

**Review Article****Enhancement of dissolution rate through design and techniques of liquisolid tablets formulation****Deeksha Tiwari\*, Vandana Sharma, Anjudip Yadav***Department of Pharmaceutics, Arya College of Pharmacy, Jaipur, Rajasthan-302028 India*

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**Abstract**

The solubility and dissolution properties of every drug are vital determinants of its oral bioavailability. A large portion of the recently evolved drugs are lipophilic and poorly water-soluble. Upgrading the dissolution and bioavailability of these medications is a main challenge for the pharmaceutical industry. During the development of another medication, it is imperative to guarantee its fundamental bioavailability. Here comes the requirement for a Liquisolid procedure which is a novel and promising way to deal with beat the outcomes. The strategy depends on the dissolving the insoluble medication in the nonvolatile solvent and admixture of drug solution with a reasonable carrier and coating materials to change over into acceptably flowing and compressible powders. The Liquisolid technique can also be used for the enhancement and retardation of drug release. The target of this article is to introduce a review of the Liquisolid strategy, the formulation, and designing of the liquisolid system and review the progress of its applications in pharmaceutics. Low cost, easy processing and great potentials in industrial production are the main advantages of this approach.

**Keywords:** Liquisolid system, liquid load factor, photostability, sustained release

**Introduction**

Out of the countless challenges in the design of pharmaceutical formulation, the most important is the solubility improvement of poorly water-soluble drugs and improvement of bioavailability (Vimalson et al., 2016).

Drugs belonging to the biopharmaceutics classification system (BCS) class II encounter the problem of low solubility, dissolution rate which leads to reduced bioavailability (Sahu et al., 2012). It is reported that about 40% of the newly developed drugs and nearly 60% of the produce chemical entities suffer from solubility issues (Liversidge et al., 2002). Consequently to enhance the solubility and dissolution of these poorly water-soluble drugs and improve their bioavailabilities is a serious matter of concern for many pharmaceutical scientists. The bioavailability of these Biopharmaceutical Classification system Class II (BCS II) drugs is regularly restricted by their solvency and dissolution rate in the gastrointestinal tract

(Amidon et al., 1999). All the drug delivery system target to give sufficient drug concentration at the site of activity and maintained the ideal concentration of the drug.

Precise information about the physiological and organic parameter of the drug is the key parameter for developing the drug transportation system. Oral drug administration has been one of the most suitable and extensively accepted routes of delivery for most of the remedial agents. It is one of the most comprehensively used routes of drug administration because of its evident advantages of ease of administration enhanced patient fulfillment, and ease. (Sudheer et al., 2014). Numerous studies have been carried out to increase the dissolution rate of drugs by decreasing the size of particles, by creating nano and microparticles. Another method of expanding the dissolution rate is the adsorption of the drug onto a high-surface-area carrier (Sworth et al., 2003). Nowadays, the synthesis of poorly soluble drugs increasing steadily. Therefore, one of the most important and promising areas of modern pharmaceutical technology is focused on a modern approach to the formulation and evaluation of solid dosage forms with enhanced bioavailability of poorly soluble

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drugs. These drugs signify up to 40% of commonly used active substances and approximately 70% of newly synthesized molecules. Of all these, the formulation of liquisolid systems represent one of the most encouraging and creative strategies for advancing dissolution rate and in-vivo bioavailability of poorly soluble drugs. The concept of "liquisolid tablets" was evolved from "Powdered solution technology" that can be Scientific literature describes some of the specific techniques for improving the solubility and bioavailability of tablets (including lowering particle size via micronization (Hiendrawn et al., 2014), the usage of surfactants (Nighute et al., 2009), lyophilization (Burra et al., 2013), the preparation of self-emulsifying drug transport structures (Qi et al., 2014) used to formulate "liquid medication". The word "liquid medication" refers to solid drugs isolated in suitable non-volatile liquid vehicles. By methods for straightforward mixing of such "liquid medication" using selected carriers and coating materials, dry-looking, non-adherent, free-flowing and promptly perfect powder admixtures can be created. The coating material is necessary to cover the surface and so maintain the powder flowability. Accordingly, as needs are, silica the coating material ought to be a fine and profoundly adsorptive powder. Liquisolid compacts are acceptably flowing and compressible powdered types of fluid drugs. The term liquid medication infers oily, fluid medications, and solutions or suspensions of water-insoluble solid drugs conveyed in a reasonable non-volatile solvent system named the liquid vehicles. A variety of grades of cellulose, starch, lactose, and so on, may be used as the carriers, whereas very fine-particle-size silica powders may be used as the coating materials (Nagabandi et al., 2011).

