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Review Article

A review on recent advancement in liquisolid technology

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Abstract

Liquisolid technique is a novel process in which a liquid can be converted into a material that flows freely, is readily compressible. The carrier material in liquisolid compact comprises the liquid part, which is the liquid drug or a drug solution in liquid vehicles that are non-volatile. Solubility is the main parameter in the circulation of blood to achieve the whole concentration of the drug for pharmacological action. The rate of dissolution of drugs enhances in liquisolid technology. This in turn increases absorption and bioavailability subsequently. This review discusses the different advances and changes to improve liquisolid technology formulations and enhancement of dissolution rate of poorly soluble drugs. Most of the new chemical entities have high lipophilicity and poor water solubility, resulting in poor bioavailability. The release rate of these drugs should be increased in order to improve bioavailability. The technique is based on dissolving the insoluble drug in the solution loaded with non-volatile solvent. Then the dissolution rate of drug which is poorly soluble will rise. The enhanced bioavailability is due to the increased surface area of drug for release, increased drug aqueous solubility or improved wetting capacity.

Keywords: Solubility, Absorption, Lipophlicity, Screening, bioavailability.

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1. Introduction

The Liquisolid technique is a method that improves the dissolution rate of water-insoluble drugs and can alter it. The drugs that are unsolvable or poorly soluble are dissolved or dispersed in a significant non-volatile solvent in the liquisolid technique and changed by the use of carrier substance into free flow powder. Dissolution is a significant issue in absorption of the drug, chiefly in the drugs which are insoluble in water or poorly soluble, the liquisolid technology can improve it. A drug's therapeutic efficacy depends on the bioavailability that depends on drug solubility of molecules. Solubility is the main factor for achieving the preferred pharmacological response concentration of the drug in circulation of blood in the body.[1] Many approaches to formulation have been developed to enhance the solubility of drugs that are very less soluble in water. Micronization technique is the normally used approach that helps to get better drug solubility due to area of surface expansion, but the agglomeration style of micronized hydrophobic drugs makes it not as much effectual to keep away from the difficulty of solubility, especially while the drug is formulated in tablets or in encapsulations. In recent years, the term solid dispersion has grown an active curiosity in research to get better the dissolution of drug. The liquisolid technique, a novel advanced system, and a method for increasing dissolution, may conquer most of the barriers. First introduced by Spireas *et al*., this technique was used to fit in water-insoluble drugs into forms of fast release of solid dosage. The liquisolid systems intend principle is to hold powdered liquid drugs (i.e. drug solutions and liquid drugs). Liquisolid systems are considered free-flowing powders which we can compressed into tablets or can filled into capsules and containing a liquid non-volatile medium and particles of solid drugs.[2] The liquid medium can dissolve the solid drug particles or partially dissolve them

i.e. drug suspended into the organic solvents. With the mixing of appropriate excipients such as carrier and coating materials, the liquid medium can be transformed into a dry-looking free-flowing powder which we can compressed. Liquisolid formulations, such as propylene glycol and polyethylene glycol, are used as liquid vehicles as orally preferable and are water-miscible organic solvents with increased boiling point. It is possible to espouse the various different grades of cellulose and lactose as carriers. On the other hand, as coating materials, simply excipients with very well particle size and greatly adsorptive properties, for instance silica powder can be used.[3]

2. Previous advancement

Liquisolid technology is used in the powdered solutions, a method which is depend on the reformation of a drug solution into a dry powder in a solvent which is non - volatile, with heavy particular surfaces primarily by liquid adsorbing. Though, for their dissolution forms, these types of manufacturing were examined even as in a form of powder dispersion, and in the form of tablets they cannot be compressed. Compression enhancers and the binders such as methyl cellulose, starch and polyethylene glycol have been included into these types of systems in next advancement on powdered solutions to get the better blend compatibilities.[4] Though, the product's stream and compression estate have never been justified and improved to the particular industrial and necessities in the examinations. Particularly, as in the form of tablets such customized powdered solutions were dense, considerable liquid-squeezed and inappropriately difficulty found with soft tablets. This slowed down the industrial function of these types of method. On the divergent, liquisolid compacts express adequate stream and compressibility. In the liquid medicine, we can simply use the drug solutions but also we can use the various emulsions and the suspensions. Thus, unlike powdered solutions, the liquisolid technology includes powdered drug solutions, suspensions, emulsions and powdered liquid drugs.

