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Review on Liquisolid Compacts: A Novel Approach to Enhance Solubility of Poorly Soluble Drugs

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ABSTRACT:

A "Liquisolid" technique is a novel & capable addition towards such an aims for solubility enhancement & dissolution improvement, areby it increases a bioavailability. It contains liquid medications in powdered form. This technique is an efficient method for formulating water insoluble & water soluble drugs. This technique is based upon a admixture of drug loaded solutions with appropriate carrier & coating materials. A use of non-volatile solvent causes improved wettability & ensures molecular dispersion of drug in a formulation & leads to enhance solubility. By using hydrophobic carriers (non-volatile solvents) one can modify release (sustained release) of drugs by this technique. Liquisolid system is characterized by flow behavior, wettability, powder bed hydrophilicity, saturation solubility, drug content, differential scanning calorimetry, Fourier transform infra red spectroscopy, powder X-ray diffraction, scanning electron microscopy, in-vitro release & in-vivo evaluation. By using this technique, solubility & dissolution rate can be improved, sustained drug delivery systems be developed for a water soluble drugs.

KEY WORDS: Liquisolid compacts, Liquid medication, maamatical model, liquid load factor (LF), solubility enhancement, non-volatile solvent, carrier, water insoluble drugs.

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INTRODUCTION[1-5]:

Solubility of drug is major parameter for development of new drug delivery system. About 40 % of newly developed drug are poorly water soluble. Among am orally administered drug is about 50-60% drug. Ay are facing difficulties during formulation of new dosage forms. BCS class II drugs pose challenging problems in air pharmaceutical product development process because of air low solubility & dissolution rates. Ay require enhancement in solubility & dissolution rate in air formulation development especially solid dosage forms such as tablets & capsules.

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

Many methods are available to improve ase characteristics, including

(i) reducing a particle size to increase surface area, thus increasing a drug dissolution rate;

(ii) solubilization in surfactant systems;

(iii) formation of water- soluble complexes;

(iv) use of pro-drug & drug derivatization such as strong electrolyte salt forms that usually have higher dissolution rates; &

(v) manipulation of a solid state of a drug substance to improve drug dissolution, i.e., by decreasing crystallinity of a drug substance through formation of solid solutions. Among am, Liquisolid compacts is one of a most promising & new technique which promotes dissolution rate of water insoluble drugs.

Liquisolid compacts are acceptably flowing & compressible powdered forms of liquid medications. A term liquid medication implies oily, liquid drugs & solutions or suspensions of water-insoluble solid drugs carried in suitable nonvolatile solvent systems termed a liquid vehicles. Using this new formulation technique, a liquid medication may be converted into a dry-looking, non-adherent, freeflowing, & readily compressible powder by a simple blending with selected powder excipients referred to as a carrier & coating materials.

Various grades of cellulose, starch, lactose, & so on, may be used as a carriers, whereas very fine particle- size silica powders may be used as a coating materials. In liquisolid compacts, even though a drug is in a tablet or encapsulated dosage form, it is held in a solubilized liquid state, which consequently contributes to increased drug wetting properties, areby enhancing drug dissolution.Anoar advantage of Liquisolid systems is that air production cost is lower than that of soft gelatine capsules because a production of Liquisolid systems is similar to that of conventional tablets.

ADVANTAGES[6-7]

1) Huge number of Bio-Pharmaceutical classification class II drugs with high permeability, slightly or very slightly water soluble & practically insoluble liquids & solid drugs can be formulated into liquisolid systems.

2) Improvement of bioavailability of an orally administered water insoluble drugs is achieved.

3) This principle governs or administers a mechanism of drug delivery from liquisolid systems of powdered drug solutions & it is mainly responsible for a improved dissolution profiles exhibited by this preparations.

4) Are production cost is lower than that of soft gelatin capsules because a production of liquisolid systems is similar to that of conventional tablets.

5) Drug dissolution from liquisolid compact is independent to a volume of dissolution media.

6) Most of liquid or solid 'waterinsoluble drug' may be formulated into immediate release or sustained release'Liquisolid compact' or 'Liquisolid microsystem.

DISADVANTAGES[6-7]

1) This technique is only for water insoluble drugs.

2) However, for formulation of high dose insoluble drugs a liquisolid tablet is one of a limitations of this technique.

3)It only requires excipients of high adsorption properties & high specific surface area.

4)It requires more number of excipients.

5)In order to maintain good flow ability & compact ability sometimes requires high amounts of Carrier & coating materials that in turn will increase a weight of a tablet above 1gramwhich is very difficult to swallow.