The word liquisolid compact alludes to sustained release or controlled release tablets or capsules, mixed with the thought of appropriate adjuvants required for tableting or encapsulating. It is been speculated that such systems exhibit enhanced release profiles. In this method, even though the drug is in a solid dosage form, it is held inside the powder substrate in solution or, in a solubilized, almost molecularly scattered state, which adds to the upgraded medicate dissolution properties. The liquisolid innovation can be used both for the enhancement and the retardation of drug release. It includes dissolving the medication in an appropriate non-volatile solvent and then adding this liquid medication to the mixture of carrier and coating materials.

#### Classification of Liquisolid system

A. Based on the type of liquid medication contained 'liquisolid compacts' is more general and it may encompass four different formulation systems namely,

- (a). Powdered drug solutions - Produced from the conversion of drug solution.

- (b). Powdered drug suspensions- Produced from the conversion of drug suspension.
- (c). Powdered drug emulsions- Produced from the conversion of drug emulsion.
- (d). Powdered liquid drugs- Produced from the formulation of liquid drugs.

B. Based on the formulation technique used:

- (a). Liquisolid compacts
- (b). Liquisolid microsystems

#### Advantages of Liquisolid System

- Improved efficacy of tablet manufacturing.
- Liquisolid system is versatile in the fact that it can be used for poorly soluble drugs
- When compared to soft gelatin capsules, the manufacturing expenditure is low.
- The drug can be formulated as a tablet or a capsule or the same as an encapsulated liquisolid microsystem.
- Instant release or continual release dosage forms can be formulated into Liquisolid compact relying upon the character of carriers used.
- Improves the bioavailability of water-insoluble drug candidates, which are given by the oral route.
- When compared to standard tablets the extent of absorption are often enhanced up to 15%
- The capability of enormous scale industrial production (Sahir et al., 2012).

#### Limitations of Liquisolid System

- It is observed that there is a rise within in the weight of tablets because of the presence of carrier material and coating materials at larger levels
- Applications of mathematical calculations are required
- The deficient hardness of liquisolid tablets results when acceptable compression isn't achieved
- The dissolution rate and bioavailability rely on the solubility of drugs in non-volatile liquids
- Low drug loading capacities (Sudheer et al., 2016)

#### Design of Liquisolid System

The powder can just hold a constrained measure of fluid medicine while maintaining adequate flowability and compressibility. During this manner, to realize a liquisolid system with sufficient flowable and compressible properties, a logical model introduced and endorsed by

Spireas is suggested to establish the acceptable amounts of carrier and coating material (Spireas et al 1999). The model depends on two basic properties of the powder, i.e., flowable liquid retention potential ( $\Phi$  value) and compressible liquid retention potential ( $\Psi$  value). The  $\Phi$  and  $\Psi$  estimations of a powder excipient represent the most amount of fluid vehicle that which will be held within powder mass without compromising flowability and compressibility (Spireas et al., 2002). The  $\Phi$  value is preferably determined by measuring the angle of slide of the prepared liquid–powder admixture. and also the  $\Psi$  value may be measured by an experiment called practicing, which is defined because the maximum crushing strength of a tablet with a tablet weight of 1gram when compressed at sufficient compression force (Spireas et al., 2002).

