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Review Article

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LIQUISOLID COMPACTION TECHNIQUE FOR ENHANCING SOLUBILTY AND IMPROVEMENT OF DISSOLUTION

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ABSTRACT

Oral route of administration has been one of the most appropriate and broadly recognized route of delivery for most of therapeutics, because of its benefits such as easily administrable, improved patient compliance and convenience. Many drugs having poor water solubility is restricted by the dissolution rates which depends on the surface area available for dissolution. Enhancement of bioavailability of drugs having poor water solubility is the most challenging aspects for drug development. A more recent technique "Liquisolid compaction technique" has been used to formulate water insoluble medications into solid release forms. It is an innovative and capable practice to overcome this concern and it is based on mixture of insoluble drug in non-volatile solvent and combination of drug loaded solution with suitable carrier and coating substance. The usage of non-volatile solvents improves wettability and assures molecular dispersal of drug in preparation and finally points to increased solubility. Surface area of drug increased with that increased bioavailability and increased aqueous solubility of drug is observed

KEYWORDS: Poorly water solubility, non-volatile, carrier, coating substance, liquisolid compacts.

INTRODUCTION[1]

Solubility is a property of substance in a particular solvent. It is one of important factor to achieved preferred drug concentration in body circulation for pharmacological response. There are many techniques to manage the drug's poor solubility but, the most capable& new method which encourages the rate of dissolution of the water insoluble drug of BCS class II & IV drugs. (liquisolid compaction technique).

Liquisolid systems are generally considered as free flowable and compressible powdered forms of liquid medicaments. (solid water insoluble drugs dissolved into water miscible non-volatile solvent system).

The liquisolid method as described by the spireas is a unique concept, in which the liquid can be converted into a free flow, which is easily compressed and possibly as a dry powder with a simple combination of blend and suitable additives. The liquid component which may be a liquid drug, suspension or drug solution in appropriate non-volatile liquid vehicles is involved in the spongy material.

Following are the major elements involved in the preparation of liquisol compacts are liquid medication, carrier & coating materials.

CONCEPT

Liquisol compaction system is a new and most assuring method that can enhance the dissolution rate. It had been found more effective in improving dissolution rate of poor water soluble drugs. According to BCS classification class II and class IV drugs having low water solubility & is frequently restricted by dissolution rate in the gastrointestinal system. The 'liquisolid' method may be usedto design liquid medicaments into powder suitable for tableting or encapsulation. Though it contain drug solution in suitable solvent so it increases the surface area of drug for dissolution. Due to increased wettability and surface area, it may be estimated to show increased release characteristics and overall improvement of oral bioavailability.

Classification of liquisolid

A) Based upon type of liquid medicaments it contained.

- Powdered solution of drug
- Powdered suspension of drug
- Powdered liquid medications

B) Based upon preparation techniques used.
- Liquisol compacts
- Liquisolid microsystems

Ideal features of components of liquisolid compact
- Drug: Poor soluble, insolvable, liquid or liphophilic, solvability at high boiling point, unsuitable water solvent.
- Carrier: good compressibility, rougher granular.
- Coating material: high surface area, good adhesive properties.
- Non-volatile liquid: water mixable, hydrophilic or lipophilic.

Advantage
- Liquid solid systems are cheaper compared to soft gelatin capsules.
- Improved bioavailability of an water insoluble drug administered orally.
- It has been widely used in drug delivery at a predetermined rate.
- Manufacture of liquisolid systems is like conventional tablets.
- The drug can be molecularly distributed in formulations.
- Capable for industrial production.
- It is used specifically for powdered liquid medications.
- It neglect the process approaches such as nanonisation, micronization technique.
- Discriminate the dosage form by mixture of colour within liquid vehicle.
- By using suitable formulation ingredients drug release can be improved.
- More surface area of drug is available for dissolution medium.

Disadvantage
- It is difficult to prepare high dosage liphophilic drugs of the liquisolid tablet.
- During compression liquid medication may be pressed out of the liquisolid tablet which results in unacceptable hardness of tablets, due to its poor compression properties.
- Mathematical calculations are required.
- The tablet weight increases by more than one gram which is tough to swallow, if more amount of carrier used for producing free flowing granules.

Mechanism of action of liquisolid systems
The three main mechanism involved in improving drug release are:

Increase in drug surface area
The drug inside the liquisolid system is completely dissolved into liquid carrier located in powder substrate still in a solubilized, molecularly distributed state.So, the surface area available for release of drug is much greater than that ofparticles within direct compressible tablets.

Increase in aqueous solubility of drug
A small amount of vehicle present in liquisolid system is insufficient to increase the drug solubility in aqueous dissolution medium. This small amount of vehicle is enough to increase the aqueous solubility of drug having poor solubility, if small amount of liquid vehicle act as co-solvent.

