Journal of Applied Pharmaceutical Science Vol. 3 (8 Suppl 1), pp. S111-S119, August, 2013
Available online at http://www.japsonline.com
DOI: 10.7324/JAPS.2013.38.S17
ISSN 2231-3354

Design and Technology of Liquisolid Compacts

Jomon N. Baby, Steffy B. Manjila, E.N. Bijin, Icey Constantine, K. Pramod, J. Valsalakumari*
College of Pharmaceutical Sciences, Govt. Medical College, Thiruvananthapuram – 695011, Kerala, India.

ARTICLE INFO

Article history:
Received on: 30/01/2013
Revised on: 04/03/2013
Accepted on: 06/07/2013
Available online: 18/09/2013

Key words:
Excipient ratio, Liquid load factor, Carrier material, Coating material, Bioavailability, Solubility.

ABSTRACT

During the emergence of a new drug it is very important to ensure its systemic bioavailability. Majority of the drugs in the developmental pipelines confronts with the problem of poor solubility; which will result in reduced dissolution rate there by hampering its bioavailability. Here comes the need of liquisolid technique which is a novel and promising approach to overcome these consequences. This technique utilizes the powder solution technology which is based upon the dissolution of the insoluble drug in the nonvolatile solvent and admixture of drug loaded solutions with appropriate carrier and coating materials to convert into acceptably flowing and compressible powders. The liquisolid technology can also be used both for the enhancement and the retardation of drug release by suitably altering the adjuvants. This aricle highlights the relevancy, formulation and designing of the liquisolid systems.

INTRODUCTION

A therapeutically effective drug should posses enhanced bioavailability; which is being governed by the solubility of drug molecules. Solubility is one of the important parameter to achieve desired concentration of drug in systemic circulation for pharmacological response to be shown (Lipinski, 2002).The slow release rate of poorly water soluble drugs is attributed to its limited solubility within the GI contents (Figure 1). The dissolution rate is often the rate determining step in the drug absorption (Amidon et al., 1999; Lbenberg and Amidon, 2000). The challenge for poorly water soluble drugs is to enhance the rate of dissolution. This in turn subsequently improves absorption and bioavailability (Darwish and El-kamal, 2001).Formulation methods targeted at dissolution enhancement of poorly soluble substances are continuously introduced. The aqueous solubility for poorly water-soluble drugs is usually less than 100 µg/ml (Horter and Dressman, 1997). Till date there are several methods to enhance the dissolution rate and hence the bioavailability of poorly water soluble chemical entities (BCS class II drugs). Figure 2 illustrates the various methods and mechanism for dissolution enhancement of BCS class II drugs (Hiremath et al., 2008; Modi and Tayade, 2006; Rasenack and Muller, 2002; Smirnova et al, 2004). Among these various methods for improving dissolution rates, liquisolid compact technology is a novel, technique for dissolution enhancement. The term liquisolid compact refers to immediate release or sustained release tablets or capsules, combined with the inclusion of appropriate adjuvant required for tabletting or encapsulating. By using this concept liquid medication like suspension, oily liquid drugs and solutions of water insoluble solids drugs in non volatile vehicles could be transformed into acceptably flowing and compressible powder.

Liquid medication may be converted in to dry-form of non adherent free flowing and readily compressible powder on simple blending with selected powder excipient referred to as the carrier and coating material. It is been speculated that such systems exhibit enhanced release profiles. In this case, even though the drug is in a solid dosage form, it is held within the powder substrate in solution or, in a solubilized, almost molecularly dispersed state, which contributes to the enhanced drug dissolution properties. The liquisolid technology can be used both for the enhancement and the retardation of drug release. It involves dissolving the drug in suitable non-volatile solvent and then adding this liquid medication to the mixture of carrier and coating materials.

* *Corresponding Author*
Prof. J. Valsalakumari, Professor of Pharmacy College of Pharmaceutical Sciences Govt. Medical College Thiruvananthapuram – 695011 Kerala, India. Ph.: +91 94465420