3. Process and theory involved in liquisolid system

The liquid medium is integrated into a carrier material when the drug is dissolved in that medium and this has in its interior surface and strictly matted fibers such as celluloses, and there is both absorption and adsorption. Its internal structure captures the liquid initially absorbed within the particles. After this method has been saturated, the liquid is absorbed onto the porous carrier particles inner and outer surfaces. Then the fabric material with elevated adsorption properties and big particular surface region offers the liquisolid structure with fluid features.

In liquid vehicle solution the drug is present in the liquisolid systems while it is concurrently transported by powder. One of the anticipated mechanisms for explaining the improved dissolution rate from the liquisolid compacts is the wet capacity of the compacts in the dissolution media.[5]

Non-volatile solvents can easily moisten drug molecules in the liquisolid compact by lowering the interface friction between the medium of solvent and the surface of the tablet. Liquisolid compacts can therefore be estimated to reveal enhanced release profiles of water-insoluble drugs due to considerable increase in wet capacity and effective surface area for dissolution. The dissolution of drugs which are non polar is the rate at which gastrointestinal absorption partial, an enhanced bioavailability of the orally taken is achieved if a drug which is insoluble is in the solution and therefore the rate of dissolution is enhanced.[9]

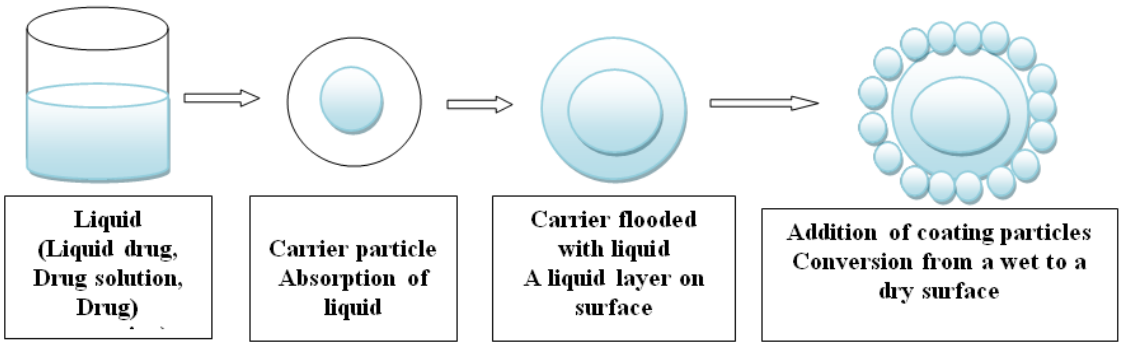

Fig. 1: Liquisolid System

3.1 Liquisolid Formulations as a tool to enhance drug release

Many poorly soluble drugs were formulated as liquisolid systems and showed enhanced release of drugs. These drug delivery systems were formulated using various liquid vehicles, carrier and coating materials.[12]

Table 1. Drugs with different liquid vehicles, carrier and coating materials for liquisolid technology