Increase in wettability
By reducing the interfacial tension amongst surface of tablet and medium of dissolution it produces wetting of drug particles in liquisolid system due to presence of non-volatile solvent in it. Thus the contact angle of this system is lowered as compared with conventional preparation hence enhanced wettability.

Components of liquisolid compact[1-3]
The main constituents of liquisolid compacts are:

Carrier material
Compression improvingcomparatively large, rather porous particles possessing enough absorption property which contributes in liquid absorption. Eg. Various grades of cellulose, starch, lactose, sorbitol, etc.

Coating material
These are flow improving, very fine (10 nm to 5000 nm in diameter), highly adsorptive coating particles (Eg. Silica of various grades, aerosol 200, etc.) contributes in covering wet carrier particles and showing a dry looking powder by adsorbing any excess liquid.

Non-volatile solvents
They decreases the interfacial tension amongst the drug and medium of dissolution. Eg. Propylene glycol, glycerin, polysorbates, fixed oils etc.

Disintegrants
The drug release rate, water solubility and wettability of liquisolid systems are increased using disintegrants. Mainly used disintegrants are crospovidone and sodium starch glycolate (explotab 13).

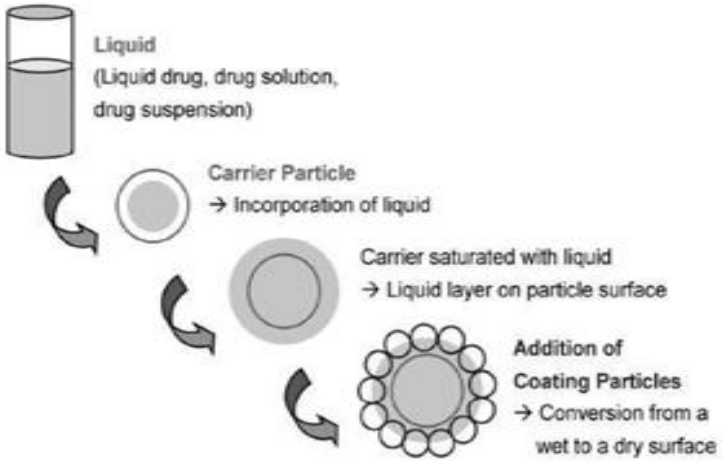

Figure 1: Schematic demonstration of liquisolid systems.

Preparation of liquid solid compacts

Accurately weighed the amount of drug and non-volatile solvent in glass beaker of 20ml and dissolve the drug in solvent by applying heat. Then the above solution is combined with proper quantities of carrier and coating materials. Admixture method is administered by 3 steps.

- Primary stage, the system is mixed at estimated admixture rate for one minute so as to equally distribute liquid medications within the powder.
- The second stage, the liquid/powder mixture is exposed on mortar surface as same layer for five minutes and permit the drug to be absorbed within powder.
- The third stage, the powder is scrapped from the surface of mortar by metal spatula and so emulsified using sodium starch glycolate for an additional thirty seconds in similar manner. It offers liquisolid formulation to be compressed.

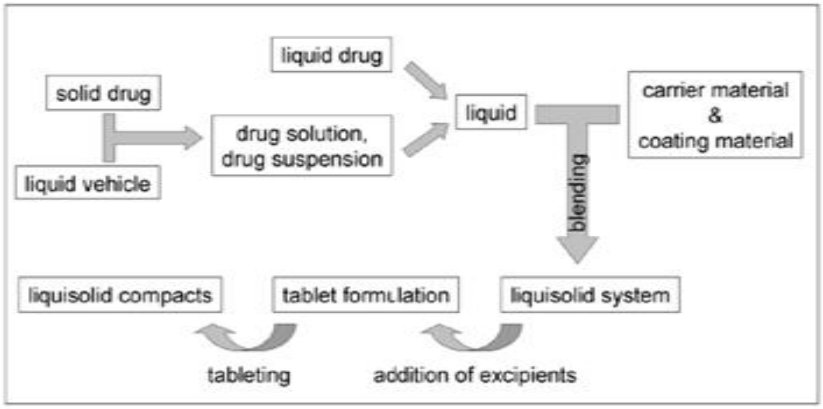

Figure 2: Schematic summary of preparation of liquisolid compacts.

Evaluation parameters of liquisolid compact[1-4]

Pre-compression studies

- The flow of liquisolid compounds is very important for the preparation of solid form. Therefore, it's essential to study the flow properties of those liquisolid powder mixtures before compression. It may be evaluated by parameters such as angle of repose, carr's compressibility index, and hausner's ratio.

- **Angle of repose**

It was determined by using a funnel fixed at proper height. Angle of repose (θ) was measured from the below calculation:

$$\Theta = \tan^{-1} h/r$$

Where "h" and "r" are the height and radius of powder cone.

