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LIQUISOLID COMPCT: A NOVEL APPROCH TO ENHANCE BIOAVAILABILITY OF POORLY SOLUBLE DRUG

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ABSTRACT

Liquisolid technique is a new and promising method that can change the dissolution rate of water insoluble drugs. According to the new formulation method of liquisolid compacts, liquid medications such as solutions or suspensions of water insoluble drugs in suitable non-volatile liquid vehicles can be converted into acceptably flowing and compressible powders by blending with selected powder excipients. It has been speculated that such systems exhibit enhanced release profiles. In this case, even though the drug is in a solid dosage form, it is held within the powder substratein solution or, in a solubilized, almost molecularly dispersed state, which contributes to the enhanced drug dissolution properties. Large scale production of fabricated drug on commercial level.succesful liquisolid tablet is a determination of optimal flowable liquid retention.

Keywords: Liquisolid compacts; Liquid medication; mathematical model; liquid load factor

INTRODUCTION

Liquisolid technique is a new and promising method that can change the dissolution rate of drugs. It has been used to enhance dissolution rate of poorly water-soluble drugs. For poorly soluble (Class II) drugs and class (Class IV) the rate of oral absorption is often controlled by the dissolution rate in the gastrointestinal tract. The new 'liquisolid'' technique may be applied to formulate liquid medications (i.e., oily liquid drugs and solutions, suspensions or emulsions of water-insoluble solid drugs carried in nonvolatile liquid vehicles) into powders suitable for tableting or encapsulation. Since, the liquisolid tablets contain a solution of the drug in suitable solvent; the drug surface available for dissolution is tremendously increased.

Due to 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. In this case, even though the drug is in a solid dosage form, it is held within the powder substrate in solution or, in a solubilized, almost molecularly dispersed state, which contributes to the enhanced drug dissolution properties. [1]

CLASSIFICATION:

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

- Powdered drug solutions
- Powdered drug suspensions
- 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.

B. Based on the formulation technique used, liquisolid systems may be classified into two categories, namely,

- Liquisolid compacts
- Liquisolid microsystems

Liquisolid compacts are prepared using the previously outlined method to produce tablets or capsules, whereas the liquisolid microsystems are based on a new concept which to produce an acceptably flowing admixture for encapsulations. [2]

ADVANTAGES OF LIQUISOLID COMPACT

1. A great number of slightly and very slightly water-soluble and practically water-insoluble liquid and solid drug can be formulated into liquisolid systems using the new formulation-mathematical mode
2. This technique is successfully applied for low dose water insoluble drug.
3. The absolute bioavability of the drug from the liquisolid tablet is 15% higher than that commercial one.
4. There production cost is lower than that of soft gelatin capsules because the production of liquisolid systems is similar to that of conventional tablets.
5. Drug dissolution from liquisolid compact is independent to the volume of dissolution media.
6. Most of liquid or solid 'water-insoluble drug' may be formulated into immediate release or sustained release 'Liquisolid compact' or 'Liquisolid microsystem. [3]

LIMITATIONS

1. This technique is not applicable for high dose insoluble drug.
2. Mathematical calculation require [4]

Components of Liquisolid Compact Formulation:

Liquisolid compact mainly includes

1. Non volatile solvent
2. Disintegrant
3. Carrier material
4. Coating material

Non volatile Solvent: Non volatile Solvent should be Inert, high boiling point, preferably water-miscible and not highly viscous organic solvent systems and compatible with having ability to solubilise the drug. The non volatile solvent acts as a binding agent in the liquisolid formulationVarious non-volatile solvents used for the formulation of liquisolid systems include Polyethylene glycol 200 and 400, glycerin, polysorbate 80 and propylene glycol.

Disintegrant: Superdisintigrants increases the rate of drug release, water solubility and wettability of liquisolid granules. Mostly superdisintigrants like sodium starch glycolate and crosspovidone.