The excipients ratio (R), which is additionally referred to as the carrier/coating ratio, is defined as follows:

$$R = Q/q \quad (1)$$

Therefore, R is that the ratio between the weights of the carrier (Q) and coating material (q). A rise within the R-value will cause to higher quantities of the carrier and lower amounts of the coating material because the R-value is linked to the flowability and compressibility properties, disintegration, and dissolution rate of the liquisolid system, an optimum value of R is recommended to be 20 (Spireas et al., 1998). Another important parameter of the liquisolid system is termed as liquid loading factor (Lf), which is defined because the mass ratio of the liquid medication (W) and also the carrier material (Q) within the Liquisolid compact system.

$$L_f = W/Q \quad (2)$$

The liquid loading factor for the fabrication of a system with adequate flowability may be dictated by:

$${}^{\circ}L_f = \phi + \Phi/R \quad (3)$$

Wherever  $\Phi$  and  $\phi$  values correspond to the flowable liquid retention capacity of the carrier and coating material, individually. within the same way, the liquid loading factor to validate acceptable compressibility of a Liquisolid system is determined by:

$${}^{\psi}L_f = \psi + \Psi/R \quad (4)$$

Where  $\Psi$  and  $\psi$ , values maintain up a correspondence to the compressible liquid retention potential of the carrier and coating material, respectively. During this manner, the optimum liquid loading factor (L0) that delivers a liquisolid system with adequate flowability and compressibility is similar to either  $\Phi L_f$  or  $\Psi L_f$ , whichever has the lower value. Seeing that  $\Phi$ ,  $\Psi$ ,  $\phi$ , and  $\psi$  values are constants proposed for each powder liquid arrangement, for an accepted excipients ratio (R), the optimum

liquid loading factor (L0) is set in line with Equations (3) or (4). Then, in keeping with sort of drug concentrations, different weights of liquid medication (W) are utilized. In this way dependent on the determined L0 and W, the acceptable measure of carrier (Qo) and coating material (qo) are often calculated consistent with the Equations (1) and (2), respectively.

### Formulation of Liquisolid compact

Liquisolid compacts formula contains a carrier, coating material, nonvolatile solvent disintegrates, lubricants, and binding agents. The carrier utilized ought to be elastic, should possess palatable retention properties for a liquid vehicle, both carrier as well as coating materials should hold a limited quantity of liquid, at the similar time it should uphold flowability and compressibility, e.g. microcrystalline cellulose (MCC) (avicel PH 200 and avicel PH 102) (Savkare et al., 2017).

### Components of liquisolid compact formulation

#### [1] Coating material

Coating materials are usually coarsely powdered particles that provide coverage to the particles that are wet by adsorbing the excess of liquid, results in a dry free-flowing powder, e. g. various grades of silica (Syloid 244FP, Cab-O-Sil M5, and Aerosil 200) (Savkare et al., 2017).

#### [2] Nonvolatile solvent

Solvents used are nonvolatile, water-miscible, inert, and not very viscous. They ought to have a high boiling point; possess good solubilization power for drugs used. Binding act can also be provided within the formulation with the aid of nonvolatile liquids. E. g:-glycerin, polysorbate 80, propylene glycol, polyethylene glycol 200, and 400 (Kulkarni et al., 2010).

#### [3] Disintegrating agents (disintegrants)

These are agents that take up water, increases wettability, water solubility, and the rate of drug release. The breakup of compacts into smaller particles is able to achieve by the use of disintegrants. E. g sodium starch glycolate and cross-povidone, exploited, and pregelatinized starch (Javadzadeh et al., 2007).

#### [4] Drug candidate

BCS class II and IV drugs are mostly chosen as a medication contender for the liquisolid system. This results in improved water solubility of such candidates, e.g. Naproxen, Digitoxin, Prednisolone.