Drug	Liquid vehicle	Carrier And Coating material
Aceclofenac	PEG	MCC and HPMC
Bromhexine HCL		MCC and Colloidal silica
Carbamazepines	PEG 200	MCC and Colloidal silica
Clofibrate (liquid)		MCC and Colloidal silica
Famotidine	PG	MCC and Colloidal silica
Fenofibrate	PEG 400	MCC and Colloidal silica
Fenofibrate	PG	MCC and Colloidal silica
Furosemide	Synperonic PE/L	MCC and Colloidal silica
Glibenclamide	PEG 400	MCC and Colloidal silica
Griseofulvins	PEG 400	MCC and Colloidal silica
Hydrochlorothiazide	PEG 200	MCC+Magnesium carbonate and colloidal silica
Hydrocortosone	PG	MCC and Colloidal silica
Hydrocortisone	PEG 400	Various silica
Ibuprofens	PEG 300	MCC and Colloidal silica
Indomethacin	PG	MCC and Colloidal silica
Indomethacins	PEG 400	MCC and HPMC
Lamotrigin	PEG 400	MCC and Colloidal silica
Methyclothiazide	PEG 400	MCC and Colloidal silica
Naproxen	Cremophore EL	MCC and Colloidal silica
Piroxicam	Polysorbate 80	MCC and Colloidal silica
Piroxicam	PG	MCC and Colloidal silica
Polythiazide	PEG 400	MCC and Colloidal silica
Prednisolone	PEG 400	Various silica
Prednisolone	PG	MCC and Colloidal silica
Prednisone	PG	MCC and Colloidal silica
Prednisone	PEG 400	Various Silica
Repaglinide	Polysorbate 80	MCC and Colloidal silica

4. Main components of liquisolid system

4.1 Coating Material and Carrier Material:

Coating material forms a uniform film around carrier particles. This prevents particle aggregation and reduces inter-particulate friction. This phenomenon improves flowability and gives a dry-looking appearance to the liquisolid by covering the wet carrier particles and absorbing any excess liquid. Usually the coating materials are very fine. Example of coating material is colloidal silica of different grades similar to Aerosil 200. And the carrier material should have porous surface and closely matted fibers in its inertial. Carriers are involved in the liquid medication sorption process that improves the effective dissolution surface area. These help the compression as well. Carriers have a sufficient adsorption property due to relatively large, preferably porous particles and matted fibers contribute to the interior. E.g. Lactose and cellulose.

4.2 Non-Volatile Solvent:

The selected solvent should have the capability to dissolve the drug adequately. Appropriate vehicles are inert; firstly they are miscible with water and having increased boiling point, like propylene glycol and fixed oils.

4.3 Disintegrant:

The formulation kind and concentration will be based mostly on the observation's purpose while the use of disintegrant. Merging of super-disintegrant is positive for studies to improve solubility. Sodium starch glycolate is the most commonly used disintegrant.

5. Mechanisms of increased drug release

The three main mechanisms proposed include increased surface area of drug available for release, increased drug aqueous solubility due to the presence of non - volatile vehicle and improved drug particle wettability due to the cosolvent effect of the used vehicle.[6]

5.1 Enhanced effectual Surface Area:

In the liquid medium whenever the drug be dissolved within the liquisolid system and it is in a molecularly dispersed condition. Consequently, the drug's surface area accessible for release in directly compressed tablets is more than that of moleculess of the drug.

Consequently, by improving the solubility of the drug content and thus increasing the portion of the drug that is not dissolved in the liquid vehicle, the release rate decreases., the discharge rates in the liquid formulation may be exposed with many of drugs and to be directly proportional to the portion of the molecularly isolated drug (F_M).[13]

According to spireas F_M as the fraction between the drug solubility, (Sd) the real concentration of the drug, (Cd) medium carried by all system.

Therefor,

$$F_M = Sd/Cd$$

Where, F_M is 1

Furthermore, it is assumed that the adsorption and absorption of molecularly dispersed drugs on the surface and inside of the carrier molecule exerts an inhanced effective surface area usually available for mass movement during the method of drug dissolution.