- **Carr's Compressibility index**

Carr's compressibility index methods are mainly used to determining the compressibility index ofthe dry mixture. Carr's compressibility index can be calculated from below equation.

$$\text{Carr's index} = \frac{(\text{tapped density} - \text{bulk density})}{\text{tapped density}}$$

- **Hausners's ratio**

It was determined using following equation.

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Poured or bulk density}}$$

Post compression evaluation

- Content of uniformity
- Weight variation test
- Hardness
- Friability test
- In-vitro disintegration test
- In-vitro dissolution studies.

Tablet dimensions

Thickness and diameter of the liquisol compact were measured using vernier calliper. Three samples from each formulation used, and mean values were calculated.

Tablet hardness

Tablets are tough to prevent breaking during normal movement and break down properly after administration. It is used to measure mechanical strength. Monsanto hardness tester is used to analyse the hardness of liquidized compact and it is denoted as kg/ cm^2.

Friability

Hardness is a not enough to determine the strength of tablet since some very hard compressed tablets losses their cap portion on abrasion. Hence friability is the method for measuring the tablets strengths. The apparatus used for testing friability of tablet is roche friabilator. 20 tablets were weighed and located in the friabilator, and was allowed torotate apparatus at 25 rpm for 4 minutes. After end of revolutions, the tablets were removed and weighed again.

Weight variation test

Weight difference testing is used to determine if the tablet contains the appropriate amount of medication. Weight difference test according to IP 2007. 20 tablets were randomly chosen and weighed. The average weight of the tablet was also determined. The deviation weight of individual of two tablet from the average weight is not more than 5% deviation.

Drug content uniformity

Randomly selected 20 tablets and their mean weight was calculated, then the tablets were crushed in a mortar and correct weight was calculated from the mixture. Then the above mixture was transferred into 100 ml volumetric flask and diluted with methanol up to a mark. The sample is stirred periodically and kept for atleast one hour for dissolution of drug. Then it is filtered and dilution prepared with suitable diluent. The drug content in each tablet was measured at λmax238 nm using blank reference.

The content uniformity was calculated from the below given formula,

Practical Yield=Absorbance/slope×Dilution Factor

% Drug content=Practical yield/Theoretical yield×100

In vitro disintegration time

The in vitro disintegration time of a tablet is decided by using disintegrating apparatus as per I.P. specification. I.P. specification: put one tablet in every of the half dozen tubes of the basket. Add a disc to every tube and run the equipment using 1.2 pH buffer maintained at 37°C ± 2°C as the immersion liquid. The assembly ought to be raised and down between 30 cycles/min.

In vitro dissolution studies

By using USP type 2 (paddle) method for 1 hour with 900 ml of 0.1 N HCL and distilled water as dissolution media at needed rpm and temperature maintained at 37 ° C + 0.5 ° C. then 10 ml sample was withdrawn at specific time intervals in minutes and fresh same amount of dissolution fluid is introduced into basket for maintaining constant volume. The samples are analysed using UV/Vis spectrophotometer.

Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry is employed to find out the interactions between excipients employed in the preparation. This may additionally indicate the successful stability studies. Once the drug is in the form of solution in liquisolid formulation it's indication of complete disappearance of characteristic peaks and hence it is dispersed molecularly within the system.

X-ray diffraction (XRD)

The diffraction (XRD) patterns are used to determining for drug, excipient utilized in preparation, physical mixture of the drug and excipient, finally for the liquisolid compact. It measures the disappearance of constructive specific drugs peak within the liquisolid preparation and retentive peaks of carrier material. It also indicates that the drug entirely transformed from crystalline to amorphous form or in solubilized form within liquisolid preparation. The amorphization or solubilization of drug within the liquisolid system contributes the resultant improvement within the apparent solubility and additionally the dissolution rate of the drug.

Fourier Transform Infrared Spectroscopy (FT-IR)

FT-IR studies to see the chemical interaction between the drug and excipients employed in the formulation. When the peaks present in drug formulation and absence of additional peaks indicates that there is no chemical interaction. The prepared liquisolid compact were exposed to FT-IR analysis and approximately minimum quantity of less than 4mg was subjected to this analysis.

CONCLUSION

One of the major challenge is to enhance the solubility and dissolution rate of poorly soluble drugs for pharmaceutical scientist. Many techniques have been reported to improve drug solubility, among them the liquisolid compact technique is one among the foremost promising approached. This system is possible stand by for formulation of water-insoluble/soluble drugs. The improved rate of dissolution of drug from liquisolid tablets is practically due to an certain increase in wetting properties and surface area of drug particles available for

dissolution. Therefore they show improved release rates and larger bioavailability. By this system, sustained drug delivery systems were even be developed for water soluble drug.

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