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Liquidsolid Compact Technology – An overview

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ABSTRACT :

The liquidsolid technique is a novel approach for delivery of drugs through the oral route. This technique is suitable for poorly soluble or water insoluble drugs, highly permeable drugs (BCS Class II drugs) and for immediate or sustained release formulations. About 40-50%drugs available marketed water insoluble drugs. It is challenge to industry to increase solubility of unit dosage forms .to overcome this liquid solid compact technology is best suitable one .on this study the pre comprisable parameters like porosity, corsaldity index, flow behavior, power bed hydrophilicity ,saturate solubility .post compressibility parameters like uniformity, weight variation ,hardness , friability , wet ability ,time. In this we can use carrier (microcrystalline cellulose, starch, and lactose), coating materials (silica gel), and disintegrating agents. In this we can do flourier transform infrared spectroscopy, differential scanning calorimeters (DSC), and differential scanning thermometer, x-ray diffraction.

Keywords: Liquidsolid compact technology,water insoluble drugs,solubility,parameters,carrier and coating materials

1. INTRODUCTION :

Combinatorial chemistry and novel high-throughput screening have led to a significant increase in our understanding of the biological and physicochemical characteristics of drug candidates, including transporters and metabolizing enzymes, as well as crystal structures and salt formation. Many active pharmacological compounds have been created as a result[1]. Unfortunately, the majority of these medications are extremely lipophilic and weakly soluble in water; over 60% of synthetic chemical entities and 40% of newly produced medications have solubility problems. [2]. Drug solubility plays a significant role in pharmaceutical formulation design, which might result in varying oral bioavailability. Drug absorption is greatly impacted by dissolution, particularly when it comes to water-insoluble or poorly soluble medications. For the majority of pharmaceutical formulations, dissolving is the rate-limiting phase [3]. Numerous methods are being used to improve the solubility of poorly soluble medications in order to address the problem of insufficient dissolving rate-related bioavailability.Hydrophilic polymers are used in several ways as solubility enhancers, working via a range of mechanisms such inclusion complexes, co-solvency, micelle formation, and amorphization. These methods have numerous positive effects on the formulation development process. However, over time, these methods typically exhibit instability and a declining success rate. A notable drawback of inclusion complexes, glass solutions, eutectic mixes, and solid dispersions is the development of sticky and hygroscopic mass, which results in poor flow properties. This setback makes the final dosage form extremely difficult to commercialize. The new developed technique by Spireas liquid solid system improves the dissolution properties of water insoluble or poorly soluble drugs. The term “liquid-solid systems” (LS) is a powdered form of liquid drug formulated by converting liquid lipophilic drug or drug suspension or solution of water-insoluble solid drug in suitable non-volatile solvent systems, into dry looking, non-adherent, free-flowing and readily compressible powdered mixtures by blending with selected carrier and coating materials [4,5]. The liquisolid technique was applied to formulate water-insoluble solid drugs into nonvolatile liquid vehicles into powders suitable for tableting or encapsulation[6]. So for this type of dosage forms that can rapidly disintegrate/dissolve to release the drug as soon as they come in contact with saliva, thus without the need for water during administration, an attempt that makes them highly attractive for pediatric and geriatric patients [7].

LIQUID SOLID COMPACT TECHNOLOGY :

Spireas et al. initially introduced the liquisolid approach, which was also linked to the integration of water-insoluble drugs into rapid discharge robust measuring frameworks. The term "fluid medicine" refers to solid medications that are dispersed in improper, unpredictable fluid carriers. Such fluid prescriptions can be combined with specific carriers and covering materials to make powder admixtures that are dry-looking, non-disciple, free-streaming, and quickly perfect. Spireas hypothesized that the particles, such as cellulose, lactose, and starch, might be used as the transporter material because of their high assimilation qualities and porous surface. For example, silica is needed as a covering material to maintain the powder's flowability by covering the surface [6]. Within these frameworks, the medication is administered as a powder when it is currently in an arranged structure within the fluid carrier. Liquidsolid innovation, thus, facilitates the conversion of fluid frameworks into robust drug delivery methods, like tablets. The liquidsolid method has been successfully linked to increasing medicine arrival of low fraction ineffectively dissolvable pharmaceuticals and improving solvent [7].

