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RESEARCH ARTICLE

Liquisolid Technique for Poorly Soluble Drugs

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ABSTRACT

It is well established that the active ingredient in a solid dosage form must undergo dissolution before it is available for absorption from the gastrointestinal tract. About 40% of the newly discovered drugs fall into poorly water soluble or water insoluble categories. The aqueous solubility of poorly water-soluble drugs is usually less than 100ug/ml. The Liquisolid compact system is a novel concept of drug delivery that can change the dissolution rate of water insoluble drugs. Formulation and manufacture of the Liquisolid compacts are quite simple method according to a new mathematical model described by Spireas et al. The technique is based upon dissolving the insoluble drug in the non-volatile solvent and admixture of drug loaded solutions with appropriate carrier and coating materials to convert into acceptably flowing and compressible powders. 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 behaviour using suitable powder excipients.

Keywords: Liquisolid, Solubility, Carrier, Super disintegrate

INTRODUCTION:

The solubility behaviour of a drug is one of the key determinants of its oral bioavailability. In recent years, the number of poorly soluble, drug candidate has increased tremendously. The formulation of poorly soluble drugs for oral delivery presents a challenge to the formulation scientists.[1] The oral route remains the preferred route of drug administration due to its convenience, good patient compliance and low medicine production costs. In order for a drug to be absorbed into the systemic

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Circulation following oral administration, the drug must be dissolved in the gastric fluids. The active pharmaceutical ingredient in a solid dosage form must undergo dissolution before it is available for absorption from the gastrointestinal tract. For hydrophobic drugs, the dissolution process acts as the rate-controlling step and, which determines the rate and degree of absorption. Consequently, many hydrophobic drugs show erratic and incomplete absorption from the gastrointestinal tract , Thus, one of the major challenges in drug development today is poor solubility, as an estimated 40% of all newly developed drugs are poorly soluble or insoluble in water. In addition, up to 50% of orally administered drug compounds suffer from formulation problems related to their low solubility and high lipophilicity 2,3 Bioavailability of poorly water-soluble drugs is limited by their solubility and dissolution rate.

Approaches to enhance the dissolution of drugs:

Pharmaceutical approach:

It involves modification of formulation e.g. modification of formulation, manufacturing process.

Pharmacokinetic approach:

The pharmacokinetics of drug are altered e.g. pharmacokinetics are altered by modifying its chemical structure.

Biologic approach:

Route of administration changed e.g. oral to parental.

Pharmaceutical approaches to enhance the dissolution of drugs.

1. **Micronization:** In which particle size of solid drug is reduced to 1to 10µ by spray drying or fluid energy mill example: sulpha drugs.

2. **Use of surfactants:** surface active agents enhance the dissolution rate by promoting wetting and penetration of dissolution fluid into solid drug particles example steroids like spironolactone.

3. **Use of salt forms:** salts have improved solubility and dissolution characteristics in comparison to the original drug. Example salt of basic drug like Atropine is more soluble than the parent drug.

4. **Alteration of pH of the Drug Microenvironment:** achieved in two ways in situ salt formation and the addition of buffers to the formulation e.g. buffered aspirin tablets.

5. **Use of metastable polymorphs:** Metastable polymorphs are more soluble than the stable polymorphs of drug that exhibits polymorphism, e.g. chloramphenicol palmitate.

6. **Solute –solvent complexation:** solvates of drugs with organic solvents generally have higher

aqueous solubility than the original drug, e.g. 1:2 griseofulvin benzene solvate.

7. Solvent deposition: In this method poorly aqueous soluble drug is dissolved in organic solvent and deposited on an inert hydrophilic, solid matrix, e.g. nifedipine is dissolved in alcohol and deposited in starch by evaporation of solvent.

8. Selective adsorption on insoluble carriers: A highly active adsorbent can enhance the dissolution rate, e.g. bentonite.

9. Solid solution-

- Use of solid solution: solid solution is a binary system comprising of solid solute molecularly dispersed in a solid solvent.
- Use of eutectic mixtures: These systems are also prepared by fusion method it is slightly differ from solid solution in that fused melt of solute –solvent show complete miscibility but negligible solid – solid solubility.
- The use of solid dispersion: These are generally prepared by solvent or co - precipitation method where both guest solute and the solid carrier solvent are dissolved in common volatile liquid such as alcohol. The liquid removed by evaporation under reduced pressure or by freeze drying which result in amorphous precipitation of guest in crystalline carrier.

