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Journal of Current Pharma Research 5 (4), 2015, 1665-1677.

Journal of Current Pharma Research
www.jcpronline.in

Review Article

Review on Liquisolid Compacts: A Novel Approach to Enhance Solubility of Poorly Soluble Drugs

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Received 15 February 2015; received in revised form 15 July 2015; accepted 16 July 2015
Available online 04 October 2015

Abstract

Solubility of drug is major challenge for the formulation and development of new dosage forms. Liquisolid compact is a new technique for enhancing the solubility of poor soluble drug. Liquisolid compact technique can change the dissolution rate of water insoluble drugs and increase the bioavailability of the drugs. This approach is suitable for immediate or sustained release formulations. Non volatile solvents enhance the solubility of water insoluble drugs by formation of micelles and act as dispersants. For immediate release liquisolid compacts, the selection of solvent is based on highly soluble drugs and for sustained release, solvents with low solubilising capacity is selected. For sustained drug release pattern, hydrophilic polymers like Hydroxy Propyl Methyl Cellulose can be the best option. Liquisolid is mainly composed of drug, non volatile solvent, carrier material, coating material, and disintegrates. In liquisolid compact, carrier and coating material should be take in the ratio and mix into the non volatile solvent and then disintegrate is added .final material is compressed into tablets. Liquisolid system is characterized by flow behaviour, wettability, powder bed hydrophilicity, saturation solubility, drug content, differential scanning Calorimetry, Fourier transform infra red spectroscopy, powder X-ray diffraction, scanning electron microscopy, *in-vitro* release and *in-vivo* evaluation.

Keywords: Bioavailability, non volatile solvent, carrier, coating agent, superdisintegrants.

1. Introduction

Solubility of drug is major parameter for development of new drug delivery system. About 40 % of newly developed drug are poorly water soluble. Among them orally administered drug is about 50-60% drug. They are facing difficulties during formulation of new dosage forms. BCS class II drugs pose challenging problems in their pharmaceutical product development process because of their low solubility and dissolution rates. They require enhancement in solubility and dissolution rate in their formulation development especially solid dosage forms such as tablets and capsules.

Therapeutic effectiveness of a drug depends up on the bioavailability and ultimately upon the solubility and dissolution rate of drug molecules. The oral route remains the preferred route of drug administration due to its convenience, good patient compliance and low medicine production costs.

Oral drug delivery system can be classified into three categories

- Immediate release
- Controlled/sustained release
- Targeted release

For immediate release liquisolid compacts, the selection of solvent is based on high drug solubility and for sustained release, solvents with least solubilising capacity is selected. For sustained release of drug hydrophilic polymer like Hydroxy Propyl Methyl Cellulose can be the best option

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Liquisolid Technique: [3]

***"*Liquisolid compacts*"*:** refers to immediate sustained-release tablets or capsules that are described under "liquisolid systems".

"Liquisolid Microsystems": refers to capsules prepared by "liquisolid systems" plus 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.

Liquid load factor (Lf): defined as the ratio of the amount of liquid medication (W) over the quantity of carrier material (Q) in the system.

$$Lf = \frac{W}{Q}$$

Carrier: Coating Material Ratio (R): Ratio between the quantities of carrier (Q) and coating materials (q) present in the formulation.

$$R = \frac{Q}{q}$$

"Carrier material": refers to a preferably porous material possessing sufficient absorption properties.

"Coating Material": refers to a material possessing fine and highly adsorptive particles.

Advantages

1) Huge number of Bio-Pharmaceutical classification class II drugs with high permeability, slightly or very slightly water soluble and practically insoluble liquids and solid drugs can be formulated into liquisolid systems.

2) Improvement of bioavailability of an orally administered water insoluble drugs is achieved.

3) This principle governs or administers the mechanism of drug delivery from liquisolid systems of powdered drug solutions and it is mainly responsible for the improved dissolution profiles exhibited by this preparations.

4) These liquisolid systems formulate into immediate release or sustained release dosage forms.

5) Optimized sustained release, liquisolid tablets or capsules of water insoluble drugs demonstrate constant dissolution rates (zero order release).