PRINCIPLE OF LIQUIDSOLID COMPACT TECHNOLOGY:

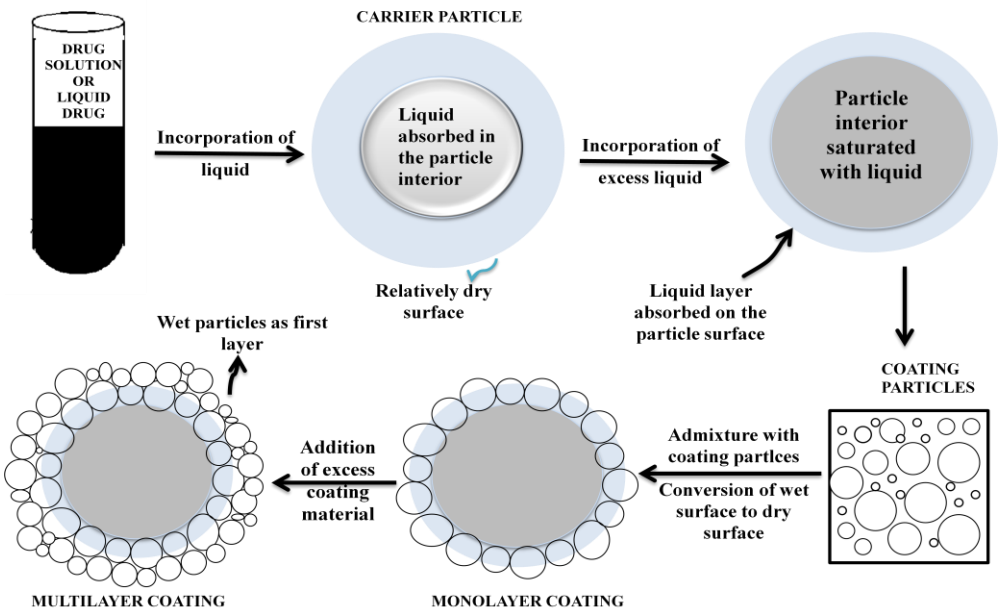


Fig 1 :- Theoretical model for Powder solutions

When the drug dissolved in the liquid vehicle is incorporated into a carrier material which has a porous surface and closely matted fiber in its interior such as cellulose, both absorption and adsorption take place. The liquid initially absorbed into the interior of the particle is captured by its internal surface. After saturation, adsorption of the liquid onto the internal and external surface of the porous carrier particle occurs. Then, coating material provides the desirable flow property to the liquisolid system due to its high adsorptive properties and large surface area.

FORMULATION ASPECTS OF LIQUIDSOLID COMPACT TECHNOLOGY:

Components of Liquidsolid compact technology

- Drug : It should be of bcs class II and IV. It should be lipophilic in nature for example Chlorpheniramine,Digoxin,Nifedipine,Clofibrate,Gemfibrozil,Etoposide,Carbamazepine,Hydrochlorothiazide. Ibuprofen [10].
- Non-volatile solvents : A liquid vehicle serves as a wetting agent or surface active agent, non-volatile solvents enhance the wetting capabilities. As a result, interfacial tension either decreases the contact angle and increases the surface area of the drug, which in turn increases its solubility, or it decreases the tension between the media and its surface
- Examples - Polyethylene glycol 400, Polyethylene glycol 200,Tween 20,Tween 80,Synperonic PE, Cremophore EL, Captex 200,captex 355 & Polysorbate [11].
- Carrier Material :- The carrier in the sorption process of liquid medication increases the surface area because of the adsorption of porous particles, as well as because it has adsorption properties and matted fibers that contribute to the interior of the liquid medication
- Examples - Starch, lactose, sorbitol, microcrystalline cellulose [12].
- Coating Material : A coating material produces a homogenous layer over the carrier particles, preventing the particles from aggregating, lowering inter-particulate friction, and enhancing flowability.
- Examples - Colloidal silica of various grades such as cab-o-sil –M5, aerosil 200, syloid 244FP [13]
- Disintegrants ; Disintegrants are compounds added to tablet formulation that encourage the tablet to break up into tiny fragments in an aqueous environment, increasing the surface area that is available and facilitating the drug's quick release.
- Examples - sodium starch glycollate, crosspovidone & crosscarmellose etc [14].