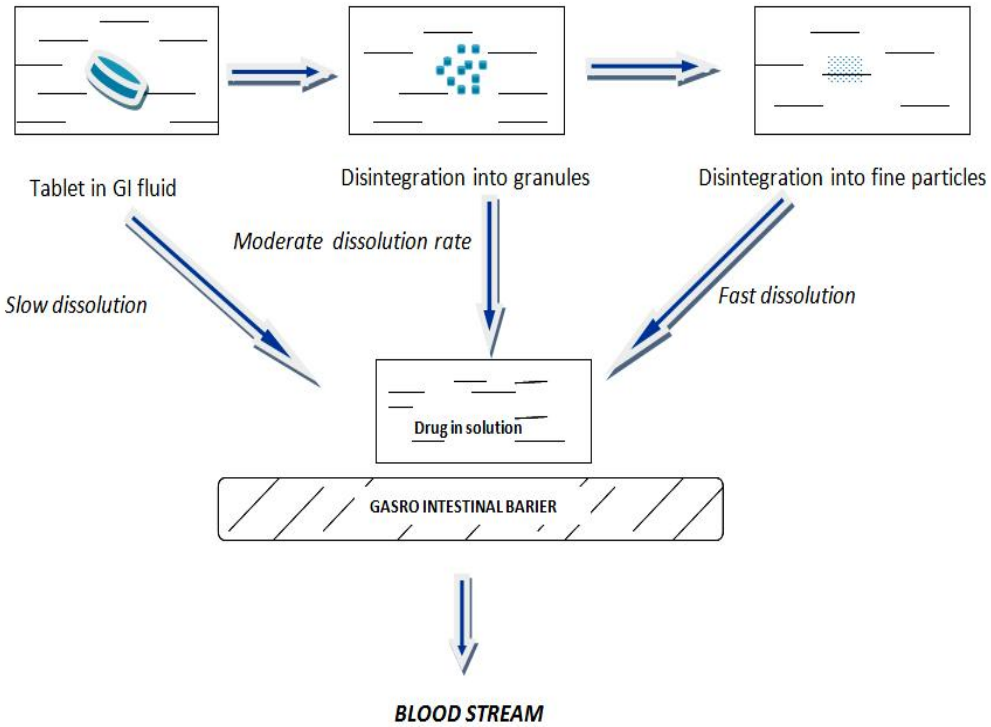

Fig. 1: Release of drug into systemic circulation.

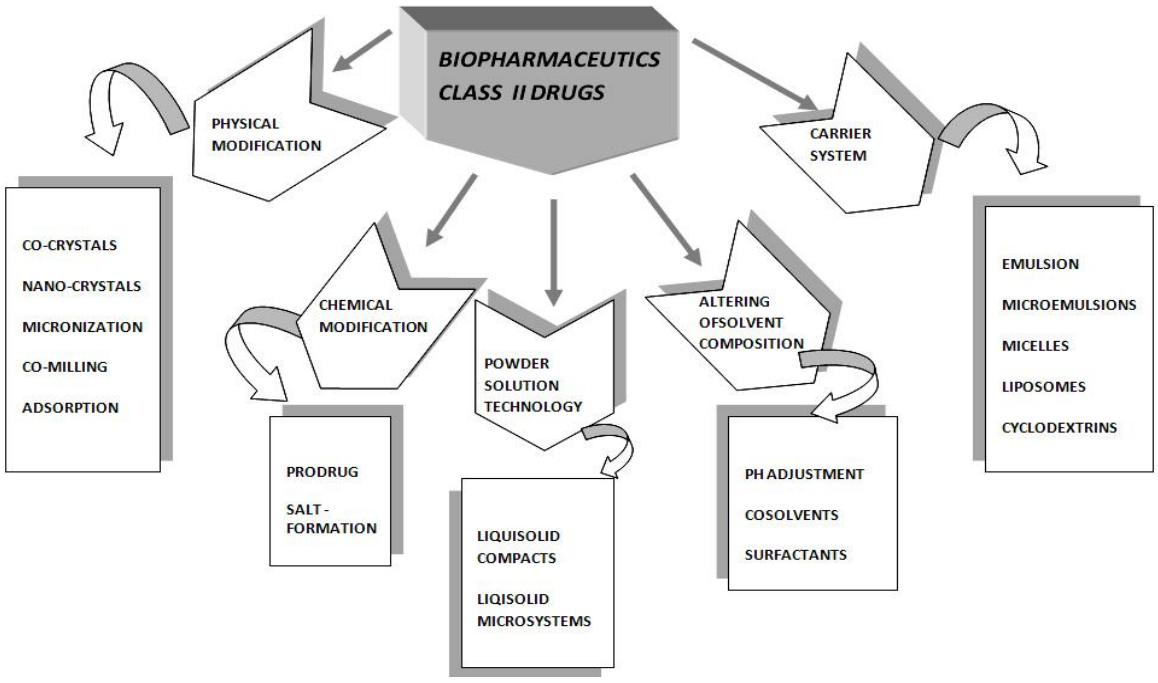

Fig. 2: Methods to enhance dissolution rate of BCS class II drugs.

Table 1: Classification of the liquisolid system.

Sl. No	Classification	Characteristics
Based on the formulation technique used		
1	Liquisolid compacts	Refers to immediate sustained-release tablets or capsules that are described under "liquisolid systems"
2	Liquisolidmicrosystems	Refers to capsules prepared by "liquisolid systems" with 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.
Based on the type of liquid medication		contained therein
1	Powdered drug solutions	Produced from the conversion of drug solution
2	Powdered drug suspensions	Produced from the conversion of drug suspensions
3	Powdered liquid drugs	produced from the formulation of liquid drugs

Mixing of this will lead to liquisolid system which is subjected to tableting by direct compression. This will result in increase in dissolution rate and in turn improvement in bioavailability is observed in case of poorly water soluble drugs. However, sustained effect is achieved in case of water soluble drugs. By use of this technique, liquid medications such as solutions or suspensions of water insoluble drugs in suitable non-volatile liquid vehicles can be easily converted into powder with acceptable flow properties and compression behavior using suitable powder excipients. Table 1 displays a brief classification of the repoted liquisolid sytems.