Disadvantages

1) This technique is only for water insoluble drugs.

2) However, for formulation of high dose insoluble drugs, the liquisolid tablet is one of the limitations of this technique.

3) In order to achieve acceptable flow ability 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. Therefore, it is impossible with conventional tablet methods to convert high dose to liquisolid tablets with a tablet weight of less than 50 mg.

4) Dissolution profile enhancement occurs in the presence of low levels of hydrophilic carrier, where coating material is not significant.

Limitations:

1) Not applicable for formulation of high dose insoluble drugs.

2) If more amount of carrier is added to produce free-flowing powder, the tablet weight increases to more than one gram which is difficult to swallow.

3) Introduction of this method on industrial scale and to overcome the problems of mixing small quantities of viscous liquid solutions onto large amounts of carrier material may not be feasible.

Historical development [5]

Historically, liquisolid compacts are descendants of 'powdered solutions', an older technique which is based on the conversion of a solution of a drug in a non-volatile solvent into a dry-looking, nonadjacent powder by mainly adsorbing the liquid onto silica of large specific surfaces. In these studies, however, large quantities of silica are still being used and the flow and compression properties of the products are never validated and standardized to industrial specifications and requirements. Specifically, when such modified powdered solutions were compressed into tablets, they presented significant "liquid-squeezing out" phenomena and unacceptably soft tablets, thereby hampering the industrial application of such systems.

Liquisolid compacts, on the other hand, are acceptably flowing and compressible powdered forms of liquid medications, and have industrial application. In addition, the term 'liquid medication' does not only imply drug solutions, as in powdered solutions, but also drug suspensions, emulsions or liquid oily drugs. Therefore, in contrast to 'powdered solutions', the term 'liquisolid compacts' is more general and it may encompass four different formulation systems namely,

1. Powdered drug solutions
2. Powdered drug suspensions
3. Powdered drug emulsions and
4. Powdered liquid drugs.

Furthermore, the older term of 'powdered solutions' seems to be inadequate even in describing the original systems, since it has not been proven that the drug remains in solution in the liquid vehicle after its deposition on the extremely large powder surfaces of silica used.The new 'liquisolid'' technique may be applied to formulate liquid medications (i.e. oily liquid drugs and solutions, suspensions or emulsions of water-insoluble solid drugs carried in nonvolatile liquid vehicles) into powders suitable for tableting or encapsulation.

- **Concept**

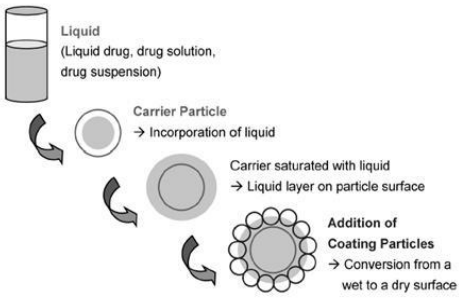

Fig. 1 Concept of Liquisolid formulation

When the drug dissolved in the liquid vehicle is incorporated into a carrier material which has a porous surface and closely matted fibers in its interior as cellulose, both absorption and adsorption take place; i.e., the liquid initially absorbed in the interior of the particles 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 occur. Then, the coating material having high adsorptive properties and large specific surface area gives the liquisolid system the desirable flow characteristics.[6]

- **Classification** [4]

Based on the type of liquid medication contained therein, liquisolid systems may be classified into three subgroups:

1) Powdered drug solutions
2) Powdered drug suspensions
3) Powdered liquid drugs

The first two may be produced from the conversion of drug solutions (e.g. prednisolone solution in propylene glycol) or drug suspensions (e.g. gemfibrozil suspension in Polysorbate 80) and the latter from the formulation of liquid drugs (e.g. clofibrate, valproic acid, liquid vitamins, etc.) into liquisolid systems [9]

Based on the formulation technique used, liquisolid systems may be classified into two categories, namely,

1) Liquisolid compacts
2) Liquisolid microsystems.