Carrier Materials: Carrier material should be porous material possessing sufficient absorption properties which contributes in liquid absorption. The carrier and coating materials can retain only certain amounts of liquid and at the same time maintain acceptable flow and compression properties hence; increasing moisture content of carrier's results in decreased powder flowability these include grades of microcrystalline cellulose such as avicel PH 102 and avicel PH 200, 20.

Coating Materials: Coating material should be a material possessing fine and highly adsorptive particles which contributes in covering the wet carrier particles and displaying a dry-looking powder by adsorbing any excess liquid. Coating material is required to cover the surface and maintain the powder flowability34.Coating material includes silica (Cab-O-Sil) M520, 35, Aerosil 20030, Syloid, 244FP 20, 35 etc.[5]

Basic theoretical aspect to formulate Liquisolid Compact: These studies are related to the flow and compression of formulation. The mathematical model of liquisolid systems is based on the flowable (Φ – value) and compressible (Ψ – number) liquid retention potentials of the constituent powders. According to the theories, the carrier (Q) and coating powder(q) materials can retain only certain amounts of liquid while maintaining acceptable flow and compression properties. Depending on the excipient ratio (R) of the powder substrate, where:

$R = Q/q$…… (1).

Which is the fraction of the weights of the carrier (Q) and coating (q) materials present in the formulation, an acceptably flowing and compressible liquisolid system can be prepared only if a maximum liquid load on the carrier material is not exceeded. Such a characteristic amount of liquid is termed the liquid load factor (Lf) and defined as the weight ratio of the liquid medication (W) and carrier powder (Q) in the system, i.e. :

$Lf = W/Q$ ….. (2)

It should be emphasized that the terms 'acceptably flowing' and 'acceptably compressible' imply preselected and desirable levels of flow and compaction which must be possessed by the final liquid: powder admixtures. Essentially, the acceptable flow and compaction characteristics of liquisolid systems are ensured and, in a way, built in during their manufacturing process via the (Φ –

value) and (Ψ – number) concepts, respectively. These are introduced for fundamental properties of powders and are referred to as their flowable and compressible liquid-retention potentials. The maximum amount of liquid loads on the carrier material, termed ‘‘load factor” (Lf). The coating/carrier ratio (R) is important for determining the ‘‘optimum flowable load factor” (Lf) which gives acceptable flowing powders and is characterized by the ratio between (W) and (Q), as shown in Eqs. 1 and 2.

Lf = Φ CA + Φ CO (1/R….. (3) Where, Φ CA is the flowable liquid-retention potential of the carrier and Φ CO is the flowable liquid-retention potential of the coating material

Preparation of liquisolid tablets: Calculated quantities of drug and non-volatile solvent is accurately weighed in 20 ml glass beaker and then heated to dissolve the drug in that solvent. The resulting hot medication is incorporated into calculated quantities of carrier and coating materials. Mixing process is carried out in three steps as described by Spireas et al.

During the first stage, the system is blended at an approximate mixing rate of one rotation per second for approximately one minute in order to evenly distribute liquid medication in the powder. In the second stage, the liquid/powder admixture is evenly spread as a uniform layer on the surfaces of a mortar and left standing for approximately 5 min to allow drug solution to be absorbed in the interior of powder particles.

In the third stage, the powder is scraped off the mortar surfaces by means of aluminum spatula and then blended with sodium starch glycolate for another 30 seconds in a similar way to the first stage. This gives final liquisolid formulation to be compressed. [7]

Pre-formulation Studies:

Pre-formulation Studies includes

1. Determination solubility of drug in different non-volatile solvents
2. Determination of angle of slide
3. Determination of flowable liquid retention potential (Φ value)
4. Calculation of liquid load factor (Lf)
5. Liquisolid compressibility test (LSC) [8]

Pre Compression Evaluations: The flowability of a powder is of critical importance in the production of pharmaceutical dosage forms in order to get a uniform feed as well as reproducible filling of tablet dies, otherwise, high dose variations will occur. In order to ensure the flow properties of the liquisolid systems that will be selected to be compressed into tablets and further evaluated, angle of repose measurements, Carr’s index and Hausner’s ratios were adopted. [9]

Post compression Evaluations:

a) Content of uniformity
b) Hardness
c) Weight variation
d) Friability
e) Disintegration
f) In - vitro dissolution studies

These are should be in the official limits prescribed by official pharmacopoeia. [10]

Evaluation of Liquisolid Systems:

Flow behavior: Flow properties are the important concern in the formulation and industrial production of tablet dosage form. Angle of repose is characteristic to the flow rate of powder. In general, values of angle of repose ≥ 40ºindicate powders with poor flowability.