10. Molecular encapsulation with Cyclodextrins:

The beta and gamma Cyclodextrins and several of their derivatives are unique in having the ability to form molecular inclusion with hydrophobic drugs having a poor aqueous solubility. These cyclodextrin molecules are versatile in having a hydrophobic cavity of a size suitable enough to accommodate hydrophilic drug as a guest; the outside of the host molecule is relatively hydrophilic. Thus the molecularly encapsulated drug has greatly improved aqueous solubility and dissolution rate. However, among them, the technique of Liquisolid compacts" is one of the most promising techniques. Low cost, simple formulation technique and capability of industrial production serve to be the advantages of this technique.

Liquisolid Technique:

The poor dissolution rate of water insoluble drugs is still a substantial problem confronting the pharmaceutical industry. A great number of new and possibly, beneficial chemical entities do not reach the public merely because of their poor oral bioavailability due to inadequate dissolution. Over the years, various solid dosage formulation techniques, to enhance the dissolution of poorly soluble substances, have been introduced with different degrees of success. The technique of, Liquisolid compacts is a new and promising addition towards such a novel aim. The

active ingredient in a solid dosage form must undergo dissolution before it is available for absorption from the gastrointestinal tract. The poor dissolution characteristics of water-insoluble drugs are a major challenge for pharmaceutical formulation scientists. The absorption rate of a poorly water-soluble drug, formulated as an orally administered solid dosage form, is controlled by its dissolution rate in the fluid present at the absorption site, i.e. the dissolution rate is often the rate- determining step in drug absorption. Several researchers have shown that the liquisolid technique is the most promising method for promoting dissolution rate of poorly water soluble drugs. [1]

The term liquisolid compacts as described by Spireas et.al indicates that immediate or sustained release tablets or capsules that are prepared using the technique of "liquisolid systems" combined with the inclusion of appropriate adjuvants required for tabulating or encapsulation such as lubricants and for rapid or sustained release action, such as disintegrate or binders, respectively. Liquisolid compacts prepared by using different solvents which dissolve the poorly soluble drug and gives better bioavailability. It has been observed that the drug release superiority of liquisolid tablets is inversely proportional to the aqueous solubility of the contained drug.[4] Liquisolid system is novel technique developed by Spireas et al[5, 6] liquisolid systems involves conversion of liquid lipophilic drugs or water insoluble solid drugs dissolved in non-volatile solvent and this liquid medication can be converted into free-flowing, non adherent, dry looking, and readily compressible powders with the use of carrier and coating materials. In case of water soluble drugs, the sustained release can be obtained. "Liquisolid systems" is formulated by converting liquid lipophilic drugs, or drug suspensions or solutions of water-insoluble solid drugs in suitable non-volatile solvent systems, into "dry" (i.e., dry-looking), nonadherent, free-flowing and readily compressible powder admixtures by blending with selected carrier and coating materials.

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

1. Powdered drug solution:

Regarding "powdered drug solutions," it must be emphasized that their preparation is not a solvent deposition technique since it does not involve drying or evaporation. Since non-volatile solvents are used to prepare the drug solution or suspension, the liquid vehicle does not evaporate and thus, the drug is carried within the liquid system which in turn, is dispersed throughout the final product depending on the

consistency of the powder substrate, the quantity of solid drug dispersed in the liquid medication and the physiochemical properties of the liquid vehicle used the acceptable liquid-to-powder percent ratio will range from 2% to 52%, the most preferable range being 10% to 35%.

2. Powdered drug suspensions

3. Powdered liquid drugs.

The first two may be produced from the conversion of drug solutions or drug suspensions and the latter from the formulation of liquid drugs into liquisolid system. [6]

Application of Liquisolid Techniques: [7]

Solubility and dissolution improvement:

This technique was successfully applied to low dose water insoluble drugs. However, the formulation of the high dose insoluble drugs as liquisolid tablets is one of the limitations of the liquisolid technique. In fact, when the therapeutic dose of a drug is more than 50mg, a dissolution enhancement in the presence of low levels of hydrophilic carrier and coating material is not significant. But by adding some materials such as polyvinyl pyrrolidone (PVP) to liquid medication (microsystems), it would be possible to produce dry powder formulations containing liquid with high concentration of drug. By adding such materials to the liquid medication, low amount of carrier is required to obtain dry powder with free flowability and good compatibility.