Optimisation of formulation for liquid solid compact technology :

1. Determination of drug solubility in different non volatile solvents
2. Angle of slide determination
3. Flowable liquid retention potential determination
4. Calculation of liquid loading factor
5. Liquisolid compressibility (LSC)

The mathematical model of the liquid solid system is used to calculate the flowability and compressibility in the liquid solid compact formulation. This allows one to determine the quantities of coating material and carrier that provide the powder's compressible liquid retention potential (Ψ-number) and flowable liquid retention potential (Ø value) [15].

1. Determining the solubility of a drug in various non-volatile solvents: To prepare saturated solutions, add excess drug to non-volatile solvents and shake for 48 hours. The solutions are then filtered through Whatman filter paper, examined with a spectrophotometer, and the best solubility solvent is chosen [16].
2. Determining the angle of slide involves weighing a carrier and placing it at one end of a polished metal plate. The plate is then gradually lifted until it is angular to the horizontal, the point at which the powder is about to slide. It is employed to gauge a powder's flow characteristics. The ideal angle for powder flow is 33°[17].
3. Determining the flowable liquid retention potential (Φ value): In order to develop a liquid/powder admixture that flows acceptably, it is defined as the greatest weight of liquid that can be kept per unit of powder material. Powders' Φ-value can be ascertained by a novel method called the liquidsolid flowability (LSF) test. Excipient amounts are calculated using the Ø value. The following is the equation for this:

$$Lf = Ø + Ø\ (1 / R)$$

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

4.Calculation of liquid loading factor (Lf)): It is defined as the ratio of weight of liquid medication (w) to weight of carrier material (Q). Different concentrations of nonvolatile solvents are taken and the drug is dissolved and the carrier coating material is added and blended.

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

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: Lf= (1/R) [18].

5.Liquisolid compressibility test (LSC): This test was developed to ascertain Ψ values and includes procedures like setting up systems for the admixture of carrier coating materials, making multiple consistent liquid/powder admixtures to tablets, figuring out average hardness, measuring the average liquid content of crushed tablets, and figuring out plasticity, sponge index, and Ψ [19].

Method of preparation of Liquidsolid compacts:

A predetermined quantity of carrier material—ideally porous and with adequate absorption capabilities—is combined with a precise amount of the produced drug solution, suspension, or liquid medication itself. The resulting wet mixture is then combined with a calculated amount of coating material and mixed to create a dry, non-adherent, free-flowing, and easily compressible powder. For this stage, excipients with fine, highly adsorptive particles work well. Liquisolid compacts are created by adding different adjuvants, such as lubricants and superdisintegrants, to the final liquisolid system prior to compression or encapsulation [7].

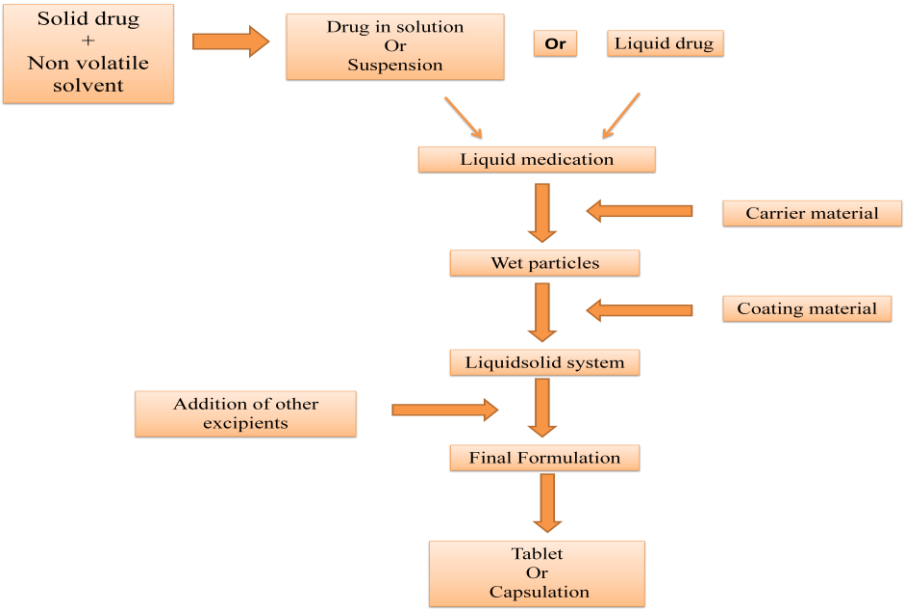


Fig 2– Preparation procedures of liquisolid system

Pre-compression parameters:

1. Flow properties of the liquid solid system
2. Scanning electron microscopy
3. X-Ray Powder diffraction (XRD) studies
4. Differential Scanning Calorimetry (DSC)

Post compression Evaluations :

a) Content of uniformity
b) Hardness
c) Weight variation
d) Friability
e) Disintegration
f) In - vitro dissolution studies

These are should be in the official limits prescribed by official pharmacopoeia [20].

