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Liquisolids-A Technique for Dosage Formulation with Improved Solubility of Active Principle

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ABSTRACT:

Liquisolid technique is a novel approach for the concept of dosage formulation to improve the bioavailability, dissolution rates and rapid disintegration of water insoluble drugs via oral route of administration. In this technique of formulation involves drugs dissolved in suitable non-volatile liquid vehicles, and converted in to powdered forms of liquid medications compact, they are compressible and acceptably industrial applicable by combination with selective powder excipients. The liquisolid technique allows the formulation transformation into solid drug delivery systems. With this technique as compare to commercial conventional tablet it shows confirmed increasing dissolution rates in addition to improved bioavailability. Approach has been successfully applied for poorly soluble drugs in release of low dose enhancement. However, for the high dose drugs one of the limitations for the formulation because of more liquid/vehicle required for the drug dissolution procedure as well high amounts of carrier and coating material are required in due course foremost to an unacceptably high tablet weight.

KEY WORDS: Liquisolids, Class II drugs, solubility enhancement, carriers coating materials, Liquid medication.

INTRODUCTION:

The liquisolid compacts defined as an used for formulating liquid medication such as oily liquid drug and solutions or suspensions of water-insoluble or poorly water soluble solid drugs in non-volatile vehicles, into acceptably flowing and compressible powders[1]

Generally poorly soluble drugs (BCS Class II drugs) correspond to a technological defy because of their poor bioavailability due to its poor water solubility ensuing in low drug absorption. Over past few decades, many of techniques to improve the solubility and dissolution of poorly soluble substances have been developed, with dissimilar degrees of accomplishment which includes micronization, lyohilization, solid dispersion, etc.[2] Out of which the Liquisolid technique is a recent approach that has emerged as a promising strategy for enhancing the release of poorly soluble drugs.[3][4]

Liquisolid solid technique is acceptably flowing and compressible powdered forms of liquid medications.3 With this technique liquisolid formulation contains non-volatile liquid vehicle drug, solid carrier, and coating materials. In liquisolid technique Solutions or suspensions of poorly soluble drugs in a non-volatile liquid vehicle that are converted into acceptably flowing and compressible powders by use of excipients like carrier and the coating material with simple physical blending. Usually, as an excipients microcrystalline cellulose and colloidal silica are used as a carrier and the coating material. Water-miscible

organic solvent systems with high boiling point such as liquid polyethylene glycols, propylene glycol, or glycerine are most excellent fitting as liquid vehicles. As the carrier is saturated with liquid, a liquid layer is formed on the particle surface which is immediately adsorbed by the fine coating particles.[5][6]

Hence, the liquisolid technology allows the transformation of liquid systems into solid/oral drug delivery systems such as tablets.

"Liquid medication" entails the drug solutions, as in "powdered solutions", drug suspensions, emulsions, or liquid oily drugs. Therefore, in contrast to "powdered solutions", the term "liquisolid compacts" is more universal and it may encompass for dissimilar formulation. Which are "powdered drug solutions", "powdered drug suspensions", "powdered drug emulsions", and "powdered liquid drug".[7]

CLASSIFICATION OF LIQUISOLID TECHNIQUES

Depends on the type of liquid medication liquisolid Technique may be classified into three categories.[8]

- Powdered drug solutions
- Powdered drug suspensions
- Powdered liquid drugs

Depends on the formulation liquisolid Technique may be classified into two categories,

- Liquisolid compacts
- Liquisolid Microsystems

The term "liquisolid compacts" refers to immediate or sustained release tablets or capsules prepared, combined with the inclusion of appropriate adjuvants required for tabletting or encapsulation, such as lubricants, and for rapid or sustained release action, such as disintegrants or binders, respectively.

The term "liquisolid Microsystems" refers to capsules prepared by combining the drug with carrier and coating materials, combined with inclusion of an additive e.g., PVP in the liquid medication wherein the resulting unit size may be as much as five times that of liquisolid compacts.[8]

COMPONENT OF LIQUISOLID TECHNIQUE

Non-volatile solvents

There are several non-volatile solvents are used in the liquisolid technique like glycerine, Polyethylene glycol 200 and 400, propylene glycol and polysorbate 80. The non volatile solvent acts as a binding agent in the liquisolid formulation.[9]

Drug candidates

Liquisolid technique mostly useful for drugs having poorly soluble or water insoluble drugs which have low bioavailability including chlorpheniramine, Losartan Pottasium, digitoxin, Lercanidipine, hydrochlorothiazide, prednisolone, polythiazide, spironolactone, and other liquid medications such as water insoluble vitamins, fish oil, etc.[10][11]

