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REVIEW ARTICLE

Liquisolid Compact Techniques – A Latest Review

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ABSTRACT

Introduction: A very large proportion of drugs that are being developed exhibits low water solubility, particularly those drugs which are presented under the (BCS) Class II. This low solubility frequently leads to the poor bioavailability, that leads to difficulties in drug formulation. This review article explores the liquisolid compacts strategy that significantly helps to overcome this problem and aims to enhance rate of drug dissolution and bioavailability of drug in the systemic circulation.

Methods: The liquisolid formulation involves the dissolving or introducing pure drug into a non-volatile liquid base, after that blending it with compatible polymer-based carrier material and coating material to compose compressible powder with no moisture. By increasing the available surface, boosting wettability and encouraging localized dissolution at the powder-solvent interface.

Results: So, this approach is adjustable for sustained-release formulations. The liquisolid formulation offers a simple and efficient method to boost both the dissolution and absorption of drugs with low water solubility.by turning them into a free-flowing moisture free powders that can be directly compressed into a tablet.

Conclusion: this method enhances the drug bioavailability in the systemic circulation and it is much more affordable than other methods and easy to apply using standard manufacturing methods.

Keywords: Bioavailability, BCS Class II Drugs, Dissolution Rate, Liquisolid Systems, Solubility Enhancement.

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INTRODUCTION

Oral dosage form is the most widely used method for delivering of drugs it is due its patient compliance and cost-effectiveness. a major challenge for oral dosage formulation is the poor aqueous solubility of drugs, which tends to limit their Disintegration profile and subsequent bio-accessibility of the drug. In order to address these issues, there are various formulation strategies that have been developed such as solid dispersion, micronisation, lyophilisation and other techniques and among these technique Liquisolid Compact Technique is one the most prominent and showing significant potential results for the enhancement of solubility in aqueous medium and rate of dissolution efficiency of the drug with required limited solubility.[1,2]

Liquisolid technology involves converting of liquid pharmaceutical agent or dissolved a pure drug in a non-volatile solvent into a powder of free flow nature and compressible nature powder, while using specific carrier and coating materials. This enhances the drug wettability and increase surface area leading to the improved dissolution and absorption of the drug. A variety of excipients including lubricant and disintegrants are incorporated to form a liquisolid compact formulation.[3,4]

Classification of liquisolid system[1,2,3]

Based on liquid formulation type

a. Powdered solution of drug substances

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b. Powdered drug dispersion(suspension)

c. Powdered form of liquid-based drugs

Based on formulation technique[6]

a. Liquisolid tablets

b. Liquisolid microsystem

Components of Liquisolid systems

Drug

Non-volatile solvents

Polymer Carrier material

Coating material

Drug[4]

The Drugs which are used in the liquisolid system are those which are sparingly soluble in aqueous media majorly belonging to Biopharmaceutics Classification System (BCS), class II and class IV pharmaceutical compounds. Class II and Class IV drugs shows poor solubility, so the liquisolid compact technique emphasis on increasing the drug solubility for example, Phenytoin, digoxin, digitoxin etc.

Non-Volatile Solvents[7]

In liquisolid formulation these non-volatile solvents work as binding agents these should be inert in nature, capable of mixing with water, and have low viscosity for example, Polyethylene glycol (PEG) 200, Polyethylene glycol (PEG) 400, Glycerine and Propylene glycol (PG) etc.

Carrier Material[7]

The material used as carrier and coating works by absorbing the drug onto them and the carrier material are highly porous, compression enhancing materials and they possess large surface areas for example, Microcrystalline grades (MC) such as Avicel ph 200, Avicel ph102, and anhydrous lactose etc.

Coating Material[5-7]

Coating materials are highly absorptive particles and they are very fine particles. They play a very important role in covering to the moist particles of the coating materials and this action helps in absorbing any excess liquid, leaving the particle dry and free flowing for example, Cab-O-Sil M5, Aerosil 200, Syloid 244FP etc.

General Method for Preparing Liquisolid Compact Formulation

Initially calculated the necessary amount of API (Active Pharmaceutical ingredient) and non-volatile liquid and incorporated the mixture into the beaker. In this stage the drug is evenly distributed in the liquid medium. After obtaining the liquid medication the acceptable amounts of the polymer carriers and the coating material particles, which were accurately measured and blended to ensure uniformly distribution of the coating and carrier particles, now left the liquid/powder formulation for 5 minutes on the surface of mortar to promote the internal adsorption of the liquid medicine into the powdered carrier particles. After 5 minutes the drug is scrapped off by the spatula from mortar surface and the mixture was then further combined with sodium starch glycolate and blended for another 30 second to ensure the uniform distribution. Now the liquisolid formulation is ready to be compressed.[3]

Mechanism of Accelerated Drug Dissolution from Liquisolid Compacts[4,7,8]

Various Mechanism have been designed to facilitate the better drug release. The primary mechanisms used to increase in surface area, enhanced water solubility and improved Drug wettability.