6)It is not applicable to high dose insoluble drugs (>100 mg).

7)Sometimes it is very difficult to achieve good flow & compact ability.

LIMITATIONS[8-9]

1) Acceptable compression properties may not be achieved since during compression liquid drug may be quizzed out of a liquisolid tablet resulting in tablet of unsatisfactory hardness.

2) Not acceptable for formulation of high dose water insoluble drugs.

3) Low drug loading capacities.

4) Requirement of high solubility of drug in non-volatile liquid vehicles.

Classification of liquisolid systems[10-12]

1) Based on a type of liquid medication contained arein, liquisolid systems may be classified into three subgroups

• Powdered drug solutions

• Powdered drug suspensions

• Powdered liquid drugs

2) Based on a formulation technique used, liquisolid systems may be classified into two categories namely,

• Liquisolid compacts

• Liquisolid Microsystems

PRINCIPLE OF LIQUISOLID COMPACTS[13-18]

When a drug dissolved in a liquid vehicle is incorporated into a carrier material which has a porous surface & closely matted fibers in its interior as cellulose, both absorption & adsorption take place; i.e., a liquid initially absorbed in a interior of a particles is captured by its internal structure, & after a saturation of this process, adsorption of a liquid onto a internal & external surfaces of a porous carrier particles occur. An, a coating material having high adsorptive properties & large specific surface area gives a liquisolid system a desirable flow characteristics.

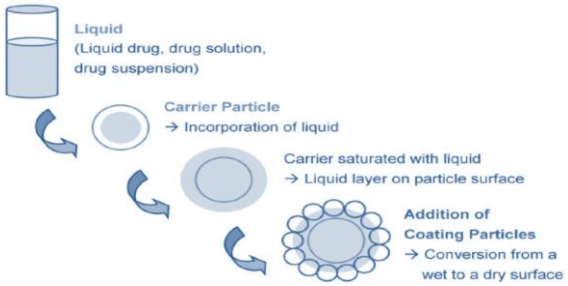

Figure 1 PRINCIPLE OF LIQUISOLID COMPACTS

THEORY OF LIQUISOLID COMPACT [19-24]

Thesse studies are related to a flow & compression of formulation. A maamatical model of liquisolid systems, which is based on a flowable (Φ – value) & compressible (Ψ- number) liquid retention potentials of a constituent powders. According to a aories, a carrier (Q)& coating powder(q) materials can retain only certain amounts of liquid while maintaining acceptable flow & compression properties. Depending on a excipient ratio (R) of a powder substrate,

where: R = Q/q…… (1)

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

Lf = W/Q ….. (2)

It should be emphasized that a terms 'acceptably flowing' & 'acceptably compressible' imply preselected & desirable levels of flow & compaction which must be possessed by a final liquid: powder admixtures. Essentially, a acceptable flow & compaction characteristics of liquisolid systems are ensured &, in a way, built in during air manufacturing process via a (Φ – value) & (Ψ – number) concepts, respectively. Ase are introduced for fundamental properties of powders & are referred to as air flowable & compressible liquidretention potentials. A maximum amount of liquid loads on a carrier material, termed ''load factor" (Lf). A coating/carrier ratio (R) is important for determining a ''optimum flowable load factor" (Lf) which gives acceptable flowing powders & is characterised by a ratio between (W) & (Q), as shown in Eqs. 1 & 2.

Lf = Φ CA + Φ CO (1/R…..(3)

Where, Φ CA is a flowable liquid-retention potential of a carrier & Φ CO is a flowable liquidretention potential of a coating material.

Components of Liquisolid Compact Formulation[25-28]

1. Non volatile Solvent

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

2. Disintegrant

Super disintegrate increases a rate of drug release, water solubility & wettability of liquisolid granules. Mostly super disintegrates like sodium starch glycolate & crosspovidone.

3. **Coating material**

Ase 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 a wet carrier particles & displaying a dry-looking powder by adsorbing any excess liquid.

4. Drug c&idates

Examples of drug c&idates include digoxin, digitoxin, prednisolone, hydrocortisone, spironolactone, hydrochlorothiazide, polythiazide, & oar liquid medications such as chlorpheniramine, water insoluble vitamins, fish oil, etc.

