrease overlap dimensions.
- Verify move conditions.
- Better dissolution

Biopharmaceuticals Classifications Scheme (BCS): Biopharmaceuticals classifications scheme is a scientific framework for categorizing of drug substance based on its liquefied solubility and abdominal permeability that coordinates *in vitro* dissolution and *in-vivo* bioavailability of pharmaceutical API .BCS drugs are classified into 4 categories according to their liquefied solubility and abdominal permeability:

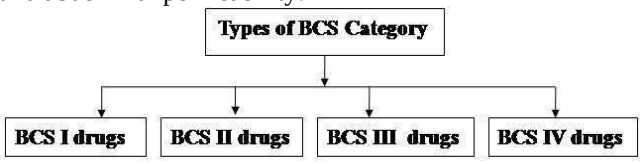

Fig. 2

***Corresponding Author Address:** Ramanpreet kaur, Department of pharmaceutics, ASBASJSM College of Pharmacy, BELA, Ropar, Punjab, India*

BCS I drugs: High Solubility, High Permeability, well absorbed, absorption rate higher than excretion rate, Metoprolol antihypertensive agent belongs to this class.

BCS II drugs: Low Solubility, High Permeability, High absorption, Low dissolution, Glibenclamide, Phenytoin belongs to this class.

BCS III drugs: High Solubility, Low Permeability, Low absorption, Cimetidine belongs to this class.

BCS IV drugs: Low Solubility, Low Permeability, Not well absorbed, Low dissolution, Bifonazole belongs to this class.

SOLID DISPERSION APPROACHES FOR SOLUBILITY ENHANCEMENT

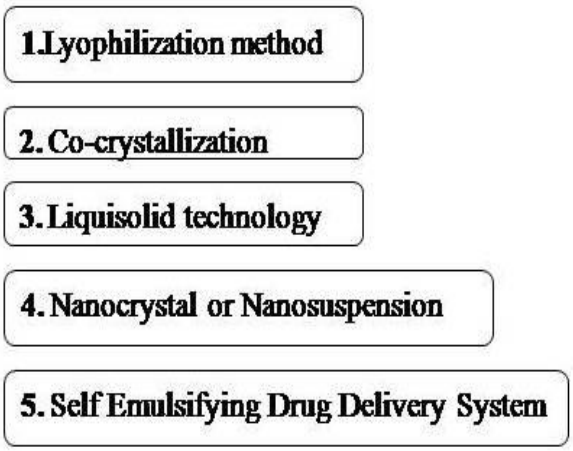

Fig. 3

Lyophilizations Techniques:

- Also called Freeze Drying Process.
- Lyophilization is a dehydration or drying process applicable to the manufacture of pharmaceuticals and biologicals that are thermolabile or otherwise unstable in aqueous solution for prolonged storage periods, but that are stable in dry state.
- It's Law based on the phenomenon of sublimation, whereby water passes directly from solid state (ice) to vapour state without passing through liquid state. Sublimation can take place at pressure and temperature below triple point (i.e. 4.579 mm of Hg and 0.0099 °C).
- Freeze drying of Pharmaceuticals is carried out at temperature of -10°to-40°c.
- Lyophilization has four step process

