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LIQUISOLID SYSTEM: A REVIEW

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ABSTRACT

The limited solubility of drugs is a challenging issue for industry, during the development of the ideal solid dosage form unit. Liquisolid technique is a novel and promising approach to overcome this consequence. 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. Water-miscible organic solvent systems with high boiling point like propylene glycol, polyethylene glycols, or glycerine are the suitable liquid vehicles. 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 and *in-vivo* evaluation. By using this technique, solubility and dissolution rate can be improved, sustained drug delivery systems be developed for the water soluble drugs. This review article explains the preparation, classification and application of liquisolid system.

Keywords: Liquisolid technique, Carriers, Coating materials.

INTRODUCTION

When a drug is administered perorally in a solid dosage form such as tablet, capsule or suspension it must be released from the dosage form and dissolved in the gastrointestinal fluids before it can be absorbed. The bioavailability of many poorly water-soluble drugs is limited by their dissolution [1]. 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 [2]. Liquisolid technology may be used to transform a liquid into a free flowing, easily compressible and apparently dry powder by simple physical mixing with selected excipients named the carrier and coating material. The liquid portion can be a liquid drug, a drug suspension or a drug solution in suitable non-volatile liquid vehicles [3]. Liquisolid system refers to formulations formed by conversion of drugs into liquid forms, as suspensions or solution in non-volatile solvents into dry, free flowing, non-adherent, and compressible powder mixtures by combining the suspension or solution with selected carriers and coating material [4]. Due to significantly increased wetting properties and surface area of drug available for dissolution, liquisolid compacts of water-insoluble substances expected to display enhanced drug release characteristics and, consequently improved oral bioavailability [5].

CLASSIFICATION

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

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

The first two may be produced from the conversion of drug solutions or drug suspensions and the latter from the formulation of liquid drug into liquisolid systems. Since non-volatile solvents are used to prepare the drug solution or suspension, the liquid vehicle does not evaporate and thus, the drug is carried within the liquid system which in turn is dispersed throughout the finalproduct [6].

Based on the formulation technique used, liquisolid systems may be classified into two categories:

1. Liquisolid compacts
2. Liquisolid Microsystems

Liquisolid compacts: - refers to immediate sustained-release tablets or capsules that are described under "liquisolid systems".

Liquisolid Microsystems: - refers to capsules prepared by "liquisolid systems" plus the inclusion of an additive resulting in a unit size that may be as much as five times less than that of a liquisolid compact [7].

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PREPARATION OF LIQUISOLID COMPACT

Before designing the liquisolid, the Preformulation studies should be performed first, these include

1. Determination of drug in different non-volatile Solvents
2. Determination of angle of slide
3. Determination of flowable liquid retention potential (Ø value)
4. Calculation of liquid load factor (L)
5. Liquid solid compressibility test (LSC)

The flow ability and compressibility of liquisolid compacts are addressed concurrently in the new formulation mathematical model of liquisolid systems, 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 (F value) and compressible liquid retention potential (Ψnumber) of the constituent powders [8].

Determination of drug in different non-volatile solvents

These are carried by preparing saturated solutions of drug in non-volatile solvents, and analyzing them spectophotometrically [9]. Saturated solutions are prepared by adding excess of drug to vehicles and shaking them on shaker for specific time period under steady vibration. After this, the solutions are filtered and analyzed spectrophotometrically.

Determination of angle of slide

The required amount of carrier is weighed and placed at one of a metal plate with a polished surface and it is gradually raised till the plate becomes angular to the horizontal at which powder is about to slide [10]. 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 (F)

It is defined as the maximum weight of liquid that can be retained per unit powder material in order to produce and acceptably flowing liquid/powder admixture. This F – value of powders may be determined using a new procedure, the liquisolid flow ability (LSF) test. The Ø value was used to calculate excipients quantities. Equation for this is as follows:

$L = \boldsymbol{Ø} + Ø\,(1 / R)$

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.

Calculation of liquid load factor (Lf)

It is defined as the ratio of weight of liquid medication (w) to weight of carrier material (Q). Different concentrations of nonvolatile solvents are taken and the drug is dissolved and the carrier coating material is added and blended [11].

