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REVIEW ARTICLE

Liquisolid Compacts Technique of Poor Water Soluble Drugs: An Overview

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ABSTRACT:
Liquisolid technique is new and promising method that can use to enhance the dissolution rate of poorly water soluble drugs. Liquisolid compact technique is based upon the dissolving the drug in a suitable non-volatile solvent by using carrier and coating material for the conversion of acceptable flowing and compressible powders. By applying the mathematical models the carrier and coating materials optimized. In this case the drug is almost solubilised in the solvent or molecularly dispersed state which contributes the enhanced drug dissolution.

KEYWORDS: Liquisolid technique, poorly water soluble drugs, dissolution rate enhancement, oral bioavailability.

INTRODUCTION:
Liquisolid technique is a new and promising method that can change the dissolution rate of poor water soluble drugs which comes under BCS Class II category. For poorly soluble (Class II) drugs, 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 liquisolid tablet by using liquid medication, carrier and coating material with super disintegrating agent. Since, the liquisolid tablets contain a solution of the drug in suitable solvent; the drug surface available for dissolution is 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 bioavailability.[1,2]

DEFINITIONS:
Liquid Medication includes liquid lipophilic drugs and drug suspensions or solutions of solid water insoluble drugs in suitable non-volatile solvent systems.

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Liquisolid System refers to powdered forms of liquid medications formulated by converting liquid lipophilic drugs, or drug suspensions or solutions of water insoluble solid drugs in suitable nonvolatile solvent systems, into dry, on adherent, free-flowing and readily compressible powder admixtures by blending with selected carrier and coating materials.

Carrier material refers to a preferably porous material possessing sufficient absorption properties, such as microcrystalline and amorphous cellulose, which contributes in liquid absorption.

Coating material refers to a material possessing fine and highly adsorptive particles, 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.[3]

ADVANTAGES:
1. The water-insoluble solid drug can be formulated into liquisolid systems.
2. The liquisolid compact can be applied to formulate liquid medication such as oily liquid drugs.
3. Simplicity.
4. Better availability of an orally administered water insoluble drug.
5. Lower production cost.

6. The production of liquisolid system is similar to the conventional tablets.
7. Can be used in controlled drug delivery.

DISADVANTAGES:
1. Liquisolid system having a low drug loading capacities.
2. The carrier and coating materials are required.
3. The liquisolid technique is not applicable to high dose insoluble drug.
4. It is only applicable to low dose drug and only water insoluble drugs.
5. It does not require chemical modification of drugs.

APPLICATIONS:
1. It is used to improve bioavailability of water.
2. Several water insoluble drugs on dissolving in different non-volatile solvents have been formulated into liquisolid compacts.
3. The rapid release rates are obtained in liquisolid formulations.
4. These can be efficiently used for water insoluble solid drugs or liquid lipophilic drugs.
5. Solubility and dissolution improvement.[4,5]

CLASSIFICATION:
1. Powdered drug solution
2. Powdered drug suspensions
3. Powdered liquid drugs.[6]

NEED OF LIQUISOLID SYSTEM:
The oral route is a preferred route of drug administration due to its convenience, good patient compliance and low production costs. In order for a drug to absorb into the systemic circulation following oral administration, the drug must be dissolved in the gastric fluids. Thus, the major challenges to drug development today is poor solubility, as an estimated 40% of all newly developed drugs are poorly soluble or insoluble in water. In addition, up to 50% of orally administered drug compounds suffering from formulation problems related to its low solubility and high lipophilicity. Bioavailability of poorly water soluble hydrophobic drugs (class II in biopharmaceutics classification system) is limited by its solubility and dissolution rate. The dissolution rate of poorly water soluble drugs can be improved by decreasing particle size surface area. The increase the dissolution rate of drugs by decreasing the particle size, to form a nanoparticles and microparticles, to overcome the dissolution problem. The technique of 'liquisolid compacts' is a new and promising approach towards dissolution enhancement. Liquisolid compacts having an acceptable flowability & compressibility properties.[7]

COMPONENT OF LIQUISOLID COMPACT:

1. Drug Candidates:
Ex. Poor water soluble drug.

2. Non-Volatile Solvents:
Different non-volatile solvents used to formulate liquisolid compact. Ex. PEG 400

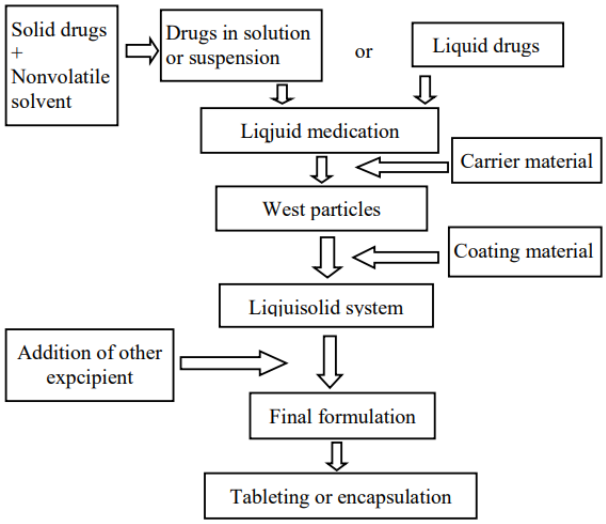
3. Carrier materials:
Carrier material having sufficient ingestion properties. Carrier material having adsorbing properties. Ex. Avicel PH 102, Avicel PH 302, Avicel PH 200

4. Coating materials:
The coating material having a fine and profoundly adsorptive particles, for example, different forms of silica, which helps in covering the wet transporter particles and showing a dry looking powder by adsorbing any over abundance fluid. The fluid parcel, which can be a fluid medication, a medication suspension or a medication arrangement in a suitable nonvolatile fluid vehicle, is consolidated into the permeable bearer material.

5. Disintegrants:
Disintegrants like sodium starch glycolate, cross caramilose sodium crosspovidone etc.[8]

Steps Involved in Formulation:
1. Suitable drug candidate is dispersed in suitable non volatile solvent like Polysorbate 80, PEG 200 etc. having different Drug: Solvent ratios.
2. In this step suitable carrier material with other excipients are added into initial mixture of drug and non volatile solvent. During this continuous mixing in the mortar should be going on.
3. In the third step suitable super disintegrants like sodium starch Glycolate or Crosspovidone is added in the prepared mixture with continuous shaking in a mortar.
4. In this step suitable coating material is added which adsorbs the layer of excess non volatile solvent over the carrier material. Due to this the liquid layer gets converted in the solid layer and this gives the dry, non adherent, free flowing powder particles.
5. The final mixture is then allowed to compress by using tablet compression machine.
6. The prepared liquisolid tablet is then evaluated for its solubility, dissolution, compressibility. [9]

Method of Preparation[10]



Pre Compression Studies:

1 Flow properties: Flow properties of liquisolid formulation were studied by angle of repose, Carr's index, and Hausner's ratio. Each analysis was carried out in triplicate. Bulk density measurements were carried by placing a fixed weight of powder in a graduated cylinder, and the volume occupied.[11]

Pre-formulation Studies:

Pre-formulation Studies includes

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

Pre Compression Evaluations

The flow ability 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.[12]

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.[13]

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 ≥ 40º indicate powders with poor flow ability.

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 studies. If the characteristic peak for the drug is absent in the DSC thermo gram, 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.

Scanning 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):

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.

Estimation of drug content:

The liquisolid compacts are powdered well and powder equivalent to 10 mg of the drug is accurately weighed and suitably diluted using methanolic sulphuric acid. The drug content is calculated by at wavelength using UV-Visible spectrophotometer. [14]

***In-vitro* drug release study:**

The *in-vitro* dissolution study is carried out for a period of 1 hour using USP XXIV type-II (paddle) method with 900 ml of 0.1 N HCl and distilled water as the dissolution media at required rpm and 37oC+0.5oC. 10 ml of the sample is withdrawn and filtered at periodic time intervals in minutes. 10ml of fresh dissolution fluid is replaced to the baskets to maintain the constant

volume (sink condition). The filtered samples are analyzed at wavelength by UV/Visible spectrophotometer. The mean of n=3 determination sis used to calculate the percentage drug release from each formulation.[15]

CONCLUSION:

Enhancement of solubility and dissolution rate of poorly water one of the most promising approaches to increase solubility and dissolution rate. This soluble drug is a major aspect in pharmaceutical scientists. So many techniques have reported to improve drug solubility as well as dissolution rate, but liquisolid compact technique is getting higher solubility and dissolution rate. Highest drug release rates are observed in liquisolid compact system and this system may be optimized by selection of liquid vehicle and carrier and coating materials. Finally this review is concluded that, various techniques are involved for the drug bioavailability enhancement, and this technique is the most promising approaches because it's simplified manufacturing method, cheaper production costs and also the prospect of industrial scale up due to the good flow and compaction properties.

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