### Methodology

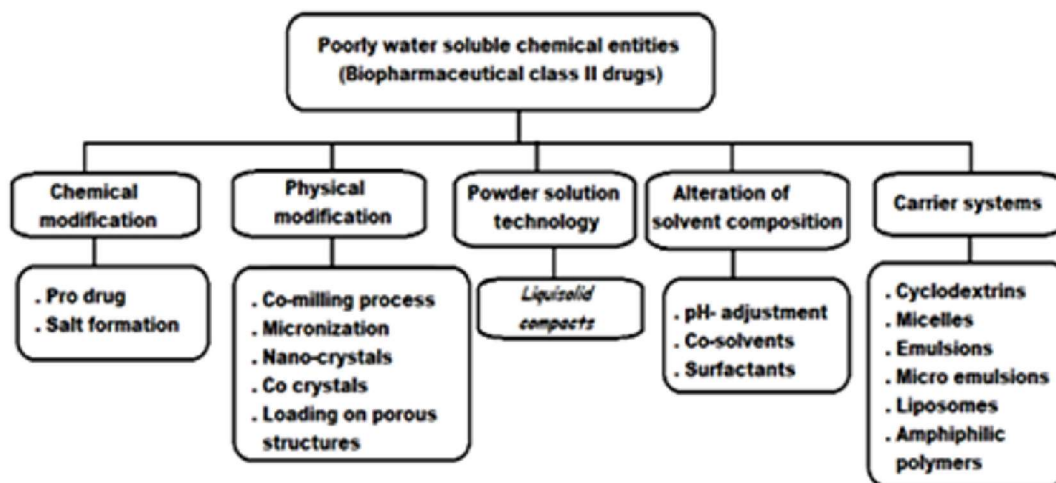


Figure 1. Methods to enhance the dissolution rate of BCS class II drugs

The requisite quantities of the drug and stated quantity of nonvolatile solvent is weighed, mixed and heated (if mandatory) results in a solution of the drug. Carrier and coating materials are included in the drug solution. The process of mixing is to be done as three stages are recommended (Sharma et al., 2012). First, stage- the weighed ingredients are to be combined at an estimated mixing rate of one rotation/second/minute, which will aid the liquid medication to contribute its role in the powder (Spireas, 1992).

Second stage- The above mixture should be spread evenly on a mortar surface for about 5 min. This results in the complete absorption of drug solution into the voids of powder particles (Spireas, 1992).

In the third stage, the above blend is to be mixed with a super disintegrant for 30 sec at a blending speed, which will result in the final blend ready for compression (Spireas, 1998).

**Preparation of Liquisolid compacts**

As displayed in Figure 3, the method of preparation of liquisolid

compacts involves these following steps:

Liquefying with non-volatile solvents:

First, a precisely calculated amount of pure drug weighted and dissolves in the appropriate amount of solvent in a molecularly dispersed state. A liquid lipophilic drug (e.g., chlorpheniramine, clofibrate, etc.) can be altered over into a liquisolid system without being additionally altered. On the other hand, but a solid water-insoluble drug (e.g., hydrochlorothiazide, prednisolone, etc.) is formulated, it should be primarily dissolved or suspended in a suitable non-volatile solvent system to make a drug solution or drug suspension of the preferred concentration.

**Addition of carrier material**

Next, an assured amount of the prepared drug solution or suspension, or the liquid drug itself, is consolidated into a particular amount of carrier material which ought to be ideally porous and possess sufficient absorption properties,

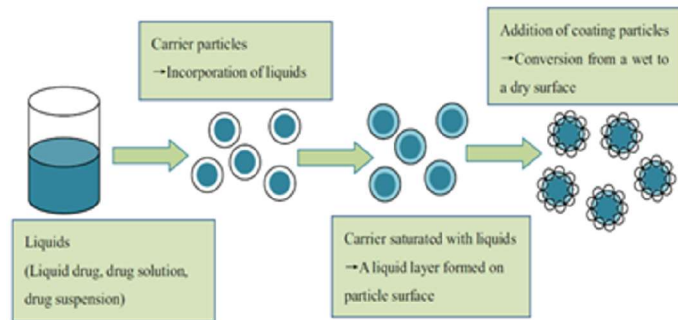


Figure 2. Mechanism of Liquisolid System Formulation.