Liquisolid compacts are prepared using the previously outlined method to produce tablets or capsules, whereas the liquisolid microsystems are based on a new concept which employs similar methodology combined with the inclusion of an additive, e.g., polyvinylpyrrolidone (PVP) in the liquid medication which is incorporated into the carrier and coating materials to produce an acceptably flowing admixture for encapsulation

Components

The major formulation components of liquisolid compacts are:

1. Carrier Material

The carrier material should possess porous surface and closely matted fibres in the interior. Carriers are involved in the sorption process of liquid medication which improves the effective surface area for dissolution. These also assist the compression. Carriers due to relatively large, preferably porous particles, possess a sufficient adsorption property and matted fibres in interior contribute in absorption of liquid medication e.g. various

grades of cellulose, starch, lactose, sorbitol etc. [61]

2. Coating Material

Coating material forms a uniform film around the particles of carrier. Thus, they prevent the aggregation of particles as well as reduce the inter-particulate friction. This phenomenon improves the flowability as well as gives the liquisolid a dry-looking appearance by covering the wet carrier particles and by absorbing any excess liquid. Coat materials are usually very fine (10 nm to 5,000 nm in diameter) and highly adsorptive coating particles e.g. colloidal silica of various grades like Cab-O-Sil M5, Aerosil 200, Syloid 244FP etc.

3 .Non-Volatile Solvent

The solvent selected should possess ability to dissolve adequate amount of the drug candidate. Inert, preferably water-miscible and not highly viscous organic solvent systems having high boiling point e.g. propylene glycol, liquid polyethylene glycols, polysorbates, glycerine, N, N-dimethylacetamide; fixed oils etc are the suitable vehicles.

I. **Poly Ethylene Glycol**

PEG is a polymer of ethylene oxide. PEGs are liquids or low-melting solids, depending on their molecular weights. PEGs can be manufactured by polymerization of ethylene oxide. PEG with different molecular weights are used in different applications and have different physical properties, (e.g., viscosity), due to chain length effects, their chemical properties are nearly identical and also have different melting points. Their hydrophilic-lipophilic balance (HLB) values range from 8 – 19 depending on chain length. Lower-molecular-weight variants are used as solvents in oral liquids and soft capsules whereas solid variants are used as ointment bases, tablet binders, film coatings, and lubricants.. [06-08]

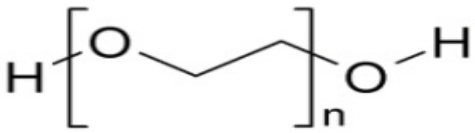

Fig. 3: General structure of Poly Ethylene Glycol

II. **Propylene Glycol**

Propylene glycol, also called 1,2-propanediol or propane-1,2-diol, is an organic compound (a diol or double alcohol) with formula C3H8O2 or HO-CH2-CHOH-CH3. It is a colorless, nearly odorless, clear, viscous liquid with a faintly sweet taste, hygroscopic and miscible with water, acetone, and chloroform. Propylene glycol is produced from propylene oxide. It is having HLB value of 11-13. It is used as a solvent in many pharmaceuticals, including oral, injectables and topical formulations. It is also used as humectants, emulsification agent, moisturizer etc.. [09]

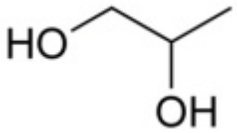

Fig. 4: Structure of Propylene Glycol

III. Polysorbate

Polysorbates are a class of emulsifiers used in some pharmaceuticals and food preparation. They are often used in cosmetics to solubilize essential oils into water-based products. Polysorbates are available in different varieties according to the presence of oxyethylene -(CH2CH2O)- groups found in the molecule, example Polysorbate 20 , Polysorbate 40 , Polysorbate 60, Polysorbate 80. Their HLB values range from 14– 20 depending on chain length. Polysorbates are used in pharmaceuticals as an excipient and it is also used as surfactant for enhancement of drug solubility. Enhanced dissolution for piroxicam is achieved by formulating liquisolid system with polysorbate80. [10]