IDEAL CHARACTERISTICS OF COMPONENTS IN LIQUISOLID COMPACTS

Drug

The biopharmaceutical class II and class IV drugs which are poorly water soluble and have slow dissolution rate could ideally designed as liquisolid compact for enhanced dissolution rate.(Spireas, 2002; Spireas and Bolton, 1999; Yadav, 2010) Those drugs with solubilbity in high boiling point much preferably choosen for formulation. Some examples of drug that have been incorporated into liquisolid system includes chlorpheniramine, digoxin, nifedipine, clofibrate, gemfibrozil, etoposide, carbamazepine, hydrochlorothiazide, methyclothiazide, spironolactone, hydrocortisone, piroxicam, indomethacin, ibuprofen etc.

Carrier material

Relatively large, preferably porous particles possessing a sufficient absorption property which contributes in liquid absorption (coarser and granular) are chosen as carrier material for liquisolid compacts. They should also exhibit excellent compressibility (Spireas, 2002; Spireas and Bolton, 1999) Example of carrier materials includes various grades of microcrystalline cellulose such as Avicel PH 102 and Avicel PH200 , lactose, eudragit RL and eudragit RS (to sustain drug delivery).

Disintegrant

Superdisintegrants are used to increase the rate of drug release, water solubility and wettability of liquisolid granules (Spireas, 2002; Spireas and Bolton, 1999). E.g. Sodium starch glycolate and crosspovidone.

Coating material

They form the integral part of liquisolid compact system (Javadzadeh, 2009). Highly adsorptive particles which contributes in covering the wet carrier particles and displaying a dry-looking powder by adsorbing any excess liquid are choosen as coating material. They must be flow enhancing and very fine (10 nm to 5,000 nm in diameter) with higher surface area. E.g. Silica of various grades like Cab-O-Sil M5, Aerosil 200, Syloid 244 FP etc.

Non volatile solvents

The non-volatile solvents must be compatible with the drug of interst and must solubilize the drug. They must be inert with higher boiling point and of sufficient water miscibility. Non volatile solvents which are highly viscous are not preffered in liquisolid formulation (Spireas, 2002; Spireas and Bolton, 1999). Propylene glycol, liquid polyethylene glycols 200 and 400, polysorbates, glycerin, N, N-dimethylacetamide, fixed oils, etc. are most suitable as vehicles.

Table 2 displays a list of various studies carried out on liquisolid compacts (Amidon et al., 1999; Gubbi and Ravindra 2009; Legrand, 2004; Nagabandi et al., 2011; Schiermeir and Schmidt, 2002; Spireas and Sadu, 1998; Tiong and Elkordy, 2009).

APPLICATIONS OF LIQUISOLID COMPACTS

To enhance bioavailability

In the liquisolid technology the drug is either in a solid dosage form or it is held within the powder substrate in solution or in a solubilized, almost molecularly dispersed state.Non volatile solvent present in the liquisolid system facilitates wetting of drug particles by decreasing interfacial tension between dissolution medium and tablet surface.

Figure 3 shows lower contact angle of liquisolid compacts than the conventional tablets and thus improved wettability. Therefore, due to their significantly increased wetting properties and surface of drug available for dissolution, liquisolid compacts of water-insoluble substances may be expected to display enhanced drug release properties, and consequently, improved bioavailability.

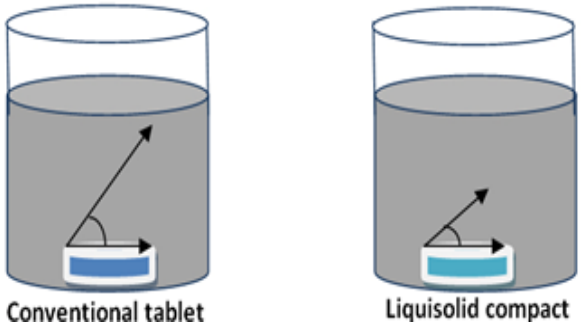

Fig. 3: Comparison of contact angle between conventional tablet and liquisolid compact.

Enhanced flowability and compressibility

To get rid from the problems of poor, erratic flowability and compressibility liquisolid compact technology confers as an efficient means. It is achieved by blending with suitable carrier and coating materials with which the drug is compatible.

This technique is also employed in tackling problems pertaining to liquid squeezing out phenomenon and unacceptable soft tablets.