Differential Scanning Calorimetry (DSC): It is necessary to determine any possible interaction between excipients used in the formulation. This will also indicate success of stability studies41. If the characteristic peak for the drug is absent in the DSC thermogram, there is an indication that the drug is in the form of solution in liquisolid formulation and hence it is molecularly dispersed within the system.

X-ray diffraction (XRD): Generally, disappearance of characteristic peaks of drug in the liquisolid formulation and retaining peaks of carrier material is observed. This indicates that drug gets converted to amorphous form or in solubilized form in the liquisolid formulation.

Electron Microscopy (SEM): After SEM study, complete disappearance of crystals of drug which confirms that drug is totally solubilized in liquisolid system and this ensures the complete solubility.

Fourier Transform Infrared spectroscopy: FTIR studies are performed to determine the chemical interaction between the drug and excipients used in the formulation. The presence of drug peaks in the formulation and absence of extra peaks indicates there is no chemical interaction. [11]

In vivo evaluation of Liquisolid tablets: Khaled et al.10 evaluated liquisolid tablets in beagle dogs. They found that absolute bioavailability of drug from

liquisolid tablets was 15% higher than marketed tablets. [12]

Dissolution testing of Liquisolid formulations: Works of many researchers revealed that dissolution rate improvement is observed in case of liquisolid formulation. It was also proved that at low drug concentrations in liquid medication, more r apid release rates are observed. This may be due to the precipitation of drug within silica pores at high drug concentration. [13]

Applications of Liquisolid Tablets: Rapid release rates are obtained in liquisolid formulations. These can be efficiently used for water insoluble solid drugs or liquid lipophilic drugs. Sustained Release of drugs which are water soluble drugs such as propranolol hydrochloride has been obtained by the use of this technique. [14]

CONCLUSION

In conclusion, liquisolid compact refers to formulations formed by conversion of solid state to liquid state, drug suspensions or drug solution in non-volatile solvents into dry, non-adherent, free-flowing and compressible powder mixtures by blending the suspension or solution with selected carriers and coating agents. The formed liquisolid tablets dosage form showed significantly greater extent of absorption due to their solubility and dissolution improvement. The technique is also used to design sustained release systems by using hydrophobic carriers instead of hydrophilic carries in liquisolid systems. Therefore, this formulation of the drug has the potential to be considered for human study in order to be manufactured on a large scale.