Standard Methodology Involved to Prepare Liquisolid Formulation[6,1]

Increased Surface Area

Within the liquisolid system the drug molecules are suspended in a liquid medium, hence it increases the surface area. Due to this enhanced surface area, it allows the greater

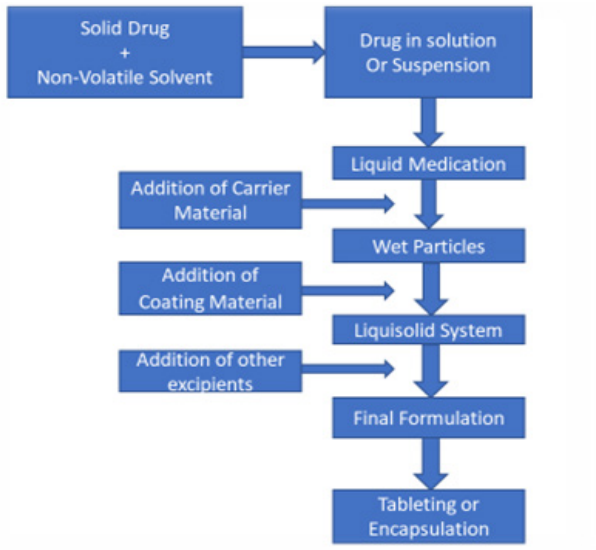

Figure 1: Methodology Used Prepare Liquisolid Formulation

interaction within the dissolution medium, which leads to a better drug solubility and a faster release rate of drug.

Enhanced Solubility in Water

liquisolid can help in increasing the drug release by improving its solubility. However, within a liquisolid system, the minimal quantity of liquid which is used is not enough to significantly improve the drugs water solubility in the liquid phase, however, at the interface between each liquid molecules and the dissolving medium particles, a small amount of liquid can be dispersed with the drug. If this solvent functions as a co-solvent, it can be significant to improve the drug solubility in the water or liquid medium.

Improvement of Wetting Properties

The liquid medium helps to improve the wettability of liquisolid primary particles may function as surfactants or help in reducing surface tension between the molecules. The wetting property of liquisolid system has been evaluated using contact angle measurement and water rising time tests.

Benefits and Drawbacks of Liquisolid Technique

Benefits[3-5,9]

a. Liquisolid compacts increases the absorption rate of poorly aqueous-soluble drugs.

b. It is well-suited for the industrial production.

c. Liquisolid system is more economical than soft gelatin capsules.

d. Utilizing suitable pharmaceutical excipients, the drugs can be modified.

e. Improved bioavailability can be achieved in comparison to traditional oral tablets.

f. Enhanced exposure of the drug surface to the dissolution medium.

g. This method is effectively utilized for poorly water-soluble drugs with low doses.

h. This liquisolid system can be formulated into sustained-release and immediate-release tablets.

i. The manufacturing process of liquisolid system, which is similar to the traditional tablets.

Drawbacks[2]

a. This method is applicable solely for drugs that are insoluble in water

b. To develop an acceptable flow property in liquisolid compacts it requires a large proportion of carrier material and encapsulating materials to achieve it, due to this, weight of the tablet can go up to 1gram which makes them difficult to swallow.

c. Liquisolid technique is not use to prepare for high-dose insoluble drugs

Pre-Compression Testing of Liquisolid Formulations[10]

Flow Properties[11]

While making a pharmaceutical product flow property plays an important role in the formulation as it helps in reducing excessive variations in dose and we use different methods to evaluate it such as Tapped density (TD), Bulk density (BD), Hausner ratio, Angle of repose, and Compressibility index.

Bulk Density[12]

The required amount of powder (W) is measured, transfer it into the measuring cylinder to measure the bulk volume (Vb), and it was measured using the formula as follows,

Bulk Density = W/Vb

Tapped Density[12,13]

The required quantity of powder is weighed (W) and further it is placed into a measuring cylinder and repeatedly to measure the tapped density (Vt) is estimated by using formula as follows,

Tapped Density = W/Vt

Compressibility Index (CI)[12]

The compressibility index can be calculate using formula as follows.

If the value of CI is less than 15% then it shows a good flow of

$$\text{Compressibillity Index} = \frac{\text{Tapped density (Td)-Bulk density (Bd)}}{\text{Tapped density (Td)}} \ 100$$

powder properties and if its value is more than 25% it shows poor flow of powder properties.