Table 2: Details of studies carried out on liquisolid compacts

Drug	Co-solvent	Carrier material	Coating material	Use
Aceclofenac	PEG 400	MCC	HPMC	NSAID
Methyclothiazide	PEG 400	MCC	SILICA	Diuretic
Carbamazepine	PEG 200	MCC	Cab-o-sil	Anti-epileptic
	Propylene glycol	Avicel PH102	Aerosil 300	
Piroxicam	Tween 80	MCC	Silica	NSAID
	Propylene glycol	MCC	Silica	
Indomethacin	2- pyrrolidone	collodionCL-M	Aerosil 300	NSAID
	Propylene glycol	MCC	Silica	
	PEG 400	MCC	HPMC	
Prednisolone	N,N-dimethyl acetamide/PEG 400 (7:3v/v)	Drug solution dispersed on various silicas (no compacts)		In rheumatoid arthritis. Anti-asthma.
	Propylene glycol	Avicel PH 101, Lactose	Cab-o sil	
	Propylene glycol	MCC	Colloidal silica	
Prednisone	Propylene glycol	MCC	Colloidal silica	In rheumatoid arthritis. Anti-asthma.
	N,N-dimethyl acetamide/PEG400 (7:3v/v)	Drug solution dispersed on various silicas (no compacts)		
Hydrochlorthiazide	PEG 200	Avicel PH 101/102	Aerosil	Diuretic
	PEG 200	MCC Magnesium carbonate	Colloidal silica	
Hydrocortisone	Propylene glycol	Avicel PH 200	Cab- o -sil	NSAID
	Propylene glycol	MCC	Colloidal silica	
	N,N-dimethyl acetamide/PEG400(7:3v/v)	Drug solution dispersed on various silicas (no compacts)		
Griseofulvin	PEG 400	MCC	Colloidal silica	Antifungal
Famotidine	Propylene glycol	MCC	Colloidal silica	Anti ulcer
Fenofibrate	PEG400	MCC	Colloidal silica	Lipid lowering agent
	Propylene glycol	MCC	Colloidal silica	
Furosemide	Synperonic PE/L81	MCC	Colloidal silica	Diuretic
Ibuprofen	PEG 300	MCC	Colloidal silica	NSAID
Repaglinide	TWEEN 80	MCC	Calcium silicate	Antidiabetic
Polythiazide	PEG400	MCC	Colloidal silica	Diuretic
Naproxen	CremophorEL	MCC	Colloidal silica	NSAID
BromhexineHCl	PG	MCC	Clolloidal silica	Expectorent
Lamotrigine	PEG400	MCC	Clolloidal silica	Antiepileptic
Gemfibrosil	Tween 80	Avicel PH 200	Cab-o-sil M5	Lipid lowering agent
Nifedipine	PEG 400	Avicel PH 200	Cab-o-sil M5	Antihypertensive
Glibenclamide	PEG 400	Avicel PH 102	Aerosil	Antidiabetic
Clofibrate	_	Avicel PH 200	Cab-o-sil M5	Lipid lowering agent
	_	MCC	Colloidal silica	

In designing controlled release tablets and sustained release tablet.

Liquisolid technique could also be used in the formulation of controlled release and sustained release tablets by suitably changing the dissolution rate of drugs (Li et al., 2007; Spireas and Bolton, 1998; Ghorab et al., 2004; Gubbi and Ravindra, 2009).

If hydrophobic carriers (Eudragit RL and RS) are used instead of hydrophilic carries in liquisolid systems, sustained release formulation can be achieved. Henceforth the liquisolid compact technology is also having the potential for the reduction of the drug dissolution rate and thereby production of sustained release and contolled release systems.

Solubility and dissolution improvement

A large extend of Bio-Pharmaceutical classification class II and class IV drugs can be formulated into liquisolid systems. Poorly soluble, insoluble liquid drugs or lipophilic drugs could be suitably formulated with enhanced solubility and dissolution improvement without any compromise to its pharmacological action.

ADVANTAGES of liquisolid compacts

The major advantage of liquisolid compacts over other conventional tablets is their enhanced bioavailability (Grover et al., 1999; Papadimitriou et al., 2008). This technology can be used for formulation of liquid medication like suspension, oily liquid drugs and solutions of water insoluble solids drugs etc. In this technique the drug can be molecularly dispersed in the formulation.

Among the various methods that are used to improve the bioavailability of biopharmaceutical class II chemical entities the liquisolid compacts utilizes powder solution technology. The other methods like physical modification, chemical modification, alteration of solvent composition etc are teadious.

The process approaches like nanonisation and micronization techniques are omitted in the liquisolid compact technique.

The liquisolid systems could also be employed to formulate immediate release or sustained release dosage forms and also in controlled drug delivery system. Apart from all these drug related benefits these techniques also confer many industrial based advantages too which includes:

- Improved efficacy of tablet manufacturing.
- Lower production cost as compared to soft gelatin capsules.
- Sustained release, liquisolid tablets orcapsules of water insoluble drugs demonstrate constant dissolution rates (zero order release) comparable only to expensive commercial preparations that combine osmotic pump technology and laser –drilled tablets.
- Capability of large scale industrial production.
- To aid direct compression.

LIMITATIONS of liquisolid compacts

Inspite of having major applications and advantages these techniques has some limitations which includes:

- Not applicable for formulation of high dose insoluble drugs
- In order to achieve acceptable flowability and compactability for liquisolid powder formulation, high levels of carrier material and coating materials should be added. This will increase the weight of tablets to above one gram which makes them difficult to swallow. Consequently, it is impossible with conventional tablet methods to convert high dose to liquisolid tablets with a tablet weight of less than 50 mg.
- Dissolution profile enhancement occurs in the presence of low levels of hydrophilic carrier, where coating material is not significant.
- Low drug loading capacities

Preparation of liquisolid compacts

As displayed in Figure 4, the method of preparation of liquisolid compacts involves these following steps:

Liquifying with non volatile solvents

A liquid lipophilic drug (e.g., chlorpheniramine, clofibrate, etc.) can be converted into a liquisolid system without being further modified. On the other hand, if a solid water-insoluble drug (e.g., hydrochlorothiazide, prednisolone etc.) is formulated ,it should be initially dissolved or suspended in a suitable non-volatile solvent system to produce a drug solution or drug suspension of desired concentration.