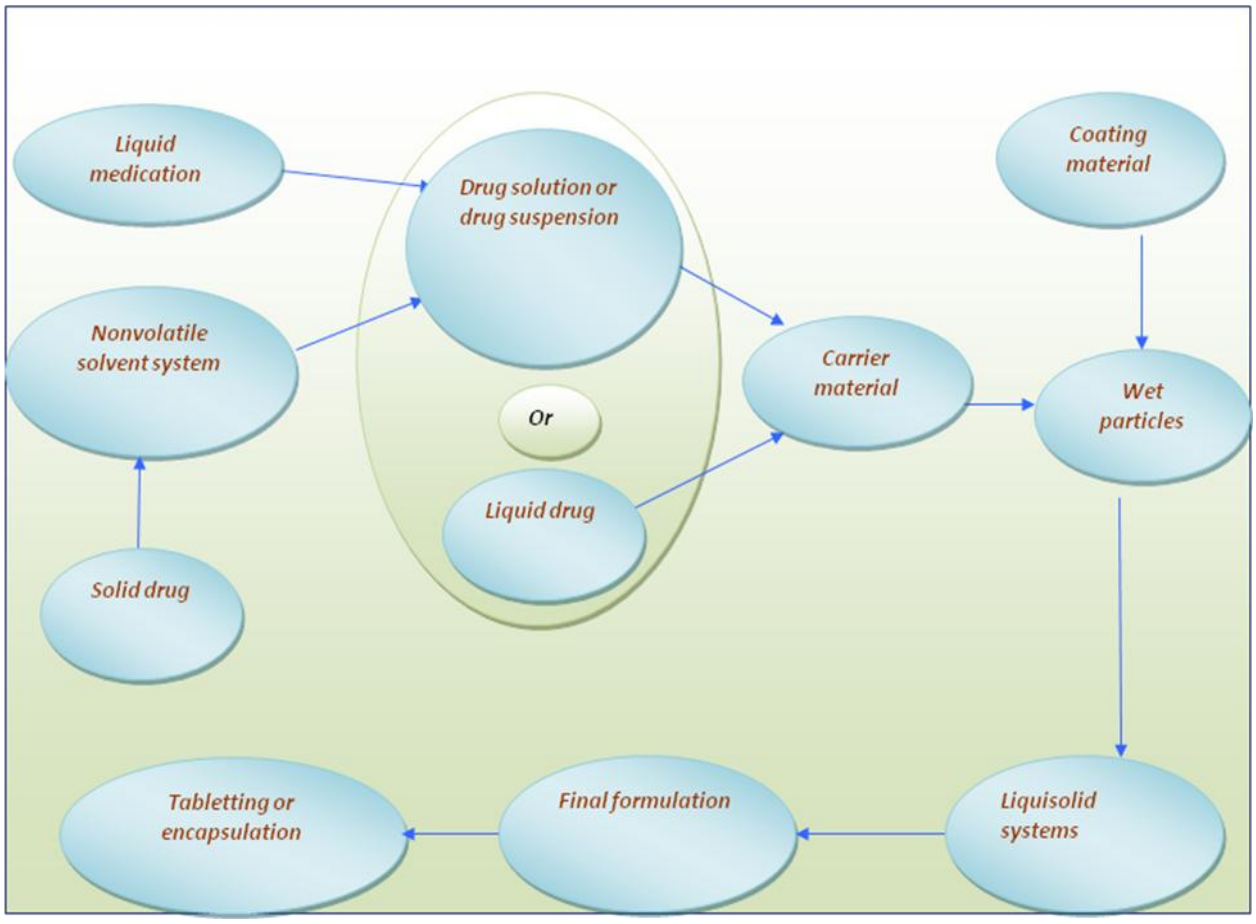

Fig 1: Steps involved in the preparation of liquisolid systems. [6]

REFERENCES

1. Stegemann S. Leveiller F. et.al. Eur J Pharm Sci, 2007; 31: 249-61.
2. Nokhodchi A. J Pharm Sci, 2005; 8(1):18-25.
3. Javadzadeh Y. Nokhodchi A. Int J Pharm, 2007; 341:26-34.
4. Spireas S. Liquisolid Systems and Methods of Preparing Same. U.S. Patent 6423339 B1 200..
5. AE Amal, T Ngiik. Eur J Pharm Biopharm, 2009; 73: 373–8.
6. Javadzadeh Y, et al. J Pharm pharm Sci, 2005; 8: 18- 25.
7. SS Spireas, CI Jarowski, BD Roher. Pharm Res, 1992; 9: 1351-8.
8. Fahmy RH, Kassem MA. Eur J Pharm Biopharm, 2008; 69: 993-1003.
9. Khaled KA, Asiri YA and El-Sayed YM. Int J Pharm, 2001; 222:1-6.
10. Smirnova I, Suttiruengwong S, Seiler M, Arlt M. Pharm Dev Tech, 2004; 9: 443-5.
11. Tayel SA, Soliman II, Louis D. Eur J Pharm Biopharm, 2008; 69: 342-347.
12. N Ali, JYousef, JN Bacharach. Int J Pharm, 2007; 341, 26-34.
13. D Louis, A Saadia, Tayel, I Iman, Soliman. Eur J Pharm Biopharm, 2008; 69, 342-7.