Flowability and compressibility:

Liquisolid compacts possess acceptable flowability and compressibility properties. They are prepared by simple blending with selected powder excepients referred to as the carriers and the coating materials. Many grades of cellulose, starch, lactose, etc. can be used as carriers, whereas silicas of very fine particle size can be used as coating materials. In order to have acceptable flowability and compactability for liquisolid powder formulation, high levels of the carrier and coating materials should be added and that in turn will increase the weight of each tablet above 1 gm which is very difficult to swallow. Therefore, in practice it is impossible with conventional method to convert high dose drugs to liquisolid tablet with the tablet weight of less than 1 gm. In such systems, the drug existed in a molecular state of subdivision and systems were free flowing, on adherent, dry looking powders. In further studies, compression enhancers were added to these powdered solutions like microcrystalline cellulose. However, the compression of these latter systems resulted in a significant Liquid Squeezing out phenomenon.[6]

Bioavailability improvement:

In the liquisolid and powdered solution systems the drug might be in a solid dosage form, it is held within the powder substrate in a solution, or in a solubilized, almost molecularly dispersed state. 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.

Classification of liquisolid systems

A. 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 or (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, liquid vitamins, etc.), into liquisolid systems.

Since non-volatile solvents are used to prepare the drug solution or suspension, the liquid vehicle does not evaporate and thus, the drug is carried within the liquid system which in turn is dispersed throughout the final product.

B. Based on the formulation technique used, liquisolid systems may be classified into two categories:

1. Liquisolid compacts
2. Liquisolid Microsystems

Preparation of liquisolid tablets

Calculated quantities of drug and non-volatile solvent is accurately weighed in 20 ml glass beaker and then heated to dissolve the drug in that solvent. The resulting hot medication is incorporated into calculating quantities of carrier and coating materials. The mixing process is carried out in three steps as described by Spireas[8] et al. During the first stage, the system is blended at an approximate mixing rate of one rotation per second for approximately one minute in order to evenly distribute liquid medication in the powder. In the second stage, the liquid/powder admixture is evenly spread as a uniform layer on the surfaces of a mortar and left standing for approximately 5 min to allow the drug solution to be absorbed into the interior of powder particles. In the third stage, the powder is scraped off the mortar surfaces by means of aluminum spatula and then blended with sodium starch glycolate for another 30 seconds in a similar way to the first stage. This gives final liquisolid formulation to be compressed.

Materials-

Drugs:

Drugs which are poorly soluble can be incorporated into liquisolid systems include: digoxin, digitoxin, Prednisolone, hydrocortisone, spironolactone, hydrochlorothiazide, polythiazide, and other liquid medications such as chlorpheniramine, water insoluble vitamins, fish oil, etc.[9, 10]

Non- volatile solvent:

These may be hydrophilic or lipophilic in nature based on the selection of type of formulation like immediate or control release. Inert, high boiling point, preferably water-miscible and not highly viscous organic solvent systems are most suitable as vehicles.

Some of them are: Polyethylene glycol, Propylene glycol, Tween 80, 20, Span 80,20, Liquid Paraffin, Cremophore L etc.

Carrier:

These are preferred to be coarser and granular for acceptable flow. These are compression-enhancing, relatively large, preferably porous particles possessing a sufficient absorption property which contributes in liquid absorption. E.g. Various grades of cellulose, lactose, sorbitol, etc. [9, 10]

Coating material:

These are flow-enhancing, very fine (10 nm to 5,000 nm in diameter), highly adsorptive coating particles (e.g., silica of various grades like Cab-O-Sil M5, Aerosil 200, Syloid 244FP etc.) contributes in covering the wet carrier particles and displaying a dry-looking powder by adsorbing any excess liquid. [9, 10]

Super disintegrant:

Most commonly used disintegrant is sodium starch glycolate, Explotab, pumogel, etc. [9]

Necessary equipments:

