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Liquid Solid Compact Technique -A Review

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ABSTRACT - Liquisolid system is the combination of liquisoild technique and orodispersible technique. The Liquisolid system is to improve dissolution rate of water insoluble drugs and to enhance dissolution rate of water soluble drugs which is a substantial problem confronting the pharmaceutical industry.The liquid-solid compact technique/powered solution technology is a new and promising technology towards the enhancement of the solubility and bioavailability of the insoluble drug moiety.This technique is based upon dissolving the insoluble drug in the nonvolatile solvent and admixture of drug loaded solutions with a carrier and coating materials to convert into acceptably flowing powders suitable for tableting or encapsulation.

Keywords: Dissolution rate, Liquisolid compacts, Liquid loading factors and poorly water-soluble drugs.

I. INTRODUCTION

Bioavailability is the major principle of a drug for its therapeutic effectiveness, which in turn depends upon the solubility of that drug in gastrointestinal fluid. Dissolvability a significant parameter to accomplish the ideal convergence of medication in fundamental flow for pharmacological reaction to appear. The drugs which are poorly water soluble will be inherently released at a slow rate owing to their limited solubility within the gastrointestinal contents. The increase in solubility in turn subsequently improves absorption and bioavailability[1]. Liquisolid compacts are powdered types of fluid meds that allude to fluid medications, arrangement, and suspensions of water-insoluble strong medications conveyed inappropriate non-unpredictable dissolvable frameworks named the fluid vehicles. The liquisolid technique was applied to formulate water-insoluble solid drugs into non-volatile liquid vehicles into powders suitable for tableting or encapsulation[2].. So for this type of dosage forms that can rapidly disintegrate/dissolve to release the drug as soon as they come in contact with saliva, thus without the need for water during administration, an attempt that makes them highly attractive for pediatric and geriatric patients.

LIQUISOLID SYSTEM

The liquisolid strategy was first presented by Spireas et al. what's more, was connected to join water insoluble medications into quick discharge strong measurements frames. The fluid medicine alludes to solid drugs which are scattered inappropriate non-unpredictable fluid vehicles. By blending such fluid prescription with chose bearers and covering materials, dry-looking, non-disciple, free-streaming and promptly perfect powder admixtures can be created. Spireas proposed that the particles have a permeable surface with high assimilation properties which might be utilized as the transporter material, for example, cellulose, starch, and lactose. Covering material, for example, silica is required to cover the surface thus keep up the powder flowability[2]. In these frameworks, the medication is as of now in arrangement structure in the fluid vehicle, while in the meantime, it is done as a powder. Thus, the liquisolid innovation helps the transformation of fluid frameworks into strong medication conveyance systems such as tablets. The liquisolid approach has been effectively connected to expand solvency and upgrade of medication arrival of low portion ineffectively dissolvable medications.

However, this technique cannot be applied to high dose poorly soluble drugs.

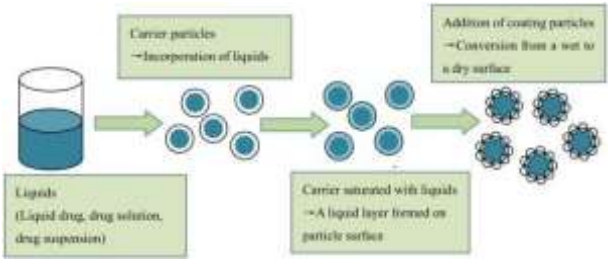

Figure 1 Theoretical Concept of Liquisolid System

CLASSIFICATION OF LIQUISOLID SYSTEM

I Based on the type of liquid medication, liquisolid systems may be Classified as:

1. Powdered drug solutions
2. Powdered drug suspensions
3. Powdered liquid drugs

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II Based on the formulation technique used, liquisolid systems are classified into two Categories:

1. Liquisolid compacts

2. Liquisolid Microsystems

Liquisolid compacts: refers as immediate sustained-release tablets or capsules

Liquisolid Microsystems: refers as capsules prepared by liquisolid systems

The wettability of the liquisoild compacts in the dissolution media is one of the proposed mechanisms for explaining the enhanced dissolution rate from the liquisolid compacts [3].