Addition of carrier material

Next, a certain amount of the prepared drug solution or suspension, or the liquid drug itself, is incorporated in to a specific quantity of carrier material which should be preferably of a porous nature and possess sufficient absorption properties,such as powder and granular grades of microcrystalline and amorphous cellulose are most preferred as carriers.

Addition of coating material

The resulting wet mixture is then converted into a dry-looking, non-adherent, free-flowing and readily compressible powder by the simple addition and mixing of a calculated amount of coating material.

Excipients possessing fine and highly adsorptive particles, such as various types of amorphous silicon dioxide (silica), are most suitable for this step. Various adjuvants are mixed with the finished liquisolid systems to produce liquisolid compacts of desired release (Figure 5).

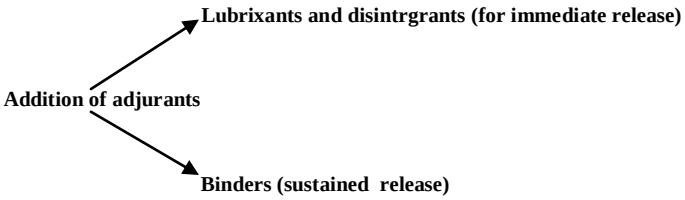

Fig. 5: Selection of adjuvants for desired drug release profile.

COMPRESSION

The liquisolid blend prepared are finally mixed with sufficient quantities of lubricants and glidants and compressed to obtain liquisolid compacts.

MECHANISM OF SOLUBILITY ENHANCEMENT

The mechanisms by which the liquisolid compacts show increased solubility and hence bioavailability include:

- Increased surface area of drug available for release
- Increased aqueous solubility of the drug
- Improved wettability of the drug particles

When the drug is dissolved or dispersed in a liquid vehicle it is located in the powder substrate still in a solubilized, molecularly dispersed state (Javadzadeh et al., 2007, Spireas and Sadu, 1998).

Therefore, the surface area of drug available for release is much greater than that of drug particles within directly compressed tablets.

The drug which is dissolved in the liquid vehicle is therefore incorporated into a carrier material which has a porous surface. The liquid initially absorbed in the interior of the particle is captured by its internal structure, and after the saturation of this process, adsorption of the liquid onto the internal and external surfaces of the porous carrier particles occurs. Both absorption and adsorption take place.

Here at the solid/liquid interface between an individual liquisolid primary particle and the release medium, it is possible that, in this microenvironment the amount of liquid vehicle diffusing out of a single liquisolid particle together with the drug molecules increases the aqueous solubility of the drug. The liquid vehicle (non volatile solvent) present in the liquisolid system can either act as surface active agent or have a low surface tension.

This improves wetting of drug particles by decreasing interfacial tension between dissolution medium and tablet surface.