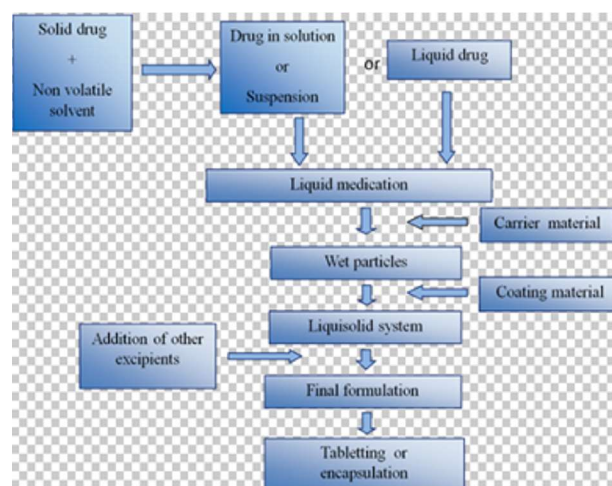


Figure 3. General preparation of Liquisolid compacts

**Table 1.** Examples of some drugs that can be incorporated into Lquisolid systems

Sr. No.	Drug Name	Use
1.	Chlorpheniramine	Antihistamine
2.	Digoxin	Cardiac glycoside
3.	Nifedipine	Antihypertensive
4.	Clofibrate	Diuretic
5.	Gemfibrozil	Hyperlipidemic
6.	Etoposide	Alkaloids
7.	Carbamazepine	Antiepileptic
8.	Hydrochlorothiazide	Diuretic
9.	Methyclothiazide	Diuretic
10.	Spironolactone	Diuretic
11.	Hydrocortisone	NSAID
12.	Fenofibrate	Lipid lowering agent
13.	Bromhexine hel	Expectorant
14.	Lamotrigne	Antiepileptic
15.	Prednisone	Anti-asthma

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 having fine and profoundly adsorptive Particles, such as various types of amorphous silicon dioxide (silica), are most suitable for this step. Various adjuncts are mixed with the finished liquisolid systems to produce Liquisolid Compacts of the desired release.

#### Addition of adjuncts

Selection of adjuvants for desired drug release profile, adjuncts are such as- lubricants and disintegrants (for immediate release), Binders (for sustained release).

#### Compression

The Liquisolid blend prepared is finally mixed with adequate amounts sufficient of lubricants and glidants and compressed to obtain liquisolid compacts.

#### The mechanism associated with improved drug release profile from Liquisolid systems

Different literature reports emphasize that the liquisolid system has been used to improve the release rate of weakly soluble and low dose drugs. The alteration of an enormous portion of water-insoluble medications can be accomplished by added substances polyvinyl pyrrolidone (PVP), hydroxyl propyl methylcellulose (HPMC), polyethylene glycol (PEG) 35000 (Javadzadeh et al., 2007). These additives can increase the liquid absorption capacity of carrier and coating material (Hentzschel et al., 2011).

The accountable mechanism for enhanced drug release is given

below:

The augmented surface area the increase in the surface area of the drug in a liquisolid system results from a complete dissolution of the drug in a liquid vehicle which represents the drug insolubilized and molecularly dispersed state (Hentzschel et al 2011).

A connection between straightforwardly compacted tablets and tablets arranged by the liquisolid procedure recommended that the drug release from the latter was at a higher rate. The molecularly dispersed fraction of drug in the liquid formulation is given by solubility of the drug divided by drug concentration which is expressed by the following equations (Hasanandini et al., 2014).

$$F_m = S/C$$

Where,

$$F_m = 1 S \geq C$$

#### Improved aqueous solubility of the drug

Enhancement in the water solubility of the medication is due to the presence of a solid-liquid boundary between liquisolid primary particles and the media nearby it. The quantity of the vehicle diffuses along with drug particles from the microenvironmental condition contributes to an increase in the aqueous solubility, which may be due to the co-solvent effect of the vehicle (Komala et al., 2015).

#### Improved wetting properties

The liquid vehicle has surface-active properties that reduce the surface tension, results in the wetting of primary particles. The wettability can be determined by contact angle measurements and the water rising time (Kumar et al., 2011).