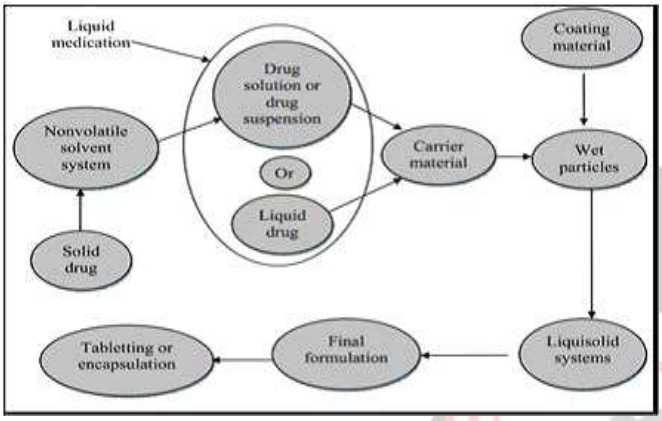

Figure 2 Steps involved in the preparation of liquisolid systems

LIMITATIONS

 Not relevant for plan of high portion insoluble medications.

 If more measure of bearer is added to create free-streaming powder, the tablet weight increments to more than one gram which is hard to swallow.

 Acceptable pressure properties may not be accomplished since during pressure fluid medication might be crushed out of the liquisolid tablet bringing about tablets of inadmissible hardness.

II.APPLICATIONS

 Rapid release rates.

 Used for water insoluble solid drugs or liquid lipophilic drugs.

 Sustained release of drugs.

 Solubility and dissolution improvement.

 Flowability and compressibility.

 Designing of controlled release tablets.

 Bioavailability enhancement.

 Application in probiotics.

 Improvement of the drug photostability.

Advantages

1. It is reasonable strategy for medications with high penetrability and ineffectively water solvent.

2. It is reasonable strategy for essentially insoluble fluids and strong medications.

3. It is appropriate strategy for upgrade of bioavailability of ineffectively water solvent medications.

4. It is reasonable method for upgrade of disintegration profiles.

5. It is reasonable method for development of uncovered medication surface territory to the disintegration medium.

6. It is reasonable method, explicitly for powdered fluid prescriptions.

7. It is reasonable method for figure into prompt discharge or continued discharge measurements shapes.

8. In this liquisolid system, generation consumption is low contrasted with delicate gelatin containers

9. It is utilized in controlled medication conveyance frameworks.

10. Medication can be molecularly scattered in the plan

11. Medication discharge can be changed utilizing appropriate detailing fixings.

12. Separate the dose structure by admixture of shading into fluid vehicle.

13. Capacity of mechanical creation is additionally conceivable.

14. To limit excipients in definition contrast and different plans like strong scatterings.

15. Preclude the procedure methodologies like nanonisation, micronization strategies.

16. Medication is figured in a tablet structure or embodied measurement structure and is held in solubilized

fluid state, which gives created or upgraded medication wetting properties in this way improving sedate disintegration profiles.

III. COMPONENTS OF LIQUISOLID SYSTEMS

The major formulation components of liquisolid compacts are.

1. Carrier material

These are compression-enhancer preferably porous particles possessing a sufficient absorption property which contributes in liquid absorption.

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E.g. starch, lactose, sorbitol, Avicel PH 102 and 200, Eudragit RL and RS, amorphous cellulose etc.

2. Coating material

These are flow-enhancing, very fine (10 nm to 5,000 nm in diameter), highly adsorptive coating particles (e.g., silica of various grades like Cab-O-Sil M5, Aerosil 200, Syloid 244FP etc.) contributes in covering the wet carrier particles and displaying a dry-looking powder by adsorbing any excess liquid.