Shaking water bath, Electric balance, Ultraviolet spectrophotometer, Single Punch tablet press, Tablet Hardness tester, Friability tester, Thickness tester, Disintegration tester, and Dissolution apparatus.[11]

Theory of Liquisolid systems: [8, 10-15]

A powder can retain only limited amounts of liquid while maintaining acceptable flow and compression properties. To calculate the required amounts of powder excipients (carrier and coating materials) a mathematical approach for the formulation of liquisolid systems has been developed by Spireas. 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 of a powder represents the maximum amount of a given non-volatile liquid that can be retained inside its bulk [w/w] while maintaining an acceptable flowability. The flowability may be determined from the powder flow or by measurement of the angle of repose.

The Ψ-number of a powder is defined as the maximum amount of liquid the powder can retain inside its bulk [w/w] while maintaining acceptable compatibility resulting in compacts of sufficient hardness with no liquid leaking out during compression. The compactability may be determined by the so-called "pactisity" which describes the maximum (plateau) crushing strength of a one-gram tablet compacted at sufficiently high compression forces.

The terms "acceptable flow and compression properties" imply the desired and thus preselected flow and compaction properties which must be met by the final liquisolid formulation.

Depending on the excipient ratio (R) of the powder substrate an acceptably flowing and compressible liquisolid system can be obtained only if a maximum liquid load on the carrier material is not exceeded. This liquid/carrier ratio is termed "liquid load factor Lf " [w/w] and is defined as the weight ratio of the liquid formulation (W) and the Carrier material (Q) in the system:

$$L f \quad W / Q \qquad \text{Eq. (1)}$$

R represents the ratio between the weights of the carrier (Q) and the coating (q) material present in the formulation:

$$R \quad Q / q \qquad \text{Eq. (2)}$$

The liquid load factor that ensures acceptable flowability (ΦLf) can be determined by:

$$\Phi Lf \quad \Phi \varphi \cdot (1/ R) \quad \text{Eq. (3)}$$

where Φ and φ are the Φ-values of the carrier and coating material, respectively.

Similarly, the liquid load factor for production of liquisolid systems with acceptable compatibility (ΨLf) can be determined by:

$$\Psi Lf \quad \Psi \psi \cdot (1/ R) \quad \text{Eq. (4)}$$

where Ψ and ψ are the Ψ-numbers of the carrier and coating material, respectively. In Table 1 examples of liquisolid formulation parameters of various powder excipients with commonly used liquid vehicles are listed.

Therefore, the optimum liquid load factor (Lo) required to obtain acceptably flowing and compressor liquisolid systems are equal to either ΦLf or ΨLf , whichever represents the lower value.

As soon as the optimum liquid load factor is determined, the appropriate quantities of carrier (Qo) and coating (qo) material required to convert a given amount of liquid formulation (W) into an acceptably flowing and compressible liquisolid system may be calculated as follows:

Q_o W / L_o Eq. (5)

And

q_o Q_o / R Eq. (6)

The validity and applicability of the above mentioned principles have been tested and verified by producing liquisolid compacts possessing acceptable flow and compaction properties.

Mechanisms of enhanced drug release from liquisolid systems: [16-20]

In the literature several mechanisms of enhanced drug release have been postulated for liquisolid systems. The three main suggested mechanisms include an increased surface area of drug available for release, an increased aqueous solubility of the drug, and an improved wettability of the drug particles. Formation of a complex between the drug and excipients or any changes in crystallinity of the drug could be ruled out using DSC and XRPD measurements.

a. Increased drug 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 solubilized, 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 the fraction of undissolved drug in the liquid vehicle the release rate decreases. With various drugs it could be shown that the release rates are directly proportional to the fraction of the molecularly dispersed drug (FM) in the liquid formulation . FM is defined by Spireas as the ratio between the drug solubility (Sd) in the liquid vehicle and the actual drug concentration (Cd) in this vehicle carried by each system

Therefore:

FM Sd / Cd Eq. (7)

Where FM 1 if Sd $\geq$ Cd .

In Fig 1 the effect of the fraction of the molecularly dispersed drug (FM) on the release rate of hydrocortisone formulated as liquisolid compacts containing various drug concentrations in varying amounts of propylene glycol as liquid vehicle is shown. It is obvious that the drug release rate increases linearly with increasing FM. Interestingly, this linear increase may be observed only above a certain FM-limit.