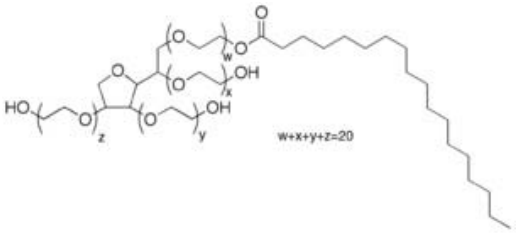

Fig. 5: General structure of Poly Sorbate

IV. Cremophor EL

Cremophor EL is a non-ionic solubilizer and emulsifier obtained by the reaction between ethylene oxide and castor oil in a molar ratio of 35 moles to 1 mole. The main component of Cremophor EL is glycerol-polyethylene glycolricinoleate, which, together with fatty acid esters of polyethylene glycol, represents the hydrophobic part of the product. The smaller, hydrophilic part consists of polyethylene glycols and ethoxylated glycerol. It appeared as a pale yellow, oily liquid having

characteristic odour. The hydrophilic-lipophilic balance (HLB) lies between 12 and 14..[11]

V. Synperonic PE/L61

Synperonic PE/L61 is a non ionic surfactant of block copolymer of polyethylene and polypropylene glycol. It is used in the manufacture of liquisolid preparation as a solubilizer for poorly soluble drug. Synperonic PE/L61 possess higher dissolution for furosemide.[12-13]

4. Disintegrants

The use of disintegrants, its type and concentration in the formulation will be mainly based on the objective of the investigation. For solubility enhancement studies, incorporation of superdisintegrants is encouraged. Most commonly used disintegrant is sodium starch glycolate (Explotab13, Pumogel etc.). While for matrix type of system intendeds for sustained release, disintegration is not required (Sandeep*et al*. 2012).

5. 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 [14]

Pre-formulation Studies [55]

Pre-formulation Studies includes

1. Determination solubility of drug in different non-volatile solvents
2. Determination of angle of slide
3. Determination of flowable liquid retention potential (Φ value)
4. Calculation of liquid load factor (Lf)
5. Liquisolid compressibility test (LS)

1. Determination solubility of drug in Different non-volatile solvents

Solubility Studies: Solubility studies were conducted for the selection of high solubility of the pure drug form in the non volatile solvents. This involves pure drug dissolved in different non-volatile solvents. Excess amounts of pure drug were added to the non-volatile solvents, followed by saturation solution transfer to a rotatory shaker for 48 hours at 25 ^{0}c under constant vibration. After a 48-hour period the saturated solution was filtered through a 0.45 μm Millipore filter and analyzed.

2. Determination of angle of slide64

The required amount of carrier is weighed and placed at one of a metal plate with a polished surface and it is gradually raised till the plate becomes angular to the horizontal at which powder is about to slide. [40] It was used to measure the flow properties of powders. The angle of 33° is optimum for flow of powder.

3. Determination of flowable liquid retention potential (Φ value)

It is defined as the maximum weight of liquid that can be retained per unit powder material in order to produce and acceptably flowing liquid/powder admixture. This Φ –value of powders may be determined using a newprocedure, the liquisolid flowability (LSF) test. The Ø valueis use to calculate excipients quantities. Equation for this is as follows:

$$\mathbf{Lf = Ø + Ø\ (1 / \mathit{R})}$$

Where

Ø and Ø are the constant Ø values of carrier and coating materials, respectively. By calculating Lf and W, we can calculate the amount of Q and q required for liquisolid systems.

4. Calculation of liquid load factor (Lf))

It is defined as the ratio of weight of liquid medication (w) to weight of carrier material (Q). Differnt concentrations of nonvolatile solvents are taken and the drug is dissolved and the carrier coating material is added and blended. [41]

$$\mathbf{Lf = W/Q}$$

W=ratio of weight of liquid medication

Q= weight of carrier material

The liquid load factor that ensures acceptable flowability (Lf), and can be measured by:

$$\mathbf{Lf = (1/R)}$$

5. Liquisolid compressibility test (LSC)

It is developed to determine Ψ values and involves steps such as preparing carrier coating material admixture systems,[42] preparing several uniform liquid/powder admixtures to tablets, determining average hardness, measuring of average liquid content of crushed tablets, as well as determining plasticity, sponge index and Ψ v

Preparation of Liquisolid Compact Tablet

1) First to **determine the solubility of drug** in different non volatile solvent .selection of the non volatile depend dosage form. For immediate release liquisolid compacts, the selection of solvent is based on high drug solubility and for sustained release, solvents with least solubilising capacity is selected.