Lf=W/Q

W=ratio of weight of liquid medication

Q= weight of carrier material

The liquid load factor that ensures acceptable flow ability (Lf), and can be measured byLf(1/R)

Liquisolid compressibility test (LSC)

It was developed to determine Ψ values and involves steps such as preparing carrier coating material admixture systems, 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 [12].

Calculated quantities of drug are added to the non-volatile solvent and then it is heated to dissolve the drug. This liquid drug solution is added to the carrier and coating materials and then it is mixed properly [13]. The mixing process is carried out in three steps

- The system is blended at a rate of one rotation per second for approximately one minute in order to distribute the drug evenly in liquid.
- This admixture is evenly spread over the motor surface and left standing for 5min.to absorbs the drug into the powder particle.
- Then powder is scraped off and then blended with other excipients for another 30sec. similar to first step. This gives the final formulation of liquisolid compact [14].

COMPONENTS OF LIQUISOLID COMPACT FORMULATION

Liquisolid compact mainly includes

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

1. 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 formulation .Various non-volatile solvents for the formulation of liquisolid systems includes Polyethylene glycol 200 and 400, glycerine, polysorbate 80 and propylene glycol.

2. Disintegrant Super disintigrants increases the rate of drug release, water solubility and wettability of liquisolid granules. Mostly super disintigrants like sodium starch glycolate and cross povidone.

3. 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 flow ability These include grades of microcrystalline cellulose such as avicel PH 102 and avicel PH 200,20.

4. 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 [15].

ADVANTAGES OF LIQUISOLID SYSTEM

1. A great number of slightly and very slightly water-soluble and practically water-insoluble liquid and solid drugs 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 bioavailability of the drug from the liquisolid tablet is 15%higher than that commercial one [16].
4. Their production cost is lower than that of soft gelatine 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 [17].

LIMITATIONS

- Not suitable for formulation of high dose water insoluble drugs.
- If more amounts of carrier is added it increase the flow properties of powder, it may increases the tablet weight too, hence it is difficult to swallow.
- It does not require chemical modification of drugs.
- Acceptable compression may not be achieved because the
- Liquid drug may be squeezed out during compression resulting in unsatisfactory tablet weight [18].

APPLICATIONS

1. It gives rapid release and sustained releases of drugs are obtained in liquisolid formulations.
2. Sustained release of drugs which are water soluble drugs such as propranolol hydrochloride has been obtained by the use of this technique.
3. Solubility and dissolution enhancement.
4. Designing of controlled release tablets.
5. Application in probiotics [19]

EVALUATION OF LIQUISOLID SYSTEMS

In order to ensure the suitability of selected excipients Differential Scanning Calorimetry (DSC), X-ray diffraction (XRD)& Scanning Electron Microscopy (SEM) studies are performed. In addition flowablity studies are also carried out to select the optimal formulae for compression prior to compression of the formulation to tablets.

Flow behaviour

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 $\geq$ 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 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.

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. After complete formulation, Tablets are evaluated by carrying out tests for weight variation, uniformity of tablet thickness and diameter, humidity content using Karl fisher method, friability, hardness, disintegration, dissolution, and content uniformity. All these tests are carried out in triplicate and according to the compendial specifications. For content uniformity test tablets should contain not less than 95% and not more than 105% of the labelled potency. The disintegration test was carried out on six tablets in distilled water at 37 ± 2 ºC using the SP disintegration apparatus [20].

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 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.

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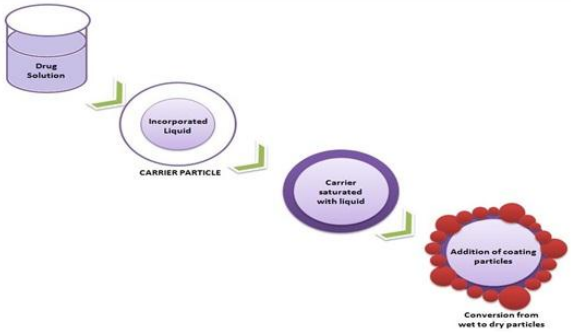
CONFLICT OF INTEREST
The authors declare that they have no conflict of interest.

Fig 1. Schematic representation of Liquisolid systems



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