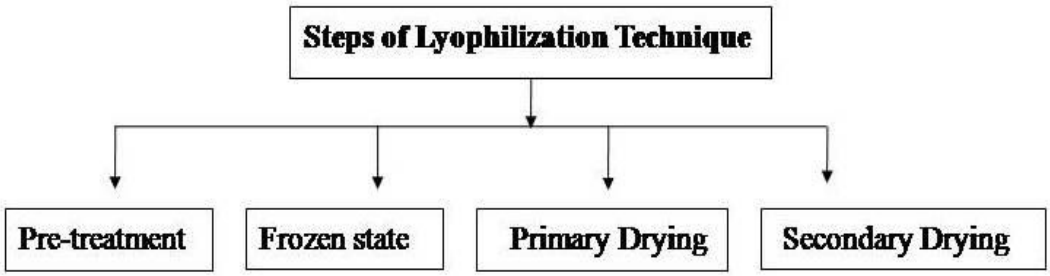

Fig 4

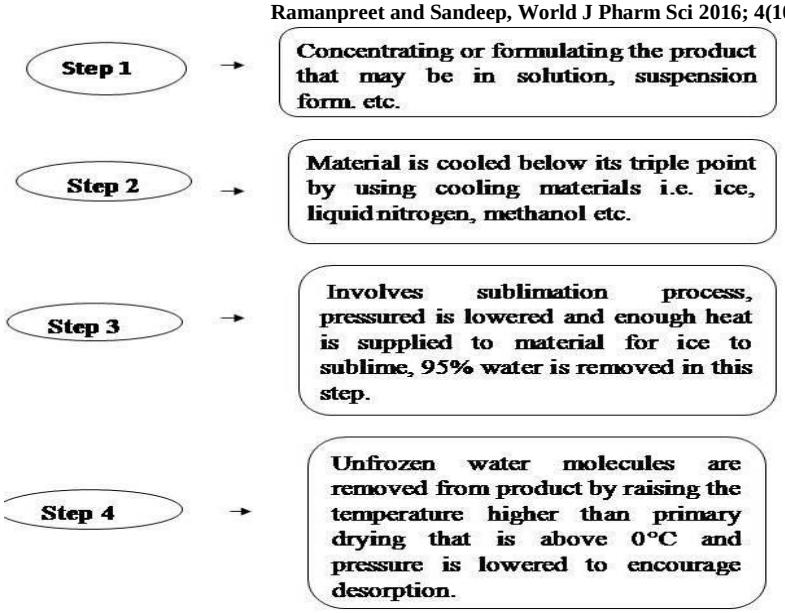

Fig 5:

FEATURES OF LYOPHILIZATION TECHNIQUE

- Ease of aseptic process in case of solutions.
- Powdered stability enhanced by removal of water molecules and to obtain dry powder.
- Water can be removed completely without excessive heating, which otherwise reduced the stability of drug.
- Drug powder reprocessing

DRAWBACKS OF LYOPHILIZATION TECHNIQUE

- Processing time is usually high.
- Required separate sterile water for injection filling during reprocessing.
- Enhancement of operation time.Requiring essential equipment for processing

Co-crystallizations method:

- rystallization is the process where a solid forms are directly unorganized in a structure known as a crystal.
- This process chemically separated the solid-liquid.
- In this solutes are transfer from liquid to a solid .
- A co-crystal may be defined as crystalline material that consists of two or more molecular species held together by non-covalent forces and are more stable as crystallising agents which are solid at room temperature.
- Examples of co-crystallising agents are saccharin, nicotinamide and acetic acid.

Processing steps for Co-crystallization

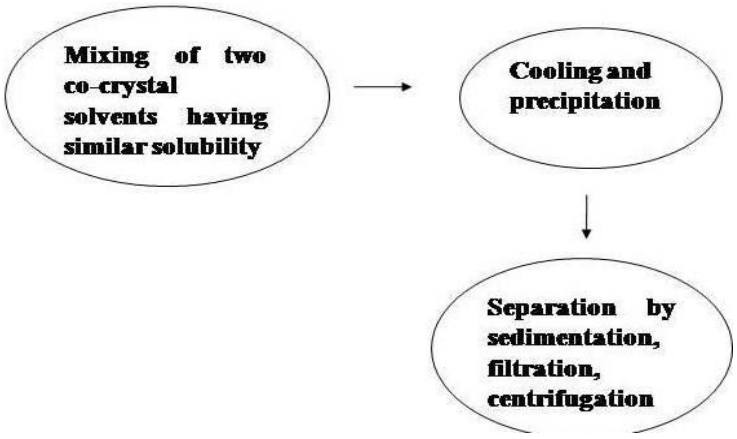

Fig 6

Co-crystallization methods:

Solution Co-crystal method: Prepare solvent mixtures for co-crystals. Saturation of co-crystals. By cooling and evaporation co-crystals are prepare.

Grinding Co-crystal method: Mixing of stiochimetric type co-crystal components together. Grinding them either manually, using a mortar or pestel or mechanically, using a ball mill or a vibratory mill. Then exhibit vapour pressures in solid co-crystals preparations.

Drawbacks of Co-crystallization method: Although preparation of co-crystals is simple but exact relationship between co-crystal structure and physical properties still unexplored. The optimum temperature range should be known for solid-state grinding because excessive heating may cause accidental phase transition. Solid state grinding method result in too small particle size and hence it is difficult to identify structure using x-ray crystallography. Phase separation of crystals only occur at relative humidity.