2) Then calculated the **liquisolid loaded factor** by using mathematical model.

Liquid load factor (L_f) and defined as the ratio of the weight of liquid medication (W) over the weight of the carrier powder (Q) in the system, which should be possessed by a acceptably flowing and compressible liquisolid system. i.e.

$$\mathbf{L_f = W/Q} \qquad \mathbf{(1)}$$

The powder excipients ratios R and liquid load factors L_f of the formulations are related as follows:

$$^{\Phi}\mathbf{L_f = \Phi_{ca} + \Phi co(1/R)} \qquad \mathbf{(2)}$$

Φ_{CA} and Φ_{CO} are the phi-values of the carrier and coating powder materials respectively

In equation no.2 **R is represent as ratio of carrier to coating**. R should be taken as 15, 20, 25,30,35,40 and so for.

- **For good result, R should be taken in 20:1 in ratio Or above.**

Finally L_f is calculated by putting phi value of carrier and coating respectively. The selection of phi value of carrier and coating depend upon solubility in non volatile solvent (from table no. 3)

3) After calculation of L_f, going for calculating **carrier material** by using following equation

L_f = W/Q (1)

W - Liquid medication (weight of drug + solvent)

Q - carrier powder

For carrier material powder **(Q) = $\mathbf{L_f}$/W**

4) Then calculation of coating material **(q) = Q/ R**

- **FOR EXAMPLE.**
  - If drug show high solubility in PEG 400

Then,

$\mathbf{L_f = \Phi_{ca} + \Phi co\ (1/R)}$

$\mathbf{L_f = 0.005 + 3.26\ (1/R)}$ ……(from table no.3 with respectively excipient)

Where,

R - 5,10,15……(If R=20)

L_f = 0.168

We know that,

L_f = W/Q

W - Liquid medication (weight of drug + solvent) (if W=20.25)

Q - Carrier powder

- Carrier powder (Q) = W/L_f, 20.25/0.168 = 120.53
- Coating Material (q) = Q/ R, 120.53/20 = 6.02

- **General Method of Preparation**

A schematic outline of steps involved in the preparation of liquisolid systems is given in the figure1.

As seen in figure 1, a liquid lipophilic drug can be converted into a liquisolid system without being further modified. On the other hand, if a solid water-insoluble drug 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. Inert, high boiling point, preferably water-miscible and not highly viscous organic solvent systems are most suitable for this process.

In the next step, certain amount of the prepared drug solution or suspension or the liquid drug itself is incorporated into a specific quantity of carrier material which should be preferably of a porous nature and possessing sufficient absorption properties. Materials with a porous surface and closely matted fibers in their interior, such as powder and granular grades of microcrystalline and amorphous cellulose are most widely used as carriers. 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. Before compression or encapsulation, various adjuvants such as lubricants and disintegrates (immediate) or binders (sustained-release) may be mixed with the finished liquisolid systems to produce liquisolid compacts like tablets or capsules (Sandeep*et al*. 2012).

- **Mechanisms of Enhancement of Drug Release**[57]

1. Increased Effective Surface Area

If the drug within the liquisolid system is completely dissolved in the liquid vehicle, it is located in the powder substrate still in a solubilised and molecularly dispersed state. Therefore, the surface area of drug available for release is much greater than that of drug particles within directly compressed tablets. Accordingly, with increasing drug content exceeding the solubility limit and

thus, increasing fraction of undissolved drug in the liquid vehicle the release rate decreases

2. Increased Aqueous Solubility

In addition to the first mechanism of drug release enhancement, it is expected that the solubility of the drug might be increased with liquisolid systems. In fact, the relatively small amount of liquid vehicle in a liquisolid compact is not sufficient to increase the overall solubility of the drug in the aqueous medium. However, in the micro-environment of the solid/liquid interface between an individual primary liquisolid particle and the release medium, it is possible that the amount of liquid vehicle diffusing out of a single liquisolid particle together with the drug molecules might be sufficient to increase the aqueous solubility of the drug if the liquid vehicle can act as a co-solvent.