#### Porosity

The liquisolid technology leads to soft structures with a high porosity which enhances the disintegration and dissolution process of liquisolid compacts of felodipine pellets.

#### Mechanism of Sustained drug release from Liquisolid system

The replacement of the usual hydrophilic carrier with the hydrophobic carrier can lead to poor wetting which results in slow disintegration and thus extends the release of the drug. It is observed that there is neither a change in the crystalline nature of neither the drug nor a complex formation that takes place during the process of liquid-solid compacts. This observation is much confirmed by X-ray crystallography and DSC measurements (Khalid et al., 1998). Another reason for decreased drug release is the influence of liquid vehicle, which was evident from the comparative study of directly compressed matrix tablets

made of Eudragit® RS or RL as matrix-forming material and lquisolid compacts, contains polysorbate 80 as the fluid vehicle. Further, retardation was observed to a higher degree for the release of the drug from the lquisolid compact in contrast to conventional matrix tablets (Tayel et al., 2008). The coalescence observed with polymer a particle in lquisolid compacts is a lot of lower than with traditional matrix tablets. The reason for decreased drug release is due to the distinct coalescence of polymer particles, which leads to decreased porosity and increased tortuosity (Resenack et al., 2003). The hydrophobicity of the polymer may contribute to the sustained release of the drug. The use of HPMC in the hydrophilic matrix system retards the drug-retaining by undergoing molecular weight dependent swelling. This system, when contact with water either swells or erodes results in zero-order kinetics (Azami et al., 2005). It is reported that the drug retardation effect from HPMC lquisolid compacts was more evident in comparison to directly compressed tablets (Ghorab et al., 2004).

#### **Mechanism of Controlled drug release from Lquisolid system**

Lquisolid technique could also be used in the formulation of controlled-release tablets by suitably changing the dissolution rate of drug. If hydrophilic carriers are used instead of hydrophobic carries in lquisolid systems, controlled release formulation can be achieved. In the future, the lquisolid compact technology is also having the potential for the reduction of the drug dissolution rate and thus the production of sustained release and controlled release systems.

#### **Preformulation studies**

Preformulation studies performed to confirm the physiochemical characterization and it includes the following studies (Stegemann et al., 2016).

- ✍ Solubility studies of the drug in solvents
- ✍ Sliding angle determination
- ✍ Flowable liquid retention potential
- ✍ Liquid load factor (LLf)
- ✍ Liquid-solid compressibility test (LSC)

The solubility of the drug in non-volatile solvents:

A saturated solution of the drug is prepared and is used for solubility studies. A surplus of the drug is added to vehicles which results in a saturated solution by employing the shaker for the solution at a given period under steady vibration. The filtrate of the drug solutions followed by analyzed spectrophotometrically.

#### **Angle of slide**

The sliding angle measures the flow behavior of powders. A

metallic plate with a smooth surface is used for the test, where the test powder is placed at one end of it, is gradually raised till the plate becomes angular to the horizontal plane, at which the powder just slides. The powder having an angle of 33° provides optimum flow characteristics.

#### **Liquid flowable liquid retention potential (Φ)**

It shows the liquid retention potential of the powder with adequate flow behavior.

#### **Liquid load factor (LLf)**

It is the proportional of the weight of liquid medication (W) to the weight of carrier material (C). This is determined by taking adequate quantities of nonvolatile solvents in which the drug is dissolved, the resulting solution is converted to a free-flowing powder by the addition of carrier and coating materials.

#### **Lquisolid compressibility test (LSC)**

This test determines the Ψ values (compressible liquid retention value). It is done by preparation of carrier and coating material admixture, converting the admixtures into tablets. The average rigidity is measured by the average liquid content of crushed tablets (Gavhane et al., 2013).