Benefits of Co-crystallization method: In place of salt formation, pharmaceutical co-crystallization may be employed to all APIs. Co-crystal formation shows polymorphic phenomenon. Co-crystallization may be used as a tool to purify API in the form of co-crystals. Synthesis of co-crystal using solvent grinding method required less quantity of solvent.

Liquisolid method: The Liquisolid technique is a novel and promising approach to overcome the problem of solubility and dissolution enhancement of poorly water soluble drugs. This technique is based upon dissolving the insoluble drug in the non-volatile solvent and mixed it with suitable carrier and coating materials to convert into free flowing compressible powders.

Processing steps for liquisolid compacts:

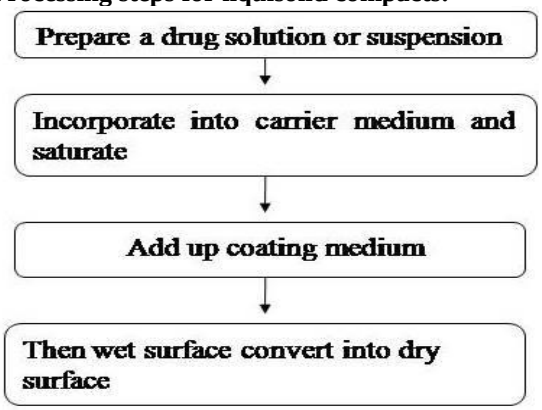

Fig 7

Drawbacks of Liquisolid method: Drug loading capacity is very low. They show maximum solubility of drug in non-volatile solvents. To maintain acceptable flow ability and compatibility for liquisolid powder formulation. Not suitable for formulation of high dose insoluble drugs.

Benefits of Liquisolid method: Increased bioavailability as compared to conventional tablets. The greater exposed surface area for dissolution medium. Cost of production is less in compared to soft gelatin capsules. BCS Class II drugs that is poorly water soluble and highly permeable can be formulated into Liquisolid systems. These systems forms immediate release or controlled release dosage forms. Improved dissolution profile of poorly water soluble drugs. Improved drug surface phenomenon.

Drug release mechanism from Liquisolid systems: Enhances particle surface area of drug. Enhances water solubility of drug. Improved surface phenomenon of drug.

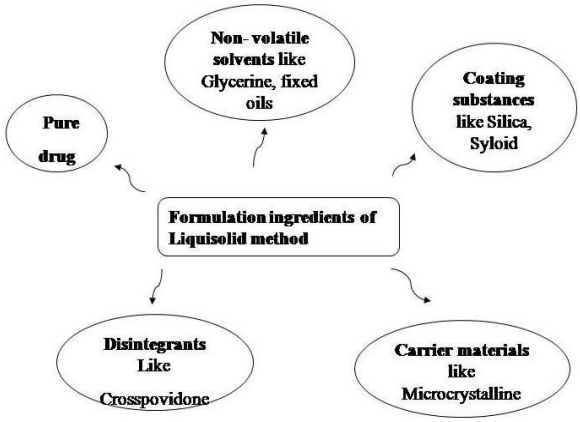

Fig.8

Nanocrystal or Nanosuspension method:

- A nanocrystal is a type of crystalline substances with at least quantity less than 1000 nm.
- Nanosuspensions are submicron colloidal dispersions of nanosized drug particles stabilized by drug surfactants.
- Nanosuspension consists of poorly water soluble drug without any matrix material suspended in dispersion.
- This technique used for both oil and water insoluble drugs.
- The particle size range in nanosuspension is usually less than one micron with an average particle size ranging between 200 nm and 600 nm

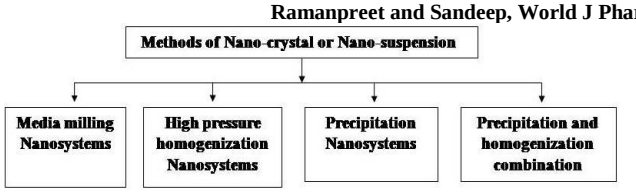

Fig 9;

Media milling Nanosystems :

- It uses high shear media mills.
- Charging of milling chamber by using milling media, pure drug, liquid, stabilizing agent on rotation at very high shear rate under controlled temperature conditions (2 to 7 days).
- The milling media is composed of glass, Zirconium oxide or highly cross-linked polystyrene resins.
- Due to impactation of drug + milling media, high shear forces are generated as a results of breakage that converts microsized particles into nanosized particles.

High pressure homogenization:

Principle based on cavitations in the aqueous phase.

