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LIQUISOLID TECHNIQUE IN PHARMACEUTICAL FORMULATION: A REVIEW

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ABSTRACT

The technique of liquisolid compacts is a promising method towards enhancing the dissolution of poorly water soluble drugs. In the liquisolid formulation, avicel PH 102 was used as carrier and aerosil was used as coat material, respectively, and polyethylene glycol 600 was used as a nonvolatile liquid to prepare liquid medication. This review article is focused on formulation of liquisolid systems, classification of liquid solid systems and its applications in the field of pharmaceutical sciences.

Key words: Liquisolid, Liquid medication, Formulation.

INTRODUCTION

Poorly water soluble drugs involve many difficulties in the development of pharmaceutical dosage forms for oral delivery systems due to their low bioavailability. In recent years, the number of poorly soluble drug candidates has increased tremendously. Solubility is the most important critical parameter of drug for its oral bioavailability. Development of solid dosage forms for water insoluble drugs has been a major challenge for pharmaceutical scientists for decades [1]. The oral route remains the preferred route of drug administration due to its convenience, good patient compliance and low medicine production costs. In order for a drug to be absorbed into the systemic circulation following oral administration, the drug must be dissolved in the gastric fluids [2]. For hydrophobic drugs, the dissolution process acts as the rate-controlling step and, which determines the rate and degree of absorption. Consequently, many hydrophobic drugs show erratic and incomplete absorption from the gastrointestinal tract. Thus, bioavailability of poorly water-soluble drugs is limited by their solubility and dissolution rate [3].

Over the years, various solid dosage formulation techniques, to enhance the dissolution of poorly soluble substances, have been introduced with different degrees of success. Different techniques are employed to enhance the dissolution of poorly soluble drugs like use of water-soluble salts and polymorphic forms, solid dispersions, reducing particle size to increase the surface area, pH adjustments, co-precipitation, polymeric modification, lyophilization, microencapsulation, inclusion of drug solutions or liquid drugs into soft gelatin capsules, solubilization in a surfactant system, Liquisolid compacts and manipulation of solid state of drug [4]. Among various techniques to achieve the better dissolution rates Liquisolid technology is one of the novel and most promising techniques for promoting drug dissolution. Advantages of this technique are its low cost, simplicity of formulation, and applicability to industrial production. Drug solution is prepared by dissolving the drug in non-volatile vehicle. Even though the drug is in a tablet, it is held in solution form. Based on the dissolution step, a pre-requisite for drug absorption may be bypassed and higher bioavailability of poorly soluble drugs obtained [5]. Among various techniques to overcome solubility problem, several researchers reported that formulation of a liquisolid tablet was one of the most promising techniques for improving drug dissolution. Employing this liquisolid technique, a liquid medication may be converted into a dry-looking, non-adherent, free flowing and readily compressible powder by simple blending with selected powder excipients referred to as carrier and coating materials [6].

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Asian J. Pharm. Res. Vol 6, Issue 2, 47-50, 2016.

Liquisolid tablets advantages over the conventional tablets

1) Liquisolid systems are low cost formulations than soft gelatin capsules.
2) Production of them is similar to that of conventional tablets.
3) Drug release can be modified using suitable formulation ingredients.
4) Drug can be molecularly dispersed in the formulation.
5) Capability of industrial production is also possible.
6) Enhanced bioavailability can be obtained as compared to conventional tablets.
7) Omit the process approaches like nanonisation, micronization techniques.
8) Differentiate the dosage form by admixture of colour into liquid vehicle.
9) To minimize excipients in formulation compare with other formulations like solid dispersions [7].

APPLICATIONS OF LIQUISOLID SYSTEMS

- Solubility and dissolution enhancement.
- Used efficiently for water insoluble solid drugs or liquid lipophilic drugs
- Rapid release rates.
- Designed for controlled release tablets.

In the liquisolid systems, even though the drug might be in a solid dosage form, it is held within the powder substrate in solution or in a solubilized, almost molecularly dispersed state. Therefore, due to their significantly increased wetting properties and surface area of drug available for dissolution, liquisolid compacts of water-insoluble substances may be expected to display enhanced drug release characteristics and consequently improved oral bioavailability [8].

Classification of liquid solid systems

The liquid solid systems are classified into two categories:
(a) based on the type of liquid medication contained
(i) powdered drug solutions
(ii) powdered drug suspensions
(iii) powdered liquid drugs
(b) Based on the formulation technique used, the liquisolid systems may be classified into two categories:
(i) liquisolid micro systems
(ii) liquisolid compacts

Based on the type of liquid medication contained therein, liquisolid systems may be classified into three subgroups

Powdered drug solution

Regarding "powdered drug solutions," it must be emphasized that their preparation is not a solvent deposition technique since it does not involve drying or evaporation. Since nonvolatile solvents are used to prepare the drug solution or suspension, the liquid vehicle does not evaporate and thus, the drug is carried within the liquid system which in turn, is dispersed throughout the final product depending on the consistency of the powder substrate, the quantity of solid drug dispersed in the liquid medication and the physiochemical properties of the liquid vehicle used the acceptable liquid-to-powder percent ratio will range from 2% to 52%, the most preferable range being 10% to 35% [9].