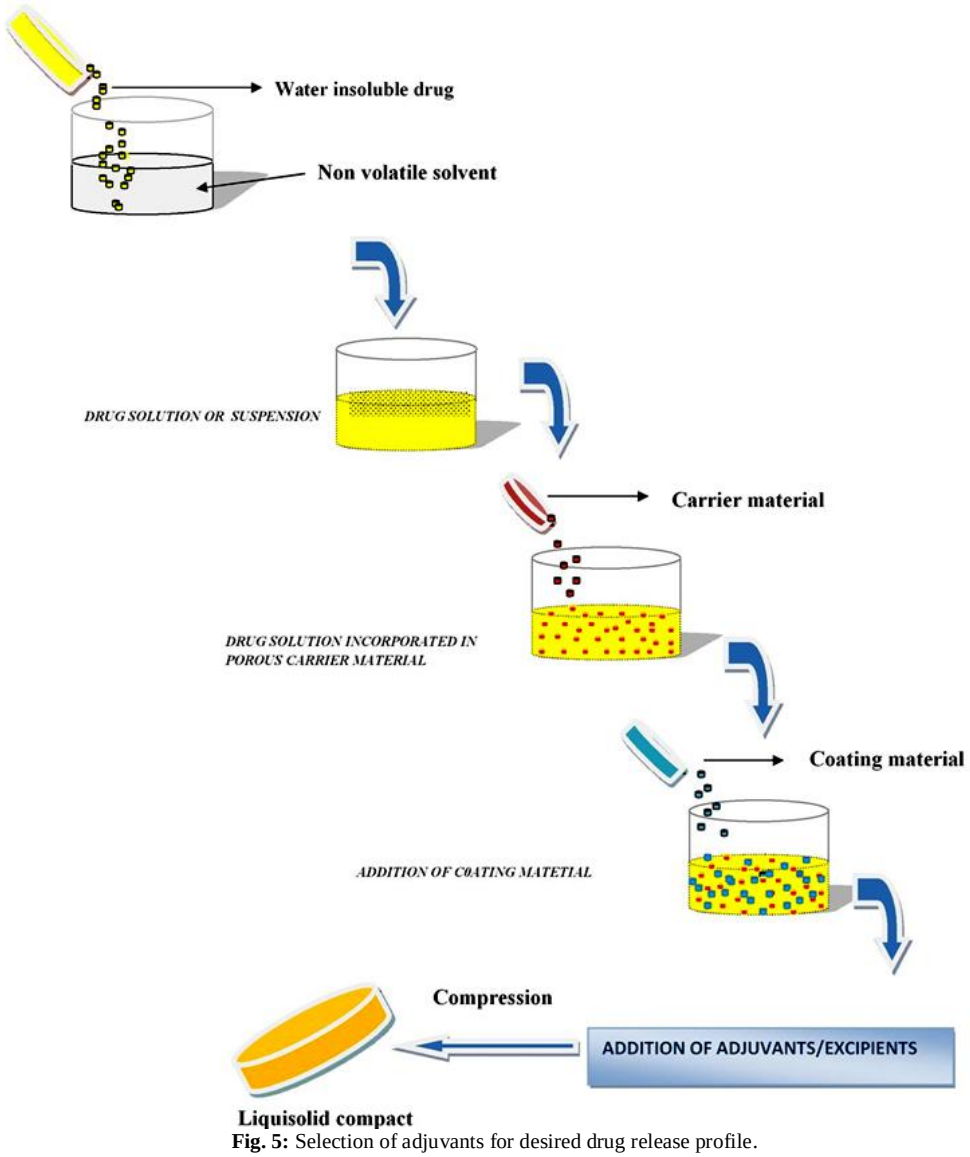

Fig. 5: Selection of adjuvants for desired drug release profile.

Design of Liquisolid Formulation

The mathematical model given by Spireas and coworkers is used as formulation design model for the liquisolid tablets (Spireas, 2002; Spireas and Bolton 1999). This approach is based on the flowable (Φ-value) and compressible (Ψ-number) liquid retention potential introducing constants for each powder/liquid combination.

The Φ-value (flowable liquid retention potential) is defined as the maximum weight of liquid that can be retained per unit weight of powder material in order to produce an acceptably flowing liquid/powder admixture.

The Ψ-value (compressible liquid retention potential) is defined as the maximum weight of liquid that can be retained per unit weight of the powder material in order to produce an acceptably compressible liquid or powder admixture i.e. being able to yield tablets of satisfactory mechanical strength without presenting any liquid squeezing out of liquisolid mass during compression. To calculate the required amounts of powder excipients for each powder/liquid combination a mathematical approach for the formulation of liquisolid systems has been developed.

$R = Q / q$ --- (1)

where R is the excipient ratio, Q is the weight of carrier and q is the weight of coating material.

Depending on this R value of the powder substrates a liquisolid system with acceptable flowability and compressibility can be obtained only if the maximum liquid load on the carrier material is exceeded. This liquid/carrier ratio is termed as liquid load factor (L_f) and is given by the expression:

$L_f = W / Q$ --- (2)

Where, L_f = liquid load factor, W = weight of liquid formulation and Q = weight of carrier material.

Preformulation and Characterization OF LIQUISOLID SYSTEMS

Before designing the liquisolid, the preformulation studies should be performed first, which comprise of:

- Determination of drug in different non-volatile solvents
- Determination of bulk properties
- Determination of flowable liquid retention potential (Φ value)
- Calculation of liquid load factor (L_f).
- Liquisolid compressibility test (LSC)
- Differential scanning calorimetry (DSC)
- Xray diffraction (XRD)
- Scanning electron microscopy (SEM)

Determination of drug in different non-volatile solvents:

These are carried out either by:

- Preparing saturated solutions of drug in non-volatile solvents, and analyzing them spectophotometrically or any other suitable analytical technique. Saturated solutions are prepared by adding excess of drug to vehicle and shaking them on shaker for specific time period under steady vibration. After this the solutions are filtered and analyzed spectrophotometrically.
- Dissolve the pure drug in different non-volatile solvents. To the non volatile solvents add excess amounts of pure drug , followed by saturation solution. Transfer the saturated solution to a rotatory shaker, kept for 48 hours at 25°C under constant vibration. After a period of 48 hrs the saturated solution is filtered through a 0.45µm millipore filter and then analyzed.

These solubility studies were conducted for the selection of high solubility of the pure drug forming the non-volatile solvents.

Determination of bulk properties

The following parameters describe a measure of the flow properties of liquisolid systems that will be selected and compressed into tablets (Liao and Jarowski, 1984).

Angle of Repose (θ)

In this method, a fixed height cone method procedure is performed in triplicate and average angle of repose is calculated.

$\tan \theta = h/r$ --- (3)

Where 'θ' is the angle of repose, 'h' is the height of cone and 'r' is the radius of the base of cone.

Bulk Density

The procedure for its determination involves the fixed height of each liquisolid powder substrate with prepared and fixed weight. The powder is placed in a graduated cylinder and the powder occupation volume is measured and from the data, initial bulk density (D_{Bmin}) is calculated.

The graduated cylinder is then allowed to tap at constant velocity until a constant volume is obtained.When the powder was considered to have reached the most stable arrangement, the final bulk volume is recorded. Final bulk density (D_{Bmax}) is then calculated.