#### **Evaluation of Lquisolid system**

Flow behaviour

Differential Scanning Calorimetry (DSC)

X-ray diffraction (XRD)

Scanning Electron Microscopy (SEM)

Dissolution testing

In vivo evaluation

#### **Flow behavior**

##### **Bulk density:**

A weighed quantity of the powder blend is transferred into a graduated measuring cylinder. The bulk volume (Vb) of the weighed quantity of the powder (W) is determined. Bulk density is given below:

$$\text{Bulk density} = W / V_b$$

##### **Tapped density:**

The weighed amount of powder mass is poured to a graduated measuring cylinder and tapped for a fixed number of times and the volume is determined (Vt). Tapped density can be given by,

$$\text{Tapped density} = W / V_t$$

#### **Compressibility index**

Compressibility index is given by the following equation:

Compressibility index = (tapped density–bulk density/ tapped density) 100

### Hausner's ratio

The indirect measurement of the flow pattern of powders is given by:

Bulk density/ Tapped density = Hausner's ratio

A value below <1.25 indicates good flow behavior, whereas >1.5 signifies poor flowability.

Hausner's ratio can vary depending on the method used for the determination, so it is not taken as a critical parameter in flow behaviour.

### Angle of repose

The powder blend is passed through a funnel that is made to ascend vertically till the funnel tip touches the pile of the powder. The height of the pile (h) and the radius of the base of powder pile (r) is measured. The angle of repose is calculated as follows (Panda et al., 2017).

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

### Differential scanning calorimetry (DSC)

The thermal behavior of the pure components and the liquisolid compacts can be evaluated by DSC studies. About 3–5 mg of the sample is vacuum-packed in aluminum pans exposed to the invariable rate of heating 10 °C/min at a temperature range of 30 to 300 °C. Aluminum pans which are vacant are used as references and by purging nitrogen, the entire thermal behavior is studied. The absence of characteristic peak of the drug in presence of excipients is an indication of incompatibility of drug with excipients as well as changes in the crystalline pattern of the drug; maybe a molecular level changes from a crystalline to amorphous pattern (Thakur et al., 2011).

### X-ray diffraction (XRD) studies

XRD studies determine the crystalline belongings of the liquisolid compact mixture by the X-Ray diffractometer. The study uses a current of 30 mA and a copper target at a voltage of 40 kV. The instrument works at a scanning angle of 5 to 70 ° and a counting rate of 0.4 s/step. The change in the peak pattern from distinct and sharp to a random pattern gives evidence about the conversion of the crystalline nature of drugs to amorphous forms of drug (Sanjay et al., 2013).

### Scanning electron microscopy

This technique helps in determining the surface behavior of the drug, which gives an idea of whether the drug is crystallized from the liquisolid system. The solubilized nature of the drug in the liquisolid system results in the disappearance of these molecular forms (Khalid et al., 2001).

### In vitro drug release studies

In vitro release studies of the liquisolid tablets are performed through USP dissolution apparatus type II. The studies are carried out in 900 ml 0.1 N HCl maintained at a constant temperature of 37 °C±2 °C at a stirring speed of 50 to 200 rpm. After adding a known amount of drug equal formulation into the media, the percentage of drug dissolved is determined by withdrawing the samples at regular intervals, and sink conditions are maintained by replacing with fresh buffer. The drug concentration can be determined spectrophotometrically (Khalid et al., 2001).

### In vivo evaluation of liquisolid tablets

The relative plasma concentration profile of the drug from the liquisolid compact in comparison to a commercial tablet should show a significant difference in the area under the plasma concentration profile, relative bioavailability, and peak plasma concentration (Aher et al., 2014).

### Applications of liquisolid technique in pharmaceuticals

#### *Liquisolid technique as a device to enhance drug dissolution*

Liquisolid technique has been widely used to improve the dissolution rate of low dose insoluble drugs, such as valsartan, ketoprofen. (Spireas, 1998).

In the case of high dose water-insoluble drugs such as carbamazepine, the feasibility of the liquisolid technique has also been discussed. Javadzadeh et al. suggested (Javadzadeh et al., 2007) that it is possible to involve liquisolid technique in the incorporation of high dose water-insoluble drugs into liquisolid systems by adding up some additives (such as PVP, HPMC, and polyethylene glycol 35000) because these additives can increase the liquid absorption capacity of carrier and coating materials. Hentschel et al. (Hentzschl et al., 2011) have shown another potential approach to load a high dose of poorly water-soluble drugs into liquisolid systems, namely by using modern carriers (such as Neusilin®) with larger SSA value and higher absorption capacity.