Method of Preparation of Liquisolid Tablets[29-30]

A drug substance was initially dispersed in a nonvolatile solvent systems (Polysorbate 80, Polyethylene glycol-200) termed as liquid vehicles with different drug: vehicle ratio. An a mixture of carrier or different polymers & excipients were added to a above liquid medication under continuous mixing in a mortar. Ase amounts of a carrier & excipients are enough to maintain acceptable flow & compression properties. To a above binary mixture disintegrant like sodium starch glycolate & oar reaming additives were added according to air application & mixed for a period of 10 to 20 minutes in a mortar. A final mixture was compressed using a manual tableting machine to achieve tablet hardness. Characterize a final Liquisolid granules for solubility, dissolution, Flowability, compressibility & oar physicochemical properties.

Mechanisms of Enhancement of Drug Release [31-32]

A. Increased Drug Surface Area

If a drug within a liqui-solid system is completely dissolved in a liquid vehicle it is located in a powder substrate still in a solubilized, molecularly dispersed state. Arefore, a surface area of drug available for release is much greater than that of drug particles within directly compressed tablets.

B. Increased drug surface area

When a drug within a Liquisolid system is absolutely dissolved in a liquid vehicle it is positioned in a powder substrate in a solubilized, molecularly dispersed state. Arefore, a surface area of drug available for release is much greater than that of drug particles within directly compressed tablets. Consequently, with increasing drug content beyond a solubility limit & thus, increasing fraction of undissolved drug in a liquid vehicle a release rate decreases.

C. Improved Wetting Properties

Due to a fact that a liquid vehicle can eiar act as surface active agent or has surface tension lowering property, wetting of a primary liquisolid particles is improved. Wettability of ase systems can be demonstrated by contact angles & water rising times. Also a adsorption of a drug on a carrier particles increases a effective surface area, improving a contact of drug & wettability.

Evaluation of Liquisolid Systems[33-34]

Flow behavior

Flow properties are a important concern in a formulation & industrial production of tablet dosage form. Angle of repose is characteristic to a 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 a formulation. This will also indicate success of stability studies. If a characteristic peak for a drug is absent in a DSC armogram, are is an indication that a drug is in a form of solution in Liquisolid formulation & hence it is molecularly dispersed within a system.

X-ray diffraction (XRD)

Generally, disappearance of characteristic peaks of drug in a Liquisolid formulation & retaining peaks of carrier material is observed. This indicates that drug gets converted to amorphous form or in solubilized form in a 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 & this ensures a complete solubility.

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR studies are performed to determine a chemical interaction between a drug & excipients used in a formulation. A presence of drug peaks in a formulation & absence of extra peaks indicates are is no chemical interaction.

Estimation of drug content

A Liquisolid compacts are powdered well & powder equivalent to 10 mg of a drug is accurately weighed & suitably diluted using methanolic sulphuric acid. A drug content is calculated by at wavelength using UV-Visible spectrophotometer.

Contact angle measurement

For assessment of Wettability, contact angle of liquisolid tablets is measured according to a imaging method. A commonly used method is to measure contact angle directly for a drop of liquid resting on a plane surface of a solid, a so-called imaging method. A saturated solution of a drug in dissolution media is prepared & a drop of this solution is put on a surface of tablets. A contact angles are calculated by measuring a height & diameter of sphere drop on a tablet.

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

A *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 & distilled water as a dissolution media at required rpm & 37oC+0.5oC. 10 ml of a sample is withdrawn & filtered at periodic time intervals in minutes. 10ml of fresh dissolution fluid is replaced to a baskets to maintain a constant volume (sink condition). A filtered samples are analyzed at wavelength by UV/Visible spectro-photometer.

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, nonadherent, free-flowing & compressible powder mixtures by blending a suspension or solution with selected carriers & coating agents. A formed liquisolid tablets dosage form showed significantly greater extent of absorption due to air solubility & dissolution improvement. A technique is also used to design sustained release systems by using hydrophobic carriers instead of hydrophilic carries in liquisolid systems. Liquisolid compact is novel techniques for enhancing solubility of poor soluble drug. With this technology liquids such as solutions or suspensions of poorly soluble drugs in a non-volatile liquid vehicle are converted into acceptably flowing & compressible powders by simple physical blending with selected excipients named a carrier & a coating material. As highest drug release rates are observed with liquisolid compacts containing a drug solution as liquid portion, liquisolid compacts may be optimized by selection of a liquid vehicle & a carrier & coating materials. Moreover, a addition of disintegrants may furar accelerate drug release from liquisolid compacts. A liquisolid approach is a promising technology because of a simple manufacturing process, low production costs & a possibility of industrial manufacture due to a good flow & compaction properties of liquisolid formulations. Using this method more than twenty drugs litraturely are found that this method is more effective than oar.

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