3. Non-volatile solvents

Inert, high boiling point, preferably water-miscible and not highly viscous organic solvent systems. E.g. Polyethylene glycol 200 and 400, glycerin, polysorbate 80 and propylene glycol, polysorbates, glycerin, N, N-dimethylacetamide, fixed oils, etc.

4. Disintegrant

The Superdisintegrants increases the water solubility and wettability of liquisolid granules and also increases drug release. So the Superdisintegrants like sodium starch glycolate and crosspovidone and croscarmellose sodium are used.

IV. MECHANISM OF DRUG RELEASE

1. Increase in surface area

The drug within the liqui-solid system is in molecularly dispersed state. So, the surface area of drug available for release is much greater than that of drug particles within directly compressed tablets.

2. Increase in wettability

The liquid vehicle can either act as surface active agent, the wetting properties of the liqui-solid primary particles is improved. Wettability of these systems has been demonstrated by measurement of contact angles and water rising times.

3. Increase in aqueous solubility of drug

To expand the general solvency in the liqui-solid conservative frameworks, moderately limited quantity of fluid vehicle isn't adequate. Notwithstanding, at the solid/fluid interface between an individual liqui-solid essential molecule and the discharge medium it is conceivable that in this microenvironment the measure of liquidvehicle diffusing out of a solitary liqui-solid molecule together with the medication particles may be adequate to expand the watery solvency of the medication if the fluid vehicle goes about as a cosolvent[8].

V. METHOD OF PREPARATION

A certain amount of the prepared drug solution or suspension or a liquid drug itself is incorporated into a specific quantity of carrier material which should be preferably of a porous nature and possessing sufficient absorption properties.

The resulting wet mixture is then converted into a dry, non adherent, free-flowing and readily compressible powder by the simple addition and mixing of a calculated amount of coating material.

Excipients possessing fine and highly adsorptive particles are suitable for this step. Before compression or encapsulation, various adjuvants like lubricants and super-disintegrants added to final liquisolid system to produce liquisolid compacts.

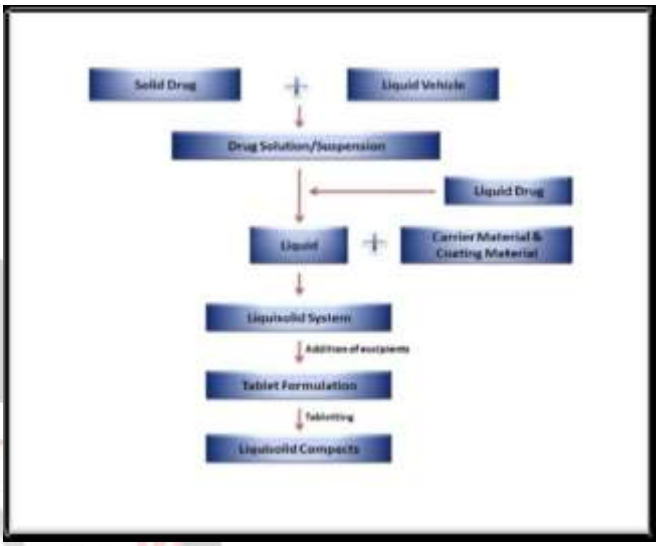

Figure 3 Method of preparation of liquisolid systems

VI. PREFORMULATION STUDIES

Preformulation studies performed to confirm the physiochemical characterization and it includes the following studies

• Solubility studies of the drug in solvents

• Sliding angle determination

The solubility of drug in non-volatile solvents

A saturated solution of the drug is prepared and is used for solubility studies. A surplus of the drug is added to vehicles which results in saturated solution by employing the shaker for the solution at a given period of time under steady vibration. The filtrate of the drug solutions are then analyzed spectrophotometrically.

Angle of slide

Sliding angle measures the flow behavior of powders. A metallic plate with a smooth surface is used for the test, where the test powder is placed at one end of it, is gradually raised till the plate becomes angular to the horizontal plane, at which the powder just slides. The powder having an angle of 33° provides optimum flow characteristics.