Carr's index (%) = $[(D_{Bmax} - D_{Bmin})/ D_{Bmax}] \times 100$ --- (4)

Hausner ratio is calculated using the following equation 5.

Hausner ratio = $D_{Bmax} \div D_{Bmin}$ --- (5)

Angle of Slide

For the determination of angle of slide, an approximately weighed amount of coating material is placed at one end of a metal plate with a polished surface. This end was raised gradually until the plate for- median angle with the horizontal at which the powder was about to slide. This angle θ represents the angle of slide. It is taken as a measure for the flow characteristics of powders. An angle of slide of 33° corresponds to optimal flow properties (Spireas et al., 1998).

Contact Angle

For assessment of wettability, contact angle of liquisolid tablets is measured according to the imaging method. To measure the contact angle, a drop of liquid is directly placed on a flat surface of the solid in the so-called imaging method. The method for preparation of liquid drop is by using a saturated solution of drug in simulated gastric fluid, simulated intestinal fluid and an excessively large amount of drug is also added to it. It is then shaken for 24 hrs at a constant rate and the supernatant solution was centrifuged. A drop of this solution is placed on the surface of the tablet, and pictures are taken using a digital camera. By measuring the height and diameter of the sphere drop on the liquisolid tablets and direct compressed tablets, contact angle is measured. Liquisolid tablet contact angle is generally less than that of direct compressed tablets.

Determination of flowable liquid retention potential (Φ value)

The amount of carrier and coating material for producing acceptably flowing and highly compactible powders is based on the powders physical properties known as 'Flowable liquid–retention potential' (Φ value) (Banker and Anderson, 1987). Here increasing amounts of liquid paraffin is added to a powdered material and mixed well. The powder absorbs or adsorbs only the liquid paraffin giving a change in flow properties. A teach concentration of the liquid paraffin added, the angle of slide is redetermined according to previously described procedure. The Φ values are calculated according to equation:

Φ value = weight of liquid / weight of solid

Calculation of liquid load factor (L_f)

An acceptably flowing and compressible liquisolid system can only be prepared if the maximum liquid on the carrier material is not exceeded ; such a characteristic amount of liquid is termed the liquid load factor (L_f). Liquid load factor (L_f) is defined as weight of liquid medicament (W) to weight of carrier (Q) and is expressed by equation 2. Different concentrations of non-volatile

solvents is taken and on to it drug is dissolved. Such liquid medication is added to the carrier-coating material ad mixture and blended.Using the above equation, drug loading factors are determined and is used for calculating the amounts of carrier and coating material since each formulation.

Liquisolid compressibility test (LSC)

It is developed to carry out Ψ values and includes steps such as preparing carrier coating material admixture systems, preparing several uniform liquid/ powder admixtures to tablets, determining their average hardness, average liquid content in crushed tablets, as well as determining plasticity, sponge index ,Ψ value and L_f.

Differential scanning calorimetry (DSC)

The thermal behaviour and the thermotropic properties of the drug, excipients used in the formulation, as well as the liquisolid system prepared are determined by DSC. It also gives any possible interaction between excipients used in the formulation. It will also indicate success of the stability studies.If the drug is in the form of solution in liquisolid formulation, i.e.,the drug is molecularly dispersed within the liquisolid matrix, then the characteristic peak for the drug is absent in the DSC thermogram (Liao and Jarowski, 1984).

X-ray diffraction (XRD)

Inorder to characterize the crystalline state, the X-ray diffraction pattern is calculated for drug, excipients, physical mixture of drug and excipients and finally for the prepared liquisolid system (Fahmy and Kassem, 2008). Absence of characteristic peaks of the drug in the liquisolid XRD indicate that drug has almost entirely converted to amorphous or solubilised form. This amorphization or solubilisation of drug in the liquisolid system contributes to the consequent improvement in the apparent solubility and therefore the dissolution rate of the drug.

Scanning electron microscopy (SEM)

Scanning electron microscopy is mainly used to determine the morphological characteristics of the raw materials and the drug–carrier systems. This study confirms if there are any crystals present, or else drug is present in completely solubilised form by absence of crystals of drug (Liao and Jarowski, 1984).

CONCLUSIONS

Liquisolid system is a novel technique for improving the dissolution rates. By this technique oily liquids and water insoluble solid drugs in non volatile vehicles can be transformed into highly flowing and compressible powders. This method can enhance as well as retard the drug release. Bioavailability is the major advantage of liquisolid compacts over other conventional techniques.This system also offers industrial advantages including large scale production capability and productin of sustained and controlled release products .

REFERENCES

Amidon GL., Lennernas H., Crison JR. A theoretical basis for Biopharmaceutics drugs. Pharm Res. 1999; 12: 413-420.

Banker, G. S., & Anderson, N. L. (1987). Tablets. In: L. Lachman, H.A. Liberman, J.L. Kanig (Eds.) The theory and practice of industrial pharmacy (pp. 293-345). Bombay; Varghese publishing house.

Darwish AM., El-Kamel AH. Dissolution enhancement of glibenclamide using liquisolid tablet technology. Acta Pharm. 2001; 51: 173-181.

