

Liquisolid Compact Technique: A Novel Approach to Solubility Enhancement

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Introduction

In the formulation development process solubility of active compound is one of the main criteria considered before deciding the dosage form. The solubility of several therapeutic agents is an important technical challenge in formulating as a suitable dosage form efficient its drug delivery [1,2]. Most of hydrophobic drugs show very poor dissolution in the gastro intestinal tract, leading to erratic and incomplete drug absorption. Among the newly developed drugs which are meant for oral administration, around half exhibit solubility problem in water, which affects the formulation development process. Due to the many advantages associated with oral route, the poor solubility of such drugs suffers with slow dissolution and poor bioavailability. The drugs belongs to the biopharmaceutical classification system (BCS) class II and IV shows very poor dissolution leads to incomplete drug release from the formulation, increased dose, large inter and intra-subject plasma concentration variation under both fed and fasted states eventually leads to poor bioavailability [3,4].

Over past few decades, many techniques have been developed, to improve the solubility and dissolution of poorly soluble substances, with different degrees of success which includes micronization, lyophilization, solid dispersion, etc. [5]. Out of which the recent research focus on liquisolid compact technique or powdered solution technique as one of the successful tool to achieve the goal.

Principles of Liquisolid Compact System

Liquisolid compacts are acceptably flowing and compressible powder forms of liquid medications. The liquid medication is the water insoluble drugs carried in suitable non-volatile solvents. This liquid medication is converted into a free flowing powder by addition of suitable excipients [6]. With these technique liquids dosage forms such as solutions or suspensions of poorly soluble drugs in a non-volatile liquid vehicle are converted into acceptably free flowing and compressible powders by simple physical blending with selected excipients named the carrier and the coating material. Usually, microcrystalline cellulose and colloidal silica are used as the carrier and the coating material, respectively. Hence, the liquisolid technology allows the conversion of liquid systems into solid drug delivery systems such as tablets. The liquisolid approach has been successfully applied in solubility and release enhancement of low dose poorly soluble drugs. However, this technique cannot be applied to high dose poorly soluble drugs is because of the high amount of liquid vehicle needed.

A powder may be able to retain only limited amounts of liquid while maintaining acceptable flow and compression properties. To calculate the required amounts of powder excipients including both carrier and coating materials a mathematical approach for the formulation of

liquisolid systems has been developed by Spireas [7,8]. The excipient and coating material are to be taken into definite ratios so as to retain the accepted amount of liquid to be converted into solid. The powder excipient ratio R is the fraction of weight of carrier (CR) and the coating material (CO) present in the formulation $R=CR/CO$. The maximum liquid load on the carrier material is termed as the liquid load factor (Lf). Lf is defined as the weight ratio of the liquid medication (w) and carrier powder (CR) in the system $Lf=w/CR$, which must be posed by an acceptable flowing and compressible preparation. The ϕ -value of a powder is the maximum amount of a given non-volatile liquid that can be retained inside its bulk (w/w) while maintaining the reasonable flow. The ψ - number of a powder is the maximum amount of liquid that can be retained by a powder within its bulk (w/w) while maintaining acceptable compactability, so that while making cylindrical compacts with enough strength 'liquid-squeezingout' phenomena does not occur. The ϕ -value and the ψ -number of powder may be determined using the procedure liquisolid flowability test (LSF) and liquisolid compressibility (LSC) test, respectively [6]. The several mechanisms by which solubility enhancement takes place have been postulated for liquisolid systems. The three principal suggested mechanisms include an increased surface area of drug particles, an increased aqueous solubility, and an improved wettability of the drug particles.

Conclusion

New chemical entities are often macromolecules with high lipophilicity show poor solubility and high permeability and present a technological challenge mainly due to their poor bioavailability, which leads to poor absorption. Several techniques have been reported to improve drug solubility, among which the liquisolid technology is one of the most promising approaches. As highest drug release rates are observed with liquisolid compact system and this system may be optimized by selection of the liquid vehicle and the carrier and coating materials. Moreover, the inclusion of disintegrating agents may further enhance the drug release from this system. The technique is also applied to design sustained release dosage forms by using hydrophobic carriers. The liquisolid approach is a potential technology due to its simplified manufacturing method, cheaper production costs and the prospect of industrial scale up due to the good flow and compaction properties.

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