LIQUISOLID TECHNIQUE: A NEW APPROACH FOR SOLUBILITY ENHANCEMENT

Monika Trivedi*, Veedhi Rathawa, Hitesh Jain, D. B. Meshram

Pioneer Pharmacy Degree College, Vadodara, Gujarat, 390019, India

ABSTRACT:

Solubility of medicine could be a major consider the planning of pharmaceutical formulation result in variable oral bioavailability. The "liquid solid" technique is a new approach for solubility and dissolution enhancement; thereby it increases the bioavailability of poorly soluble drugs. This technique is an efficient method for formulating water insoluble and water soluble drugs. It contains liquid medication in powdered form. Liquid medication such as solution and suspension 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. In this, we can use carriers such as microcrystalline cellulose, starch, lactose, coating materials like silica gel and disintegrating agents. It is advantageous because of formulation of dosage form in different release patterns like control release, sustained release and also in immediate release. Sustained drug delivery system can be developed for the water soluble drugs. Mostly the hydrophobic drug shows a very poor dissolution in gastro intestinal tract which lead to incomplete drug absorption, directly results into poor bioavailability. Change in surface area, aqueous solubility and wettability of the drug particles, it will be automatically affect the formulation performance. This technique has simplified manufacturing method, less production cost and also fulfil the industrial requirements, so liquisolid approach is a newer technology for solubility enhancement.

Keywords: Solubility, Dissolution, Wettability, Excipients

Access this Article Online	Quick Response Code:
Website: http://heb-nic.in/cass-studies	
Received on: 06/03/2019	
Accepted on: 08/03/2019 © HEB All rights reserved	

INTRODUCTION

Because of high patient compliance and drug development oral route is most preferable route for drug administration. Plasma drug concentration may not reach due to some problems in this oral route, as solubility of a drug is a major concern. Solubility is phenomenon in which solute is dissolved in unit volume of solvent. Solubility is considered as a major factor for desired concentration of drug in a systemic circulation.

The poorly water soluble drugs may have poor dissolution rate and incomplete bioavailability. Dissolution is the rate limiting step for hydrophobic drugs which are sparingly soluble, slightly soluble or very slightly soluble. Solubility and dissolution of drug affects the bioavailability which directly affect the therapeutic response of the drug for pharmaceutical response of a drug in systemic circulation, solubility is an important factor achieve optimum concentration. [1]

The poorly water soluble drug release at a slow rate due to their limited solubility within the GI contents. To overcome this problem, we can enhance the solubility by using liquisolid technique. The development of new chemical entities and generic drug are facing a major problem due to low aqueous solubility. This technique helps to formulate drug solution into solid dosage form. Non-volatile water miscible solvents are generally used to prepare drug solution. Thus, the tablet prepared contains drug held in the solution and a better bioavailability of poorly soluble drugs can be achieved. [2]

Advantages [3]

- Compared to conventional tablets enhanced bioavailability is obtained.
- Production cost is low than soft gelatine capsules.
- Suitable technique for formulation of liquid oily drugs.
- Drug is held in soluble liquid phase to improve wettability which increases drug solution profile.[4-6]
- Dissolution media experiences greater surface area.
- This system can be formulated as immediate release, sustained release or controlled release.
- This technique can formulate tablet or capsules with pH independent drug release profile.

Components of Liquisolid Compact Formulation[7]

- **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 solubilize the drug. The non volatile solvent acts as a binding agent in the liquisolid formulation. Various non-volatile solvents used for the formulation of liquisolid systems include Polyethylene glycol (PEG) 200 and 400, glycerine, polysorbate 80 and propylene glycol (PG).

- **Disintegrants**

Superdisintigrants increases the rate of drug release, water solubility and wettability of liquisolid granules. Mostly superdisintigrants like sodium starch glycolate and crosspovidone are used.

- **Drug candidates**

This technique is successfully applied for low dose BCS class II and class IV drugs which are poorly water soluble and have slow dissolution rate. Examples of drug candidates include carbamazepine, famotidine, piroxicam, indomethacin, hydrocortisone, naproxen and prednisolone, digoxin, digitoxin, prednisolone, hydrocortisone, spironolactone, hydrochlorothiazide, polythiazide, and other liquid medications such as chlorpheniramine, water insoluble vitamins, fish oil etc.

- **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 flowability. These include grades of microcrystalline cellulose such as avicel PH 101 and avicel PH 102, lactose, eudragit RL and eudragit RS (to sustained drug delivery) etc.