Fahmy RH., Kassem MA. Enhancement of Famotidine Dissolution rate through Liquisolid tablet formulation: In vitro and In vivo Evaluation. Eur J Pharm Biopharm. 2008; 69: 993-1003.

Ghorab MM., Salam HM., EL-Sayad MA. Tablet formulation containing meloxicam and β-cyclodextrin: mechanical characterization and bioavailability evaluation. AAPS PharmSciTech. 2004; 5: 1-6.

Grover R., Spireas S., Wang T. Effect of powder substrate on the dissolution properties of methchrothiazide liquisolid compacts. Drug Dev Ind Pharm. 1999; 25: 163-168.

Gubbi S., Ravindra J. Liquisolid technique for enhancement of dissolution properties of bromhexine hydrochloride. Research J Pharm and Tech. 2009; 2 (2): 382-386.

Hiremath SN., Raghavendra RK., Sunil F., Danki LS., Rampure MV., Swamy PV., Bhosale UV. Dissolution enhancement of gliclazide by preparation of inclusion complexes with cyclodextrin. Asian J Pharm. 2008; 2: 73-76.

Horter D., Dressman JB. Influence of physicochemical properties on dissolution of drugs in the gastrointestinal tract. Adv Drug Deliv Rev.1997; 46: 75-87.

Javadzadeh Y., Shariati H., Movahhed-Danesh E., Nokhodchi A. Effect of some commercial grades of microcrystalline cellulose on flowability, compressibility, and dissolution profile of piroxicam liquisolid compacts. Drug Dev Ind Pharm. 2009; 35(2): 243-251.

Javadzadeh Y., Siahi MR., Asnaashari S., Nokhodchi A. An investigation of physicochemical properties of piroxicam liquisolid compacts. Pharm Dev Tech. 2007; 12: 337-334.

Lbenberg R, Amidon GL. Modern bioavailability, bioequivalence and biopharmaceutics classification system. New scientific approaches to international regulatory standards. Eur J Pharm Biopharm. 2000; 50: 3-12.

Legrand E. Aceclofenac in the management of inflammatory pain. Exp Opin Pharmacother. 2004; 5: 1347-1357.

Liao CC., Jarowski CI. Dissolution rates of corticoid solutions dispersed on silicas. J Pharm Sci. 1984; 73: 401-403.

Li XS., Wang JX., Shen ZG., Zhang PY., Chen JF., Yun J. Preparation of uniform prednisolone micro crystals by a controlled micro precipitation method. Int J Pharm. 2007; 342: 26-32.

Lipinski C. Poor aqueos solubility an industry wide problem in drug discovery. Am Pharm Rev. 2002; 5: 82-85.

Modi A., Tayade P. Enhancement of dissolution profile by solid dispersion (kneading) technique. AAPS PharmSci Tech. 2006; 7(3): 2-17.

Papadimitriou SA., Bikiaris D., Avgoustakis K. Microwave-induced enhancement of the dissolution rate of poorly water-soluble tibolone from poly (ethylene glycol) solid dispersions. J Appl Polymer Sci. 2008; 108: 1249-1258.

Rasenack N., Muller BW. Dissolution rate enhancement by in situ micronization of poorly water-soluble drugs. Pharm Res. 2002; 19: 1894- 1900.

Schiermeier S., Schmidt PC. Fast dispersible ibuprofen tablet. Eur J Pharm Sci. 2002; 15: 295-305.

Smirnova I., Suttiruengwong S., Seiler M., Arlt M. Dissolution rate enhancement by adsorption of poorly soluble drugs on hydrophilic silica aerogels. Pharm Dev Tech. 2004; 9: 443-452.

Spireas S., Bolton M. Liquisolid systems and method of preparing same. US patent 5968550, 1999.

Spireas S., Bolton S. sustained release liquisolid compacts. In: 25th international symposium on controlled release of bioactive materials. Nevada, USA (pp. 138–139), 1998.

Spireas S. Liquisolid systems and method of preparing same. US patent 6423339 B1; 2002.

Spireas S., Sadu S. Enhancement of prednisolone dissolution properties using liquisolid compacts. Int J Pharm.1998; 166: 177-188.

Spireas S., Sadu S., Grover R. In vitro release evaluation of hydrocortisone liquisolid tablets. J Pharm Sci. 1998; 87(7): 867-872.

Tiong N., Elkordy A.A. Effects of liquisolid formulations on dissolution of naproxen. Eur J Pharm Biopharm. 2009; 73: 373-384.

Nagabandi VK., Ramarao T., Jayaveera K.N. Liquisolid compacts: A novel approach to enhance bioavailability of poorly soluble drugs. Int J Pharm Bio Sci. 2011; 1(3): 89-102.

Yadav VB. Enhancement of solubility and dissolution rate of biopharmaceutical class II pharmaceuticals by nonaqueous granulation technique. International Journal of Pharma. Research & Development. 2010; 1(12). 1-12.

How to cite this article:

Jomon N. Baby, Steffy B. Manjila, E.N. Bijin, Icey Constantine, K. Pramod, J. Valsalakumari. Design and Technology of Liquisolid Compacts. J App Pharm Sci. 2013; 3 (8 Suppl 1): S111-S119.