5.2 Enhanced Aqueous Solubility:

For enhancing drug unharness to the primary methodology, the liquisolid systems are doubtless to boost the drug's solubility. In fact, in a very liquisolid compact, the comparatively bit of liquid vehicle isn't adequate to extend the drug's overall solubility within the liquid medium. Though, within the the small - setting of the solid / liquid interface between a personal primary liquid particle and therefore the unharness medium, the quantity of liquid vehicle that spreads from one liquid particle along with the drug molecules could also be adequate to extend the drug's liquid solubility if the liquid vehicle will act as a cosolvent. In varied studies, the common raise in drug solubility and caused by liquisolid systems was established.[7]

5.3 Better Wetting Properties:

Because the liquid medium may also perform as a surface active agent or enclose stumpy tension on the surface, it boosts the various wetting properties of the molecules of main liquisolid. Contact angles[215] and water-rising times can demonstrate the wettability of these systems. The drug's adsorption on the carrier particles also increases the effective surface area, enhancing drug contact.

6. Optimization of liquisolid formulation for enhanced drug release

Optimizing the liquisolid method is mostly intended on improving the dissolution rate of drug formulation and flow properties. Since the releasing rates in formulation of liquid are directly proportional to the part of drug dispersed molecules (F_M), elevated drug dose needs more liquid entities for the preferred discharge profile. In addition, high levels of carrier and coating materials are required to get liquisolid systems with acceptable flowability and compactability. This leads to an increase in tablet weight, however, ultimately difficulty in processing and swallowing manufacturing. Therefore, several formulation parameters need to be optimized to overcome these and various other liquisolid technology issues. These factors are shown in the table 2.

Table 2. Formulation parameters for liquisolid system with rapid drug release

Formulation parameters	Optimization	Effects
Liquid Vehicle	High solubility of drug in the vehicle	Increased fraction of the molecularly dispersed drug (F_M)
Carrier and coating Materials	High specific area of surface	Increased liquid load factor (L_f)
Addition of excipients	Polyvinyl pyrrolidone (PVP)	Increased liquid load factor (L_f) Increased viscosity of liquid vehicle Inhibition of precipitation
Excipient ratio (R)	High R-value	Fast disintegration Inhibition of precipitation

7. Alternative technologies

The techniques that compete with the liquisolid technique are as shown in Table 3. Different solubilizers or hydrophilic polymers are used in solid dispersion technology. Different methods such as melting, solvent evaporation, condensation or cooling can be used to prepare solid dispersions; but the problem in this type of system involves the use of volatile solvents. Jain *et al* [8] studied the effect of powder processing performance on Fenofibrate formulations dissolution rate. It was discovered that milling a fenofibrate / excipient mixture was useful over milling the raw drug alone. In process C, a fast rate of release was studied. This method, however, involves using jet milling to reduce the active constituent's size. Complexation with cyclodextrins as a carrier seems to be a very effective process of inclusion. In terms of scale-up aspects, the process, involving simple stirring for a few hours and then filtering the complex, which is further dried, is very useful. However, this method's effectiveness is limited due to the cost of cylodextrins. Huang *et al* [10]. They used an emulsion solidification process to prepare ultrafine fenofibrate powder. The emulsion solidification process consisting of emulsifier, water and molten drug as oil phase was used without the use of any organic solvent. The effects on particle size and morphology of stirring velocity and volume ratios of hot emulsion to cold water as well as the impacts of various emulsifiers on emulsion were discussed. The property of dissolution was found to be improved enough than bulk fenofibrate. Although this process appears to be simple, during emulsification it requires high expertise and higher costs of emulsifier as well. Vogt *et al* [11] used technologies such as micronization with jet milling and then media milling with ball milling to obtain nanosized particles. Thereafter, spray

drying was also performed. Their limitations include high - end friction and spray drying technologies. Using an evaporative precipitation technique appears to give much smaller particle size down to nanometers, but this involves using an HPLC pump, heat exchanger, and a specially manufactured nozzle. Considering the limitations of the above technologies, liquisolid formulations can be said to be less expensive, easy to formulate, and high-performance dissolution and bioavailability systems. The above liquisolid technique advantages are based on available literature data and subject to case differences.[15]