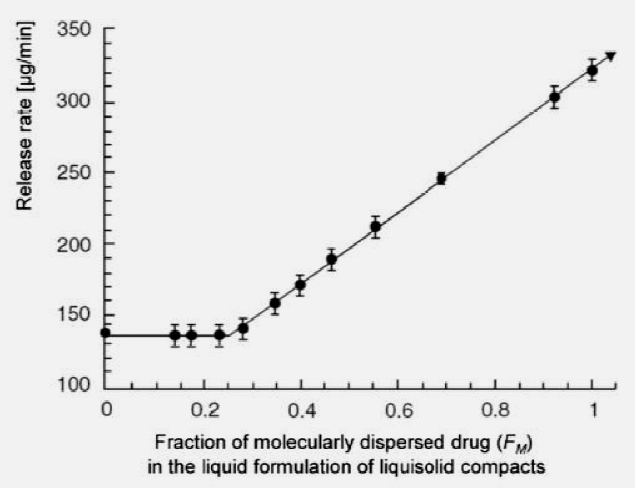

Fig.1 Effect of the fraction of molecularly dispersed drug (FM) on the hydrocortisone release rate at 30 min of liquisolid compacts (means ± SD, n = 3)

Accordingly, lower FM-values and a higher fraction of undissolved drug in the liquid vehicle, respectively, are not sufficient to increase the percentage of drug released at 30 min. However, this may not be transferred to other time points of drug release.

b. Increased aqueous solubility of the drug

In addition to the first mechanism of drug release enhancement it is expected that Cs, the solubility of the drug, might be increased with liquisolid systems. In fact, the relatively small amount of the liquid vehicle in a liquisolid compact is not sufficient to increase the overall solubility of the drug in the aqueous dissolution medium. However, 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 might be sufficient to increase the aqueous solubility of the drug if the liquid vehicle acts as a cosolvent. The overall increase in the solubility of drugs caused by liquisolid systems was confirmed.

c. Improved wetting properties

Due to the fact that the liquid vehicle can either act as a surface active agent or has a low surface tension, wetting of the liquisolid primary particles is improved. Wettability of these systems has been demonstrated by measurement of contact angles and water rising times.

Pre-formulation Studies

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 (LSC)

Solubility studies

Solubility studies are carried out by preparing saturated solutions of the drug in non-volatile solvent and analyzing them spectrophotometrically. Saturated solutions are prepared by adding an excess of drug to non volatile solvent and shaking them on shaker for a specific time period under constant vibration. After this, the solutions are filtered and analyzed spectrophotometrically.

Determination of angle of slide

Angle of slide is used as a measure of the flow properties of powders. Determination of the angle of the slide is done by weighing the required amount of carrier material and placed at one end of a metal plate with a polished surface. The end is gradually raised till the plate becomes angular to the horizontal at which powder is about to slide.

This angle is known as the angle of the slide. Angle of 33º is regarded as optimum.

Determination of flowable liquid retention potential (Φ value)

The term "flowable liquid-retential potential" (Φ-value) of a powder material describes its ability to retain a specific amount of liquid while maintaining good flow properties. The Φ-value 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 flowing liquid/powder admixture.

The Φ values are calculated according to the equation

Φ value = weight of the liquid / weight of solid … (1)

Calculation of liquid load factor (Lf)

Different concentrations of non-volatile solvents are taken and the drug is dissolved. Such liquid medication is added to the carrier-coating material admixture and blended. Using equation (2) drug loading factors is determined and used for calculating the amounts of carrier and coating materials in each formulation.

Lf = weight of liquid medication / weight of carrier material… (2)

Liquisolid compressibility test (LSC)

The Liquisolid compressibility test is used to determine Φ values and involves steps such as preparing carrier coating material admixture systems, preparing several uniform liquid or powder admixtures, compressing each liquid or powder admixtures to tablets, assessing the average hardness, determination of the average liquid content of crushed tablets, as well as determining plasticity, sponge index and Φ value and Lf.