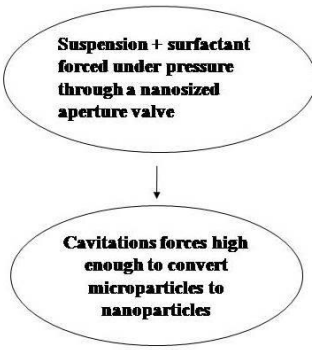

Fig 10

Precipitation Nanosystems

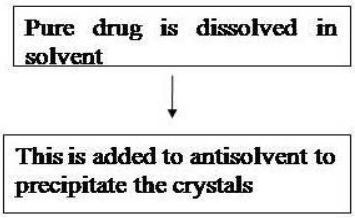

Fig. 11

Precipitation and homogenization combination :

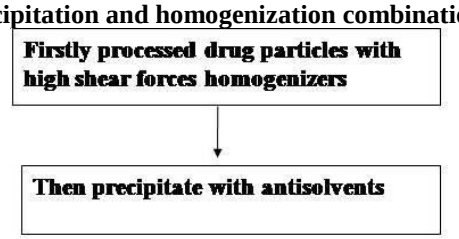

Fig. 12

Benefits of Nanosystems: Improve the solubility and oral availability of drugs. Hydrophilic drugs are good candidates for this. Achievement of high drug loading capacity. Low dose is required. Enhances the physical and chemical stability of drug. Provides a passive targeting. Accessibility of aseptic production

Drawbacks of Nanosystems: Nanosuspensions contaminated with materials eroded from balls may be problematic in media filling nanosystem. Media filling process is time consuming. Fraction of particles occurs in micrometer range in case of media filling nanosystem. Not easy to scale up due to mill size and weight. Growing of crystal needs to be limited by surfactant addition in precipitation system.

Self Microemulsified Drug Delivery Systems:

- SEDDS OR SMEDDS are the methods used to improve the solubility and dissolution of poorly water soluble drugs.
- SEDDS are defined as isotropic mixture natural or synthetic oils, solid or liquid surfactant, or alternative or one or more hydrophilic solvent and co-solvent/surfactant.
- SEDDS produce emulsions having a droplet size range between 100-300 nm while SMEDDS from transparent micro-emulsion with a droplet size range less than 50 nm.
- Upon mild agitation followed by dissolution in aqueous media, such as GI fluids these system can form fine oil in water (o/w) emulsion or micro-emulsions.

Benefits of self microemulsified systems: Enhances oral bioavailability by reduction in dose. Scale up and manufacturing are not difficult. Drug having high drug loading capacity. Protection of drug from degradation in body. Consistence and reproducible.

Drawbacks of self microemulsified systems: High surfactant concentration effects GIT. Chemical instability of drug and surfactant in formulation.

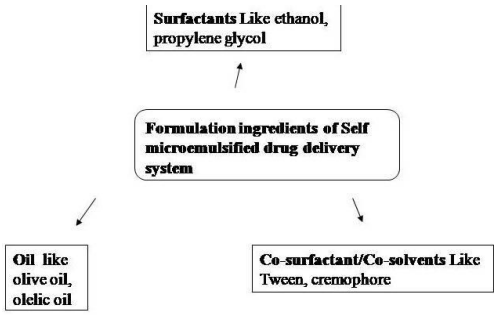

Fig. 13

CONCLUSION

Most of the drugs are poorly water soluble that means low solubility and dissolution rate results in low bioavailability of drug which produces lower therapeutic effects. In the present day low solubility drugs is the main aspects for formulation of ideal dosage form. This problem can be solved by improving the dissolution rate of drug because dissolution is a rate limiting step for oral absorption of drug from GIT. Various techniques are used for solubility and dissolution enhancement of poorly water soluble drugs to ensure the goals of formulation of stable dosage form having good oral bioavailability, reduce in dosage frequency and better patient compliance with a low cost of production.