Table 3. Competing technologies with liquisolid technique

Sr. No.	Technique	Mechanism
1	Solid dispersion	Hydrophilic polymers
2	Processing with excipients using mills	Processing of the bead mill and subsequent spraying
3	Inclusion complexation	Inclusion of active into clycodextrin structure
4	Ultrafine active development	Solidification process from emulsion
5	Micronization	Particle size reduction increasing surface area
6	Nanosizing	Bead mill processing and subsequent spray drying
7	Evaporative precipitation into aqueous solution	Precipitation of the drug in an aqueous surfactant solution dissolved in volatile solvent

8. Conclusion

Low water solubility is an inertial prolem with newly developed drugs changing to higher lipophilicities. The whole bioavailability for such drugs is frequently not achieved by standard formulation strategies. By increasing the release of drug, liquisolid technology has proven to be a beneficial innovative tool to improve bioavailability. It is an efficient technology in terms of manufacturing capacity and formulation's low cost. This technology therefore has the potential for manufacturing on a large scale.

References

[1]. Patel UB, Modi DC, Shah DP *et al*. Liquisolid compacts: A review. *International Journal of Advances in Pharmaceutics*. 2017; 06(07): 110-113.

[2]. Patel BB, Shah CN *et al*. Recent research on liquisolid technology for solubility enhancement- A review. *International Journal of Advance in Pharmaceutics.* 2016; 345-394.

[3]. Balaji A, Umashankar MS, B.Kavitha B. *et al*. Liquisolid technology- A latest review. *International Journal of Applied Pharmaceutics*. 2014; 6(1): 11-9.

[4]. Rajesh K, Rajalakshmi R, Umamaheswari J *et al*. Liquisolid technique a novel approach to enhance soluability and bioavailability. *International Journal of Biopharmaceutics*. 2011; 2(1): 8-13.

[5]. Yadav VB. Yadav AV *et al*. Liquisolid granulation technique for tablet manufacturing: an overview. *Journal of Pharmacy Research* 2009; 2(4): 670-674.

[6]. Nagabandi VK, Ramarao T, Jayaveera KN *et al*. Liquisolid Compacts: A Novel Approach to Enhance Bioavailability of Poorly Soluble Drugs. *International Journal of Pharmacy and Biological Sciences*. 2011; 89-102.

[7]. Sowmya C, Reddy CS, Amrutha V *et al*. Liquisolid technology: A novel approach to enhances solubility and bioavailability of BCS class 2 drugs. *Inernational Research Journal of Pharmacy*. 2012, 3(7).

[8]. Jain RA, Brito L, Straub JA, *et al*. Effect of powder processing on performance of Fenofibrate formulations. *Eur J Pharm Biopharm* 2008; 69: 727-34.

[9]. Hiremath SN, Raghavendra RK, Sunil F, *et al*. Dissolution enhancement of gliclazide by preparation of inclusion complexes with beta-cyclodextrin. *Asian J Pharm* 2008; 2: 73-6

[10]. Huang QP, Wang JX, Zhang Z-B, *et al*. Preparation of ultrafine Fenofibrate powder by solidification process from emulsion. *Int J Pharm* 2008; 368:160-64.

[11]. Vogt M, Kunath K, Dressman JB. Dissolution enhancement of Fenofibrate by micronization, co-grinding and spray-drying: comparison with commercial preparations. *Eur J Pharm Biopharm* 2008; 68: 283-88.

[12]. Sharma A, Jain CP. *et al*. Techniques to enhance solubility of poorly soluble drugs: a review. *J. Global Pharm. Tech.* 2010; 2:18-28.

[13]. Bindu MB, Kusum B and David Banji, Novel Strategies for Poorly Water Soluble Drugs, *International Journal of Pharmaceutical Sciences Review and Research*, 2010; 4(3): 1-5.

[14]. Saharan VA, Kukkar V, Kataria M, Gera M. *et al*. Dissolution enhancement of drugs. Part II: effect of carriers. *Int. J. Health Res.* 2009; 2:207-23.

[15]. Srinivas L, Vinai Kumar T, Ramya P, Manasa P. Preparation and biopharmaceutical evaluation of piroxicam liquisolid systems. *Indo American J of Pharma Res*. 2014.