Evaluation of Liquisolid Systems

Flow behavior

Flow properties are the important concern in the formulation and industrial production of tablet dosage form. Angle of repose is characteristic to the flow rate of the powder. In general, the values of the angle of repose ≥ 40º indicate powders with poor flowability.

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 of the drug is absent in the DSC thermogram, there is an indication that the drug is in the form of solution in liquisolid formulation and hence it is molecularly dispersed within the system.

X-ray diffraction (XRD)

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

Scanning Electron Microscopy (SEM)

After SEM study, complete disappearance of crystals of the drug which confirms that the drug is totally solubilized in liquisolid system and this ensures the complete solubility.

After complete formulation, Tablets are evaluated by carrying out tests for weight variation, uniformity of tablet thickness and diameter, humidity content using the Karl fisher method, friability, hardness, disintegration, dissolution, and content uniformity. All these tests are carried out in triplicate and according to the compendial specifications.

For content uniformity test tablets should contain not less than 95% and not more than 105% of the labeled potency

The disintegration test was carried out on six tablets in distilled water at 37 ± 2 ºC using the USP disintegration apparatus.

Dissolution studies of Liquisolid tablet

Generally Dissolution studies of Liquisolid tablet are carried out using dissolution apparatus USP II at 37ºC ± 2ºC. Many researchers revealed that at low drug concentrations in liquid medication, more rapid release rates are observed. The consistency and higher dissolution rate displayed by liquisolid compacts will improve the absorption of the drug from the gastrointestinal tract.

In vivo evaluation of Liquisolid tablets

The improvement in oral bioavailability was confirmed by estimating the pharmacokinetic

parameters in various animals such as a rabbit beagle dog.

Results show that absolute bioavailability of drug from liquisolid tablets was much higher than marketed tablets.

Contact angle measurement

For assessment of wettability, contact angle of liquisolid tablets is measured according to the imaging method. The commonly used method is to measure contact angle directly from a drop of liquid resting on a plane surface of the solid, the so-called imaging method. A saturated solution of the drug in dissolution media is prepared and a drop of this solution is put on the surface of the tablets. The contact angles are calculated by measuring the height and diameter of the sphere drop on the tablet .

Advantages of Liquisolid Compact

1. A great number of slightly and very slightly water-soluble and practically water-insoluble liquid and solid drugs such as Digitoxin, Prednisolone and Hydrocortisone etc. can be formulated into liquisolid systems using the new formulation-mathematical model.

2. Better availability of an orally administered water-insoluble drug is achieved when the drug is in solution form.

3. Though the drug is in a tabletted or encapsulated dosage form it is held in a solubilized liquid state, which consequently contributes to increased drug wetting properties, thereby enhancing drug dissolution.

4. The production cost of liquisolid systems is lower than that of soft gelatin capsules.

5. Advantage of liquisolid systems, particularly for powdered liquid drugs, during dissolution of a liquisolid tablet, after the disintegration process is completed, the drug solution or liquid drug, carried on the suspended and thoroughly agitated primary particles, is dispersed throughout the volume of the dissolution medium; such a phenomenon does not extensively occur during the dissolution process of soft gelatin capsule preparations. Therefore, since more drug surface is exposed to the dissolving medium, liquisolid systems exhibit enhanced drug release. [21]

6. Optimized rapid-release liquisolid tablets or capsules of water-insoluble drugs exhibit enhanced in-vitro and in-vivo drug release as compared to their commercial counterparts.

7. Optimized sustained-release liquisolid tablets or capsules of water-insoluble drugs exhibit surprisingly constant dissolution rates (zero-order-release) comparable only to expensive commercial preparations that combine osmotic pump technology and laser-drilled tablets.

Conclusion-

Liquisolid technique is an efficient method of formulation of water insoluble solid drugs and liquid lipophilic drugs. Liquisolid technique gives a design to enhance the absorption as well as dissolution rate their by it may enhance the bioavailability of a poorly soluble, insoluble or lipophilic drug and to formulate them into immediate release or sustain or control release by selection of suitable solvent and carrier. With this technology liquid such as solution 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. Liquisolid formulations show better flowability, compressibility, improve solubility, dissolution and hence better absorption.The technique is also used to design sustained release systems by using hydrophobic carriers instead of hydrophilic carries in liquisolid systems.

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