Carrier materials

Microcrystalline cellulose (MCC) PH 101,MCC PH 200,Lactose,Methyl cellulose ,Ethyl cellulose, starch1500,Ethocel etc. are porous material contributes in liquid absorption. Carrier and coating materials are to maintain acceptable flow and compression properties.[12][3]

Coating materials

It is having fine and highly adsorptive property, such as various types of silica, which contributes in covering the wet carrier particles and displaying a dry looking powder by adsorbing any excess liquid. In liquisolid technique liquid may altered to free flowing, compressible dry powder by simple mixing with several excipients like carrier and coating material.[8]

Disintegrants

Generally sodium starch glycolate (Explotab, Pumogel, etc.) used as disintegrant.[13]

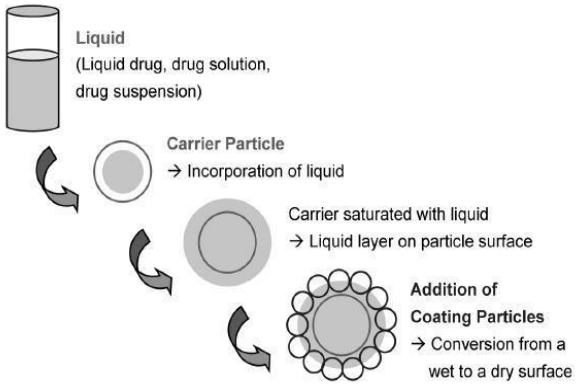

Figure 1: Schematic diagram of liquisolid technique.

METHOD OF PREPARATION FOR LIQUISOLID DOSAGE FORM

PROCEDURE :

As shown in figure 2, a liquid lipophilic drug (eg. Chlorpheniramine, clofibrate, etc.) is formulated

Drugs should be dissolved firstly in suitable non-volatile solvent to prepare drug solution or drug suspension.

⇩

Convinced amount prepared drug solution or suspension, or the liquid drug itself is integrated into a specific quantity of carrier material which should be porous and possessing adequate absorption properties.

⇩

After it, calculated amount of coating material is added to above mixture to achieve dry-looking, non adherent, free-flowing and readily compressible powder by the simple addition and mixing. Excipients possessing fine and highly adsorptive particles like amorphous silicon dioxide (silica), are most suitable for this step.

⇩

Before compression or encapsulation, various adjuvants such as lubricants and disintegrants (immediate) or binders (sustained-release) may be mixed with the finished liquisolid technique to produce liquisolid compacts i.e. tablets or capsules.[14]

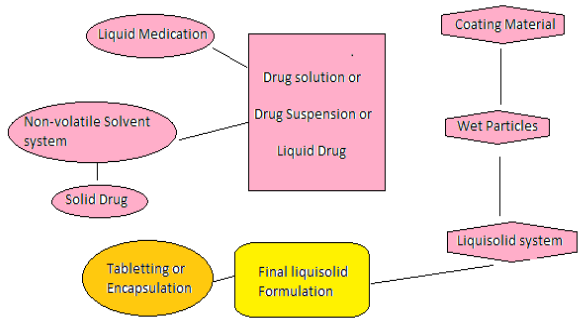

Figure. 2: Schematic outline of steps involved in the preparation of liquisolid formulation.

Evaluation of liquisolid techniques:

In liquisolid compacts flowability and compressibility are addressed simultaneously at the preparation of mathematical model for liquisolid technique, which was used to calculate the appropriate quantities of the carrier and coating materials required to produce acceptably flowing and compressible powders based on new fundamental powder properties called the flowable liquid retention potential (Φ - value) and compressible liquid retention potential (Ψ - number) of the constituent powders.[15][16]

Determination of drug in different non-volatile solvents: Prepare saturated solution of by using drug in non-volatile solvents. And analyse saturated solution of drug with use of spectrophotometer[17]

Determination of angle of glide: Collect the required amount of carrier at metal plate with polished surface and it is gradually increase till the plate becomes horizontal from angular at which powder is about to glide.20 It was used to measure the flow properties of powders. The angle of 33° is optimum for flow of powders.

Determination of liquid flowable liquid retention potential (Φ): when maximum liquid weight is retained per unit powder material in order to produce acceptably flowing liquid/powder admixture is called as flowable liquid retention potential (Φ). Excipients quantities was calculated by the Ø value .This Φ –value of powders may be determined using a new procedure, the liquisolid flowability (LSF) test.