Powdered liquid drugs

The first two may be produced from the conversion of drug solutions or (e.g. prednisolone solution in propylene glycol) or drug suspensions (e.g. gemfibrozil suspension in Polysorbate 80), and the latter from the formulation of liquid drugs (e.g. clofibrate, valproic acid, liquid vitamins, etc.), into liquisolid systems [10].

Liquisolid Microsystems

The term liquisolid Microsystems refer to the capsules prepared by combining the drug with a coating material ad with a carrier together with the inclusion of an additive example: PVP in the liquid medication wherein the resulting size may be as much as 5 times that of liquid solid

Liquisolid compact systems

The powder can retain only limited amount of liquid while maintaining acceptable flow and compression properties. Liquisolid compacts are prepared using the previously outlined method to produce tablets or capsules, whereasthe liquisolid micro systems are based on a new concept which to produce an acceptably flowing admixture for encapsulations [11].

LIQUID LOAD FACTOR

In liquisolid system, the carrier and coating materials can retain only certain amounts of liquid while maintaining acceptable flow and compression properties depending on the excipients ratio used. The excipients ratio R (R = Q/q) of powder is defined as the ratio between the weights of carrier (Q) and coating (q) materials present in the formulation. Preparation of a liquisolid system with an acceptable flowability and compressibility is possible if a maximum liquid on the carrier material is not exceeded. This characteristic amount of liquid is termed the liquid load factor (Lf). The Lf is defined as the weight ratio of the liquid medication (w) and carrier powder (Q) in the system (i.e., Lf = W/Q) [12].

Requirements for Preparation of Liquisolid Systems
Drug candidates

Examples of drug candidates include digoxin, digitoxin, prednisolone, hydrocortisone, spironolactone, hydrochlorothiazide, polythiazide, and other liquid medications such as chlorpheniramine, water insoluble vitamins, fish oil, etc

Asian J. Pharm. Res. Vol 6, Issue 2, 47-50, 2016.

Non-volatile Solvents

Various non-volatile solvents used for the formulation of liquisolid systems include Polyethylene glycol 200 and 400, glycerin, polysorbate 80 and propylene glycol

Carrier Materials

These include grades of microcrystalline cellulose such as Avicel PH 102, Lactose11, Eudragit RL and RS12

- Coating Material

Coating material include silica (Cab-O-Sil M5 8, 9, Aerosil 20013, Syloid, 244FP8,

- Disintegrants

Most commonly used disintegrant is sodium starch glycolate (explotab13, pumogel [13].

Recent studies on liquisolid compact technique

Swamy *et al.*, 2013 studied on formulation and evaluation of telmisartan liquisolid tablets.Improved release telmisartan liquisolid tablets were formulated using Avicel Ph 102 and Aerosil 200 as the carrier and coating material respectively .The drug undergoes dissolution in the non volatile liquid(Polyethylene glycol 400) which leads to a molecular dispersion of the drug in the formulation that could result in faster dissolution of the drug from the formulation [14]. Debnath *et al*., 2015worked onformulation, development and in-vitrorelease kineticsof telmisartan tablet prepared by liquisolid technique. In-vitrodrug release of Telmisartan compacts showed increase in dissolution rate of Telmisartan. So PEG 400, PG, Tween 80 could be economic substitute as dissolution enhancing agent [15]. Ashokbhai *et al.,* 2015 studied theformulation, optimization and evaluation of liquisolid tablets containing tadalafil.*In-vitro* drug release of liquisolid tablets were higher compared to control and marketed tablets due to its less contact angle and more wettability. Significantly improved dissolution profile was observed for all liquisolid formulation as compared to that of marketed formulation as indicated from *in-vitro* dissolution study (108.33%) which was due to presence of polyethylene glycol which increase fluid penetration in to formulations. Moreover the desirability value of various dependent variables was found to be nearer to one [16]. Jain *et al.,* 2014 studied on comparison of liquisolid and inclusion complexation technique for dissolution rate enhancement of valsartan. The drug undergoes dissolution in the non volatile liquid which leads to a molecular dispersion of the drug in the formulation that could result in faster dissolution of the drug from the formulation. The increased dissolution rate may be due to increased wetting and increased surface area of the particles [17]. Javaheri *et al*., 2014 studied on wet granulation to overcome liquisolid technique issues of poor flowability and compatibility: a study to enhance glibenclamide dissolution.The aim of this study is to apply wet granulation on liquisolid powders to overcome issues of poor powder flowability and compressibility especially with using high viscosity liquid vehicles. This new technique is the wet granulation process to be applied with liquisolid powders just before the compaction stage of the powders into tablets. Consequently, it was found that by application of wet granulation to liquisolid powder admixture, the large-scale production of liquisolid compacts is feasible and can be easily applied by pharmaceutical industry [18].

CONCLUSION

Liquisolid formulations are designed to contain liquid medications in powdered form, and hence possess drug delivery mechanisms similar to that of soft gelatin capsule preparations containing liquids. This novel technique is found to be efficient method for formulation of water insoluble solid drugs and liquid lipophilic drugs. Rapid disintegration rates are observed compared to conventional tablets and therefore, they show improved release rates and hence greater bioavailability. The use of nonvolatile solvent in the formulation causesincreased wettability of water insoluble drugs and ensures molecular dispersion of drug in the formulation. Modification of formulation by use of certain agents cause sustained release of drugs from the liquisolid tablets.

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Nil

CONFLICT OF INTEREST

No interest

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