- **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 so maintain the powder flowability. Coating material includes silica (Cab- O-Sil) M5, Aerosil 200, Syloid, 244FP etc. A formulation mathematical model by Spireas of liquisolid systems enabled calculation of the appropriate amounts of both the carrier and the coating material to be added to produce acceptable flow and compressibility.[8]

The excipient ratio R of the powder substrate is defined in the following equation as:

$$R = Q / q$$

where R is the fraction of the weights of carrier Q and coating q materials present in the formulation. The amounts of excipients used to prepare the tablets are related to the amount of liquid medication W through the Liquid Load Factor (Lf) as shown in the following equation:

$$L_f = W / Q$$

For a given excipient ratio R, there exists a specific Flowable Liquid Load Factor denoted as $ØL_f$, as well as a specific compressible Liquid Load Factor denoted as ψLf.

$$\Phi L_f = \Phi + \Phi\ (1/R)$$

The optimum liquid load factor Lo that produces acceptable flow and compression characters is equal to either $ØL_f$, or ψL_f, whichever possesses the lower value.

Powder excipient or system	Φ Values (Flowability index)			Ψ values (Compressibility index)		
	Propylene Glycol	PEG 400	Tween 80	Propylene Glycol	PEG 400	Tween 80
Avicel PH102	0.16	0.005	0.003	0.224	0.242	-
Avicel PH200	0.26	0.02	-	0.209	0.232	-
Cab-O-Sil M5 (silica) with Avicel PH 101	3.31	3.26	3.95	0.560	0.653	-
Cab-O-Sil M5 (silica) with Avicel PH 200	2.56	2.44	-	0.712	0.717	-

Table 1: Examples of liquisolid formulation parameters of various powder excipients with commonly used liquid vehicles [8]

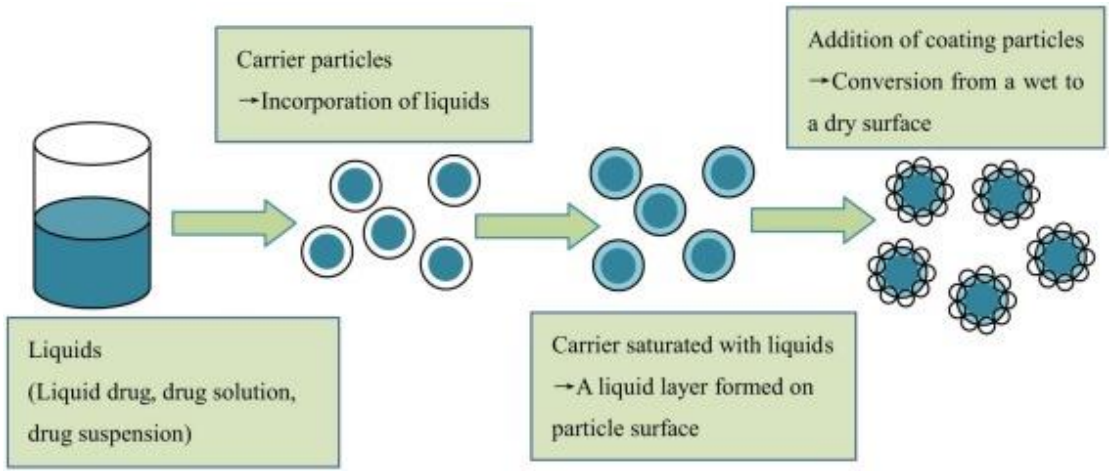

Figure: 1 - Mechanism of Liquisolid compact

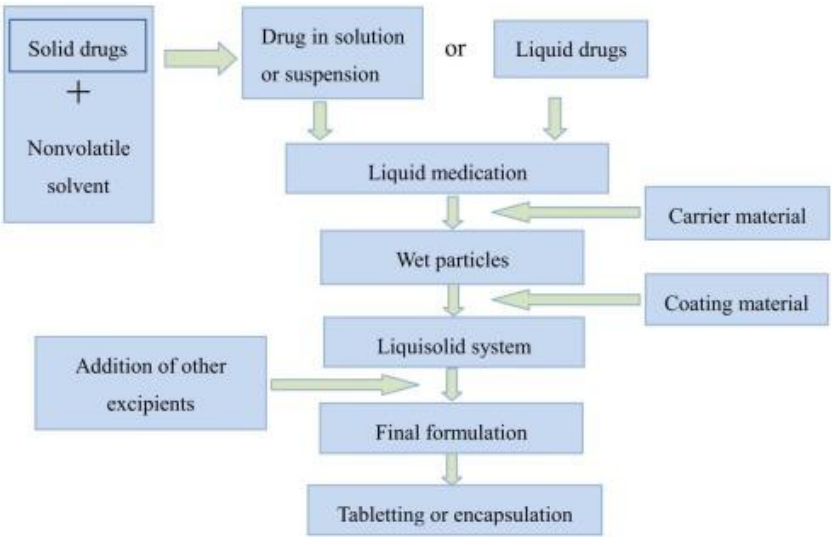

Figure: 2 - Preparation procedure of Liquisolid compact.

Characterization of Liquisolid compact

1. Flow behaviours [9,10]

The prepared liquisolid compacts are evaluated for their flow characteristics such as bulk density, tapped density, angle of repose, Carr's index and Hausner's ratio.

2. 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[11,12].