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VII. EVALUATION OF LIQUISOLID SYSTEM

- Flow behaviour
- Differential Scanning Calorimetry (DSC)
- X-ray diffraction (XRD)
- Scanning Electron Microscopy (SEM)
- Dissolution testing

Flow behavior

Bulk density

Weighed quantities of the powder blend is transferred into a graduated measuring cylinder. The bulk volume (Vb) of the weighted amount of the powder (W) is determined. Bulk density is given below: nt of crushed tablets

$$\text{Bulk density} = W/Vb$$

Tapped density

The weighed amount of powder mass is poured to a graduated measuring cylinder and tapped for a fixed number of times and the volume is determined (Vt). Tapped density can be given by,

$$\text{Tapped density} = W/Vt$$

Compressibility index

Compressibility index is given by the following equation:

Compressibility index = (tapped density – bulk density)/tapped density *100

Compressibility index values lower than 15 % shows good flow characteristics of powders and values higher than 25 % indicate poor flow nature.

Hausner's ratio The indirect measurement of flow pattern of powders is given by:

Hausner's ratio = Tapped density / Bulk density

A value below<1.25 indicates good flow behavior, whereas>1.5 signify poor flowability. Hausner's ratio can vary depending on method used for the determination, so it is not taken as a critical parameter in flow behaviour[4].

Differential scanning calorimetry (DSC) Thermal behavior of the pure components and the liquisolid compacts can be assessed by DSC studies. About 3–5 mg of the sample is vacuum-packed in aluminum pans exposed to the invariable rate of heating 10 °C/min at a temperature range of 30 to 300 °C. Aluminum pans which are vacant are used as references and by purging nitrogen, the entire thermal behavior is studied. The absence of characteristic peak of the drug in presence of excipients is an indication of incompatibility of drug with excipients as well as changes in the crystalline pattern of the drug, may be a molecular level changes from a crystalline to amorphous pattern.

X-ray diffraction (XRD) studies

XRD studies determines the crystalline property of the liquisolid compact mixture by X-Ray diffractometer. The study uses a current of 30 mA and copper target at a voltage of 40 kV. The instrument works at a scanning angle of 5 to 70 ° and a counting rate of 0.4 s/step. The change in the peak pattern from distinct and sharp to random pattern gives evidence about the conversion of crystalline nature of drugs to amorphous forms of drug.

Scanning electron microscopy

This technique helps in determining the surface behavior of the drug, which gives an idea whether the drug is crystallized from the liquisolid system. The solubilized nature of the drug in liquisolid system results in the disappearance of these molecular forms.

***In vitro* drug release studies**

In vitro release studies of the liquisolid tablets is performed using USP dissolution apparatus type II. The studies are carried out in 900 ml 0.1 N HCl maintained at a constant temperature 37 °C±2 °C at a stirring speed of 50 to 200 rpm. After adding a known amount of drug equal formulation into the media, the percentage of drug dissolved is determined by withdrawing the samples at regular intervals and sink conditions are maintained by replacing with fresh buffer. The drug concentration can be determined spectro-photometrically.

VIII. CONCLUSION

Liquisolid technology is the impending move towards enhancing the solubility of the water-insoluble drug by using a simple industrialized process and lower production cost by the use of relatively inexpensive excipients. Due to the enhanced water solubility and dissolution rate, the extent of absorption of drugs can be increased. It can also be employed to design immediate and sustained release system by means of hydrophilic and hydrophobic carriers. Liquisolid technology employs liquid portion as suspensions or solution of poorly soluble drugs in a suitable nonvolatile liquid vehicle which are then changed to effortlessly smooth and compactable powders by simple physical blending with particular ingredients such as carrier and coating agent. This technology is found to be truly promising as the solubility and dissolution related problems of drugs, especially BCS class II and IV which leads to poor bioavailability.

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