3. Improved Wetting Properties

Due to the fact that the liquid vehicle can either act as surface active agent or has surface tension lowering property, wetting of the primary liquisolid particles is improved. Wettability of these systems can be demonstrated by contact angles and water rising times. Also the adsorption of the drug on the carrier particles increases the effective surface area, improving the contact of drug and wettability

- **Application of the Mathematical Model for Designing the Liquisolid Systems** [58]

The flowability and compressibility of liquisolid compacts were addressed simultaneously in the 'new formulation mathematical model of liquisolid systems', which was used to calculate the appropriate quantities of the excipients (carrier and coating materials) required to produce acceptably flowing and compressible powders based on new fundamental powder properties called the flowable liquid retention potential (Φ -value) and compressible liquid retention potential (Ψ -number) of the constituent powders.

The flowable liquid retention potential of a powder is defined as the maximum amount of a given non-volatile liquid that can be retained inside its bulk (w/w) while maintaining acceptable flowability. This Φ-value is determined by recording powder flow.

The compressible liquid retention potential (Ψ) of a powder is the maximum amount of liquid, the powder can retain inside its bulk (w/w) while maintaining acceptable compactability to produce compacts of suitable hardness and friability with no liquid squeezing out phenomenon during the compression process.

The phi value of powders may be determined using a new procedure, the liquisolid flowability (LSF) test, which employs recording powder flow rate for the flow characterization of tested liquid/powder admixtures. The Ψ number of powders may be determined using a new method termed the liquisolid compressibility (LSC) test, which employs the recently proposed 'pactisity theories' to evaluate the compaction properties of liquid/ powder admixtures.

According to the new theories, the carrier and coating powder materials can retain only certain amounts of liquid while maintaining acceptable flow and compression properties. The excipients ratio (R) : the carrier to coating ratio of the powder system used, where,

$$R = Q/q$$

As R represents the ratio between the weights of carrier (Q) and coating (q) materials present in the formulation. An acceptably flowing and compressible liquisolid system can be prepared only if a maximum liquid on the carrier material is not exceeded; such a characteristic amount of liquid is termed as liquid load factor (L_f) and defined as the ratio of the weight of liquid medication (W) over the weight of the carrier powder (Q) in the system, which should be possessed by an acceptably flowing and compressible liquisolid system. i.e.

$$L_f = W/Q \qquad (1)$$

The powder excipients ratios R and liquid load factors L_f of the formulations are related as follows:

$$^{\Phi}L_{f} = \Phi_{ca} + \Phi co(1/R) \qquad (2)$$

Φ_{CA} and Φ_{CO} are the phi-values of the carrier and coating powder materials respectively.

In order to calculate the required ingredient quantities, the flowable liquid retention potentials (Φ-values) of powder excipients are utilized. So to calculate the required weights of the excipients used, first, from Eq. (2),Φ_{CA} and $\Phi_{CO}$and are constants, therefore, according to the ratio of the carrier/ coat materials (R), L_f is calculated. next, according to the used liquid vehicle concentration, different weights of the liquid drug solution (W) will be used. So, by knowing both L_f and W, the appropriate quantities of carrier (Q) and coating (q) powder materials required to convert a given amount of liquid medication (W) into an acceptably flowing and compressible liquisolid system could be calculated from equations (1) and (2).

- **Liquisolid System for Controlled Drug Delivery** [59]

Development of sustained release oral dosage forms is beneficial for optimal therapy in terms of efficacy, safety and patient compliance. Ideally, a controlled release dosage form will provide therapeutic concentration of the drug in the blood that is maintained throughout the dosing interval. There are several techniques for preparation of sustained release formulations, among which control of drug dissolution is one of the best and most successful methods due to its simplicity and low cost . To achieve this aim, several methods have been developed such as preparation of salt form of drug, coating with special materials and incorporation of drugs into hydrophobic carriers. It is suggested that liquisolid technique has the potential to be optimized for the reduction of drug dissolution rate and thereby production of sustained release systems. If hydrophobic carriers such as Eudragit RL and RS are used instead of hydrophilic carries in liquisolid systems, sustained release systems can be obtained.The mechanism of release prolongation is likely to be a more efficient encapsulation of drug particles by the hydrophobic polymers.