3. 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[13,14]

4. 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[15-18]

Applications of liquisolid technique [19-20]

- Liquisolid technique as a tool to enhance drug dissolution and solubility.
- Liquisolid technique as a tool to sustained drug release.
- Liquisolid technique as a tool to minimize the influence of pH variation on drug release.
- Liquisolid technique as a promising tool to improve drug photo stability in solid dosage form.
- Rapid release rate.
- Application in probiotics.
- To improve flowability and compressibility.

CONCLUSION

There are many techniques described to enhance the bioavailability of drug. This is one of the most promising approach for enhancement of solubility. Practically it is effective for increasing bioavailability of water insoluble drugs. Recently, most of the research work is focusing on the formulation development of liquisolid systems. Future studies of exposure measurements at high doses of drugs that are insoluble in water and in vivo assessment of the liquisolid system should be studied and strengthened.

References

1) Mei LU. Liquisolid technique and its application in pharmacy. *Asian. J. Pharm. Sci.* 2017; 115:123 – 12.

2) Elkordy AA, Essa EA. Spironolactone release from liquisolid formulations preapared with Capryol™ 90 as a non-volatile liquid vehicle. *Eur. J. Pharm. Biopharm.* 2013; 203:223 – 83.

3) Khames A. Liquisolid technique: a promising alternative to conventional coating for improvement of drug photo stability in solid dosage form. Drug Deliv.2013; 1335:1343 – 10.

4) Javadzades Y, Nokhodchi A. Liquisolid technique as a new approach to sustained propranolol hydrochloride release from tablet matrices. *Int. J. Pharm*. 2008; 102:108 – 362.

5) Hammadi M, Awad N. Investigating the use of liquisolid compacts technique to minimize the influence of pH variation on loratadine release. *Pharm. Sci. Tech*. 2012; 53:58 – 13.

6) Badawy MA, Kamel AO, Sammour OA. use of biorelevent media for assessment of poorly soluble weakly basic drug in the form of liquisolid compacts: in vitro and in vivo study. Drug Deliv. 2016; 818:827 – 23.

7) Gavali S, Pacharane S, Sankpal S, Jadhav K, Kadamet V. Liquisolid Compact: A New Technique for Enhancement of Drug Dissolution. *Int J Res Pharma and Chem* 2011; 705:713 – 1(3).

8) Spireas S, Bolton S. Liquisolid systems and methods for preparing same. United States patent. 2000; 96:337 – 6.

9) Vaskula S, Vemula S, Bontha V, Garrepally P. Liquisolid Compacts: An Approach to enhance the Dissolution Rate of Nimesulide, *A Journal of Applied Pharmaceutical Sciences* 2012; 2(5): 115-121.

10) Gold G, Duvall R, Palermo B, Slater J. Powder flow studies II: Effects of glidants on flow rate and angle of repose. *J Pharm Sci* 1966; 1291:1295 – 55.

11) Gare A, Sadeghi F, Badiee A, Mostafa A, Rajabisiahboomi R. Crystal habit modifications of ibuprofen and their Physicochemical Characteristics. Drug Development and Industrial Pharmacy 2001; 803:809 – 27(8).
12) Pathak A, Goyal R, Agrawal P, Rajput S, Tiwari G, Shivhare R. A Review on Liquisolid Technology. *World J Pharma Res* 2012; 500:512 – 1(3).
13) Abdou H. (Ed.). Dissolution, bioavailability and bioequivalence. Easton, Mack Pub. Co., PA; 1989; 53:72.
14) El-Hammadi M, Awad N. Investigating the Use of Liquisolid Compacts Technique to Minimize the Influence of pH Variations on Loratadine Release. *AAPS Pharm Sci Tech* 2012; 53:8 – 13(1).
15) Yala P, Srinivasan M, Alladi S, Zalaki S. Solubility enhancement of a model etoricoxib drug using Liquisolid compacts. *International Journal of Biological and Pharmaceutical Research* 2012; 577:585 – 3(4).
16) Ibrahim E, El-Faham T, Mohammed F, El-Eraky N. Enhancement of solubility and dissolution rate of domperidone by utilizing different techniques. *Bul. Pharm Sci* 2011; 105:120 – 34(2).
17) Gare A, Sadeghi F, Badiee A, Mostafa A, Rajabisiahboomi R. Crystal habit modifications of ibuprofen and their Physicochemical Characteristics. Drug Development and Industrial Pharmacy 2001; 803:809 – 27(8).
18) Al-sarraf M, Hussein A, Abdul A. Dissolution enhancement of telmisartan by liquisolid compacts. *International Journal of Pharmacy and Pharmaceutical Sciences* 2014; 1:7 – 6(2).
19) Bonthagarala B, Sai PDL, Venkata SK, et., al., Enhancement of dissolution rate of clofibrate by using liquisolid compact technology. *Int. J. Biomed*. 2015; 288:298 – 6.
20) Tonnensen HH, Formulation and stability testing of photolabile drugs. *Int. J. Pharm.* 2001; 1:14 – 225.