Equation for this is as follows:

Lf= Ø + Ø (1 / R)

Where Ø and Ø are the constant Ø values of carrier and coating materials, respectively. By calculating Lf and W, we can calculate the amount of Q and q required for liquisolid systems.[13]

Calculation of liquid load factor (Lf)) It is defined as the ratio of weight of liquid medication (w) to weight of carrier material (Q). The drug is dissolved in various concentrations of non-volatile solvents the carrier coating material is added with blending.[18]

Lf=W/Q

W=ratio of weight of liquid medication

Q= weight of carrier material

The liquid load factor that ensures acceptable flowability

(Lf), and can be measured by:

Lf= (1/R)

Liquisolid compressability test (LSC)

It was developed to determine Ψ values and it involves carrier coating material admixture preparation system,[19] preparing several uniform liquid/powder admixtures to tablets, determining average hardness, measuring of average liquid content of crushed tablets, as well as determining plasticity, sponge index and Ψ value and Lf.

Flow behavior: Angle of repose, Carr's index and Hausner's ratio were used to make sure the flow properties of the liquisolid technique.[20] In the pharmaceutical dosage forms production powder flowability is important in order to reduce high dose variations.[21]

Pre compression studies of the prepared liquisolid Powder systems: For the ensured the suitability of the selected excipients, several studies are to be performed like Fourier Transform Infra Red Spectroscopy, Differential scanning Calorimetry, X-ray Diffraction and Scanning Electron Microscope. In addition, for the select the optimal formulae for compression, flowability studies are also to be carried out prior to the compression of the powders the dosage forms such as into tablets and capsules.

Contact angle measurement: Method is imaging method for to determine contact angle directly for a drop of liquid latent on a plane surface of the solid, so it is called imaging method. It is for the measuring of or assessment of wettability, contact angle of liquisolid tablets is determine according to the imaging method. In this method dissolution media is prepare of saturated solution of drug and drop from the same is put on the surface of tablets. Finally measure the height and diameter of sphere drop on the tablet for calculating the contact angles.[22]

In vitro dissolution studies: As forwarding to moving parts of research regarding this technique revealed that technique of liquisolid compacts could be a promising alternative for formulation of water-insoluble drugs. This technique has been successfully useful for the improvement of the in-vitro drug release of poorly water soluble drugs as like Carbamazepine, hydrocortisone, Piroxicam etc. As well as several water insoluble drugs have shown higher bioavailability in rats as compared to their commercial counterparts.

In vivo evaluation of liquisolid systems: The liquisolid technique is a important technique for increasing bioavailability of drug by enhancing solubility of the drug of poorly water soluble drugs. The absorption characteristics of Hydroclorothiazide liquisolid compacts in comparison with commercial tablets were studied in beagle dogs. Bioavailability of the liquisolid and the commercial tablets were observed through significant differences in the area under the plasma concentration-time curve, the peak plasma concentration and the absolute. However, for the mean residence time, the mean absorption time, and the rate of absorption no significant differences were found. The absolute bioavailability of the drug of liquisolid compacts was 15% higher than that from the commercial formulation was found.[23]

MERITS OF LIQUISOLID SYSTEMS

- Formulating liquid medication.
- Simple method for preparation.
- By the liquisolid system there are several water-insoluble solid drug can be formulated.
- Enhanced oral administration of poorly soluble drugs.
- New approach for conventional dosage form.
- Feasible for industrial production.
- As compared to commercial counterparts Exhibits are Standard for in-vitro drug release.
- Can be used in controlled release, Optimized sustained release drug delivery liquisolid drug formulation demonstrate with constant dissolution rate.
- Drug can be molecularly dispersed in the formulation.

DEMERITS OF LIQUISOLID SYSTEMS

- Suitable for only lower dose lipophilic drugs.
- Particle agglomeration: because of more surface charge on isolated small particles.

List of Drugs that can be incorporated into liquisolid systems [24][25][26]

- Atovaquone
- Albuterol Sulfate Inhalation Aerosol
- Calfactant
- Drospirenone and Estradiol

- Fluocinolone Acetonide Oil Ear Drops
- Rizatriptan Benzoate
- Metronidazole
- Tretinoin Cream

CONCLUSION:

According to liquisolid technique, Conventional dosage form like tablet, capsule can be formulate by converting acceptably flowing and compressible powders, from the liquid medications such as solutions or suspensions of poorly water soluble drug dissolving with suitable non-volatile vehicle through simple physical blending. It acceptably suitable for large scale production in industry due to simple method, low cost and capability. Liquisolid technique is promising alternative for achieving improved bioavailability and dissolution properties of water insoluble drugs as compare to commercial drugs.

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