REFERENCES

1. Madhok Shivangi, Madhok Akankasha. Enhancement of solubility and dissolution of carvidilol by solid dispersion technique using rota evaporation and lyophilisation technique . Int Journal of drug research and technology 2015 ; 5(2) : 81-102.
2. Chandel P et al. A liquisolid technique : an approach for enhancement of solubility. Journal of drug delivery and therapeutics 2013; 3(4) : 131-137.
3. Lakshmi M S et al .A Novel Approach for Improvement of Solubility and Bioavailability of Poorly Soluble Drugs: Liquisolid Compact Technique. International Journal of Research in Pharmaceutical and Biomedical Sciences 2012; 3(4): 1621-1632.
4. Soni S et al. Nanosuspension: An Approach to Enhance Solubility of Drugs. IJPI's J. Pharmaceutics and Cosmetology 2012; 2(9): 49-63.
5. Chaudhari A et al. Enhancement of solubilisation and bioavailability of poorly soluble drugs by physical and chemical modification, A recent review. Journal of advance pharmacy education and research 2012; 2(1): 32-67.
6. Ketan T et al Drug Solubility: Importance and Enhancement Techniques.International Scholarly Research Network ISRN Pharmaceutics Volume 2012.
7. Zaheer A et al . Solubility enhancement of poorly water soluble drugs International Journal of Pharma tech 2011; 3(1) : 807-823.
8. Patil S k et al. Strategies for solubility enhancement of poorly soluble drug. International journal of pharmaceutical science review and research 2011; 8(2): 74-80.
9. Vikash Dash, Asha Kesari. Role of biopharmaceutical classification system in drug development program.Journal of Current Pharmaceutical Research 2011; 5 (1): 28-31.
10. Ning Qiao et al. Pharmaceutical co-crystals : An overview. International Journal of Pharmaceutics 2011.
11. Bandarkar FS, Khattab IS et al. Lyophilized gliclazide - poloxamer solid dispersions for enhancement of in-vitro dissolution and in-vivo bioavailability. Int J Pharm Pharm Sci 2011; 3: 122 – 127.
12. Patil J S et al. Inclusion complex sytem. A novel techniques to improve the solubility and bioavailability of poorly drug: a Review. International journal of pharmaceutical sciences 2010; 2(2): 29-34.
13. Mohanachandran P S . Enhancement of solubility and dissolution rate : an overview. International Journal of Comprehensive Pharmacy 2010; 4: 1-10.
14. Khan M et al. Crystal engineering of pharmaceutical co-crystals: application of methyl paraben as molecular hook.J Am Chem Soc. 2010 ; 132, 5254–5263.
15. kulkarrni A S et al. Liquisolid system : a review. International journal of science and nanotechnology 2010; 3(1): 795-803.
16. Ahire B R et al. Solubility Enhancement of Poorly Water Soluble Drug by Solid Dispersion Techniques. International Journal of Pharm tech Research 2010;2: 2007-2015.
17. Aggarwal S et al. Solid dispersion as an eminent strategic approach in solubility enhancement of poorly soluble drugs. International Journal of Pharmaceutical Sciences and Research 2010; 1: 1-13.
18. V R Vemula et al. Solubility enhancement techniques.International Journal of Pharmaceutical Sciences Review and Research 2010; 5(1) : 41–51.
19. Bindu MB et al. Novel strategies for poorly water soluble drugs. International Journal of Pharmaceutical Sciences Review and Research 2010; Volume 4, Issue 3.
20. Sharma A, Jain C P .Techniques to enhance solubility of poorly soluble drugs: a review. J. Global Pharm. Tech. 2010; 2: 18-28 .
21. D. Sharma. Solubility enhancement - eminent role in poorly soluble drugs Research Journal of Pharmacy and Technology 2009; 2(2) : 220–224.
22. Sharma D et al.Solubility Enhancement -Eminent Role in Poorly Soluble Drugs. Research Journal of Pharmacy and Technology 2009; 2: 220-224.
23. D. Sharma et al. Solubility enhancement-eminent role in poorly soluble drugs. Research Journal of Pharmacy and Technology 2009; 2(2) :220–224.
24. Sabiruddin Mirza et al . co-crystals: an emerging approach for enhancing properties of pharmaceutical solids,Dosis 2008; 4(2).
25. Bansal et al .Solid self-nanoemulsifying delivery systems as a platform technology for formulation of poorly soluble drugs. Crit. Rev. Ther. Drug Carrier System 2008; 25: 63-116.
26. Javadzadeh Y et al. Liquisolid technique for dissolution rate enhancement of a high dose water insoluble drug (carbamazepine). Int. J. Pharm. 2007; 341: 26-34 .
27. Chokshi RJ et al . Improving the Dissolution Rate of Poorly Water Soluble Drug by Solid Dispersion and Solid Solution: Pros and Cons., Drug Deliv 2007; 14(1) : 33-45.