#### *Liquisolid technique as a device to sustain drug release*

Liquisolid technique is originally designed to enhance the dissolution rate of poorly water-soluble drugs. In the past few years, extensive studies indicated that the liquisolid technique could be utilized as a promising method for preparing sustained-release formulations of different drugs (Hentzschl et al., 2011, Javadeh et al., 2008). Sustained-release formulations are designed to release the drug slowly at a predetermined rate for a certain period with high efficacy, high patient compliance, and minimum side

effects. One of the primary points of interest in applying the liquisolid procedure in delaying drug release is the likelihood to accomplish a liquisolid system with zero-order release kinetics.

#### ***Liquisolid technique as a device to minimize the influence of pH variation on drug release***

The solubility of weak acids and bases is dependent on the ionization constant (pKa) of the compound and pH of the local environment. Therefore, the dissolution and bioavailability of these drugs are greatly influenced by the pH of gastrointestinal fluids. This further leads to a high degree of inter and intra-variability in drug bioavailability and therapeutic effects (Badawy et al., 2016). El-Hammadi et al. (Hammadi et al., 2012) first investigated the chance of utilizing a liquisolid procedure to limit the impact of pH variation on the release of loratadine. Numerous liquisolid formulations were prepared using propylene glycol as a liquid vehicle, MCC as a carrier, and silica as a coating material. The dissolution profile of the prepared liquisolid tablets was investigated in three buffered media with pH values of 1.2, 2.5 and 5 respectively (Chella et al., 2014).

#### ***Liquisolid technique as a promising device to improve drug photostability in solid dosage forms***

A loss of drug potency during the photodegradation process may result in toxic degradation products and causing potential side effects, thus the photostability study is an indispensable part of pre-formulation studies for photosensitive drugs. (Khames et al., 2013). designed a study to evaluate the possibility of using the liquisolid technique as a promising alternative to conventional coating for the improvement of drug photostability.

#### **Future Perspective**

The low oral bioavailability of a large number of drugs is a result of their poor solubility. Drugs falling in class II of the BCS fail to reach the systemic circulation in required amounts due to poor solubility.

Large number of drugs in spite of their excellent pharmacological activity *in vitro* cannot be formulated as an oral dosage form because of their low bioavailability.

Liquisolid compaction is a simple technique feasible at industrial scale. The formulation prepared using liquisolid compaction presents the drug in solubilized form ready to be absorbed. Thus, the technique is likely to be adopted by the industries in the coming years. It is very suitable for BCS class II drugs that are administered at low doses.

Even the step of granulation for the preparation can be avoided if choice of suitable excipients is done. Thus, it is a preferable method for enhancement of oral bioavailability of drugs

having low solubility.

#### **Conclusion**

To enhance the solubility and dissolution of poorly water-soluble drugs is still a matter of concern for pharmaceutical scientists. A review of extensive literature demonstrates that the improvement of the liquisolid technique is advancing very fast in the past few years. 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. Liquisolid technique is not only a useful tool to improve the dissolution rate of poorly water-soluble drugs, but also an inventive and magnificent strategy to prepare sustained-release tablets with zero-order release pattern. Thus, a constant plasma level will be reached, which is maintained throughout the dosing interval. Besides, the method has displayed incredible potential in diminishing the impact of pH variation on drug release and improving drug photostability in solid dosage forms. This system also offers industrial compensation including large scale production capability and production of sustained and controlled release products. The *in vitro* dissolution study confirmed enhanced drug release from liquisolid compacts compared with directly compressed counterparts and this was independent of the type and volume of the dissolution medium. For sustained-release liquisolid compacts, the choice and the concentration of the excipients such as a liquid vehicle, retarding agent (matrix-forming material) as well as carrier and coating material play an important role.

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