- **Evaluation of liquisolid tablets**

Thickness, Hardness test, Friability test, Weight variation test, Disintegration time,

Uniformity of contents, In-*vitro* dissolution study, *In-vivo* dissolution study

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 studies41. 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 thesystem[30]

X-ray diffraction (XRD)

Generally, disappearance of characteristic peaks of drug in the liquisolid formulation and retaining peaks of carrier material is observed30. This indicates that drug gets converted to amorphous form or in solubilized form in the liquisolid formulation.

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.

Fourier Transform Infrared spectroscopy (FTIR) (Bhise et al., 2009)

FTIR studies are performed to determine the chemical interaction between the drug and excipients used in the formulation. The presence of drug peaks in the formulation and absence of extra peaks indicates there is no chemical interaction.[60]

Conclusion

In conclusion, liquisolid compact refers to formulations formed by conversion of solid state to liquid state, drug suspensions or drug solution in non-volatile solvents into dry, nonadherent, free-flowing and compressible powder mixtures by blending the suspension or solution with selected carriers and coating agents. The formed liquisolid tablets dosage form showed significantly greater extent of absorption due to their solubility and dissolution improvement. The technique is also used to design sustained release systems by using hydrophobic carriers instead of hydrophilic carries in liquisolid systems. Liquisolid compact is novel techniques for enhancing solubility of poor soluble drug .Liquisolid compact approach is a promising technology because of the simple manufacturing process, low production costs and the possibility of industrial manufacture due to the good flow and compaction properties of liquisolid formulations. With this technology liquids such as solutions or suspensions of poorly soluble drugs in a non-volatile liquid vehicle are converted into acceptably flowing and compressible powders by simple physical blending with selected excipients named the carrier and the coating material

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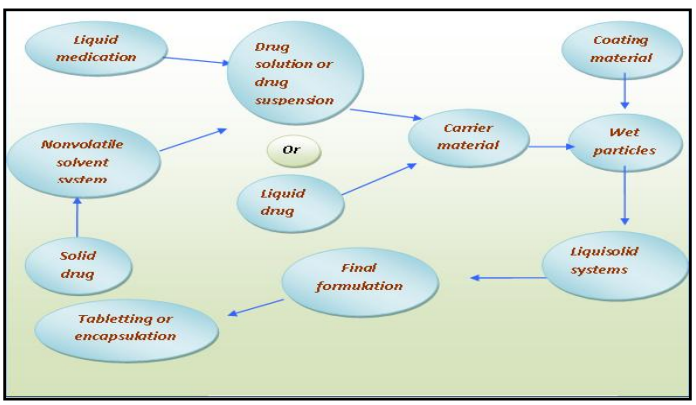

Fig. 2 Steps involved in the preparation of liquisolid

Table no.1 Excipient use in liquisolid compact**.**

Non Volatile Liquids	Poly Ethylene Glycol 200, Poly Ethylene Glycol 300, Poly Ethylene Glycol 400, Glycerine, Propylene Glycol, fixed oils.
Carrier Materials	Microcrystalline Cellulose PH 101, Microcrystalline Cellulose PH 200, Lactose, Methyl Cellulose, Ethyl Cellulose, Starch1500, Ethocel, Eudragit RL, Eudragit RS 12, Hydroxy Propyl Methyl Cellulose K4M, Hydroxy Propyl Methyl Cellulose K100M, Xanthum Gum, Guargum.
Coating Materials	Aerosil 200, Silica (Cab-O-Sil M5), Syloid 244FP, and Colloidal Silicon Dioxide.
Disintegrants	Sodium Starch Glycolate (Explotab, Primogel), Croscarmellose Sodium, Cross Polyvinyl Pyrrolidine, Pregelatized Starch.
Glidant	Talc
Lubricant	Magnesium Stearate
Release retardant material	Eudragit RS, RL, Hydroxy Propyl Methyl Cellulose K100M, K15M, K4M.