Angle of Repose[12-14]

It is done by using a funnel and it can be measured by letting the powder properly flow through the funnel, placed on burette stand, until the tip reaches to the surface of the powder pile. This can be determined by formula as follows:

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

Where,

h= powder pile height

r= powder pile radius

Hausner's ratio[13]

This parameter is essential for assessing the flow properties of powders and granules, and it was determined using the formula.

$$\text{Housner' s Ratio} = \frac{\text{Tapped density (Td)}}{\text{Bulk density (Bd)}}$$

Post-Compression Evaluation Studies Of Liquisolid Compacts

Hardness Testing[14,10]

For the testing of hardness, Monsanto apparatus can be used. The tablet is placed between a stationary jaw and a moving jaw, with the indicator reset to zero. By turning screw knob, force is gradually applied to the tablet until it breaks. The readings are recorded and were denoted in kg/cm.

Thickness[14]

The tablet thickness is determined with a Vernier caliper and noted in millimeters, with allowing variation of ± 5% of the tablet's size.

Weight variation[14,15]

A random selection of 20 tablets from the batch is selected and weighed individually to assess any variation in the weights.

Table 1: Limits for Angle of Repose

Flow Property	Angle of Repose (°)
Excellent	25 –30
Good	3–35
Fair flow	36–40
Passable	4–45
Poor	46–55
Very Poor	56–65
Extremely Poor	66 or above

Friability[14,15]

The tablets friability is measured using a Roche Friabilator and it is denoted as percentage (%). Initially, a total of 10 tablets are weighed (Wi) and placed in a friabilator, which operates at 25 Revolution Per Minute (RPM) for a duration of 4 minutes. Following the completion of time, the tablets are reweighed (Wf) and friability of liquisolid compacts was measured by the formula as follows:

$$\% \text{ Friability} = \frac{Wi-Wf}{Wi} 100$$

Where,

Wi = initial weight

Wf = Final weight

Disintegration test [15,16]

Six tablets from each batch were randomly selected and placed in the basket of the USP Disintegration Apparatus Type II. The apparatus was set to operate for 10-minutes Upon completion, the basket was initially removed from the liquid and the tablets were observed to determine if they had completely disintegrated.

Differential Scanning Calorimetry (DSC)[17,18]

Thermal behavior through DSC is carried out to check the behavior of liquisolid compacts and to detect any type of potential interactions between the API and excipients. The absence of characteristic drug peaks in the DSC thermogram indicates that the drug may not exist in its crystalline state, implying that the molecules could be dispersed within the system and showed successful complexation.

Fourier Transform Infrared Spectroscopy (FT-IR) [18,19]

Fourier transform infrared spectroscopy is helpful in detecting any potential chemical interactions between the API and the excipient in the formulation. If the drugs distinct peaks remain unchanged in the formulation without any additional peaks it indicates that no chemical interaction has occurred.

Applications[17,18]

1. The liquisolid technique offers an effective strategy to enhance the dissolution rate of poorly water-soluble drugs, particularly for low-dose medications. This method has been successful in improving the solubility of drugs such as atorvastatin and piroxicam leading to better absorption and therapeutic effect.
2. The liquisolid compacts achieve fast drug release rates.
3. The liquisolid compacts increases the solubility of drug and dissolution rate.
4. It can also be used in probiotic formulation.

CONCLUSION

The liquisolid formulation method emerges as a valuable strategy for improving the bioavailability of poorly water-soluble drugs and drug dissolution rate with low aqueous solubility. as it converts the drug into a fluid state and with the help of various carrier and coating materials it converts it into a excellent flow property and compressible powders which helps to increase their overall absorption. And since it can enhance the bioavailability of drugs more than that of conventional tablets it can be a promising alternative for Industrial Production.

Table 2: Liquisolid-based Formulations Designed to Improve Drug Release Efficiency.

Drug	Liquid Vehicle	Carrier material	Coating material	Reference
Itraconazole	Polyethylene glycol 400 (PEG)	Avicel pH 102	Aerosil 200	(20)
Prednisolone	Propylene glycol	Avicel pH 200	Cab-O-Sil	(21)
Valsartan	Propylene glycol	Avicel pH 102	Aerosil 200	(22)
Atorvastatin Calcium	Propylene glycol	Avicel pH 102	Aerosil 200	(23)
Piroxicam	Polyethylene glycol 400(PEG)	Avicel pH 102	Aerosil 200	(24)
Rosuvastatin Calcium	Propylene glycol	Avicel pH 102	Aerosil 200	(25)
Meloxicam	Polyethylene glycol 200	Avicel pH 102	Aerosil 200	(26)
Nilvadipine	Propylene glycol	Avicel pH 102	Aerosil	(27)
Flurbiprofen	Polyethylene glycol 400(PEG)	Avicel pH 102	Aerosil 200	(28)
Loperamide	Propylene glycol	Avicel pH 102	Aerosil	(29)

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