Tablel no.2 Drug candidate used in liquisolid compact

Release Drug	**Non-volatile vehicle**	**Carrier and coating material**
Aceclofenac	Propylene glycol, PEG 400 and Tween 80	MCC[15]
Aceclofenac	PEG 400	MCC and colloidal silica[16]
Atorvastatin calcium	Propylene glycol, Polyethylene glycol 400	MCC and colloidal silica[17]
Bromhexine HCL	Propylene glycol	MCC and colloidal silica[18]
Carvedilol	PEG 400	MCC and colloidal silica[19]
Carbamazepine	PEG 200	MCC and colloidal silica[20]
Clofibrate (liquid)	---------	MCC and colloidal silica[21]
Diclofenac sodium	Propylene glycol	MCC and colloidal silica[22]
Etoricoxib	PEG 400	MCC and colloidal silica[23]
Famotidine	Propylene glycol	MCC and colloidal silica[24]
Fenofibrate	Propylene glycol	MCC and colloidal silica[25]
Fenofibrate	PEG 400	MCC and colloidal silica[26]
Furosemide	Synperonic® PE/L 81, Caprol® PGE-860 and PEG 400	MCC and colloidal silica[27]
Glibenclamide	PEG 400	MCC and colloidal silica[28]
Griseofulvin	PEG 400	MCC and colloidal silica[29]
Glipizide	PEG 400	MCC and colloidal silica[30]
Hydrochlorothiazide	PEG 200	MCC and colloidal silica[31]
Hydrocortisone	PEG 400	MCC and colloidal silica[32]
Ibuprofen	PEG 400	MCC and silica gel[33]
Indomethacin	PEG 200, Glycerine	MCC and colloidal silica[34]
Indomethacin	Propylene glycol	MCC and colloidal silica[35]
Indomethacin	PEG 400	MCC and HPMC[36]
Ketoprofen	Propylene glycol and Tween80	Dicalcium phosphate and silica gel[37]
Ketoprofen	PEG 400	MCC, starch, dicalcium phosphate, lactose and silica gel[38]
Lamotrigine	PEG 400	MCC and colloidal silica[39]
Methyclothiazide	PEG 400	MCC and colloidal silica[40]
Naproxen	Cremophor EL, Synperonic PE/L61 and PEG400	MCC and colloidal silica[41]
Nifedipne	PEG 400	MCC and colloidal silica with HPMC [42]
Piroxicam	Tween 80	MCC and colloidal silica [43]

Polythiazide	PEG 400	MCC and colloidal silica[44]
Prednisolone	Tween 80, PEG 400, propylene glycol, Glycerine	MCC and colloidal silica[45]
Prednisolone	N,N dimethylacetamide /PEG400 (7:3v/v)	Various silicas[46]
Prednisone	Propylene glycol	MCC and colloidal silica[47]
Propanolol HCL	Tween 80	Eudragit RS or RL and colloidal silica with HPMC[48]
Repaglinide	Tween 80	MCC and calcium silicate[49]
Rofecoxib	PEG 600	MCC and colloidal silica[50]
Simvastatin	PEG 400	MCC and colloidal silica[51]
Theophylline	Tween 80	Eudragit RS or RL and colloidal silica with HPMC[52]
Tramadol HCL	Propylene glycol	MCC and colloidal silica with HPMC[53]
Valsartan	Propylene glycol	MCC and colloidal silica[54]

Table No.3 Examples of liquisolid formulation parameters of various powder excipients with commonly used liquid vehicles are listed

Powder excipient	**Flowability index Φ-values**		**Compressible Liquid Retention PotentialΨ-numbers**	
	Propylene glycol	PEG 400	Propylene glycol	PEG 400
Avicel PH 102	0.16	0.005	0.224	0.242
Avicel PH 200	0.26	0.02	0.209	0.232
Cab-Sil(silica)with Avicel PH 102	3.31	3.26	0.560	0.653
Cab-O-Sil (silica) with Avicel PH 200	2.57	2.44	0.712	0.717

Source of Support: Nil.

Conflict of Interest: None declared

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