Enhanced drug release mechanism from liquisolid systems :

Three main mechanisms are involved for enhancement of drug release from liquisolid systems are as follows:-

1. Enhanced drug surface area

A larger surface area for drugs Because the drug in the liquisolid system is completely dissolved in the liquid vehicle and present in the powder substrate still in a solubilized, molecularly dispersed state, the surface area of drug available for drug release in the liquisolid system is significantly greater than that of drug particles within directly compressed tablets [22]. when a result, when the drug content grows, so does the solubility limit, raising the proportion of undissolved drug in the liquid medium and lowering the release rate. The fraction of the drug that is molecularly dispersed (FM) directly correlates with the medication's release rate in the liquid solid formulation. The ratio of the drug's solubility (Sd) to its actual concentration (Cd) is what Spireas termed as FM

$$FM = Sd/Cd$$

Where $FM = 1$ $Sd \geq Cd$

Fig 3: increased drug surface area

2.Enhanced Increased aqueous solubility of the drug

Liquisolid systems have the potential to boost a drug's solubility. The solubility of the drug in the aqueous dissolving medium cannot be increased by the minimal amount of liquid vehicle present in a liquisolid compact. The low water soluble drug's aqueous solubility can be increased if the modest amount of liquid vehicle functions as a cosolvent in the liquid-solid system [23].

Fig 4: Dispersion

Fig 5: clear solution

3.Increased wettability

The liquisolid system's non-volatile solvent facilitates drug particle wetting by reducing the interfacial tension between the tablet surface and the dissolution medium. This results in a smaller contact angle in the liquisolid system compared to the standard formulation, which enhances wettability [24].

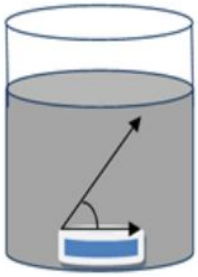


Fig 6: Conventional tablet

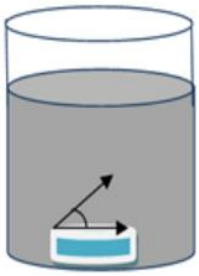
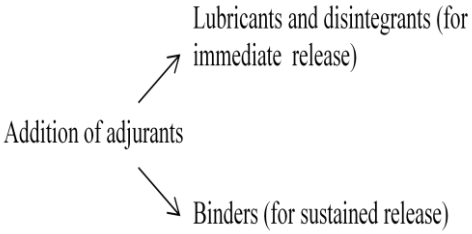


Fig 7: Liquidsolid comapact tablet

Applications of the liquisolid technology:

1. Drug dissolution enhancement:-The liquid suspension (LS) technique has been extensively researched to improve the dissolution and bioavailability of poorly soluble APIs [26]. Mechanisms of improved drug dissolution include increased drug surface area available for release, enhanced aqueous solubility, and improved wetting properties of powder particles [27].
2. Development of liquisolid orally disintegrating tablets:-Optimized formulations contained 5mg of felodipine, carrier (MCC PH 102 or silicified MCC), colloidal silicon dioxide as a coating agent, crospovidone as a superdisintegrant, and suitable excipients for taste correction. The optimized formulations exhibited fast disintegration both in vitro and in vivo, with disintegration times ranging between 7 and 11 seconds [28,29].
3. Development of modified release preparations:- Liquisolid technology has been proposed as a method to enhance the bioavailability of immediate release preparations and achieve sustained drug release. This approach involves adding a binder/matrix forming agent like HPMC to a common LS formulation. Different approaches have been proposed, such as using Eudragit® RL or RS as hydrophobic carriers and using polysorbate 80 as a solvent for highly water-soluble APIs [30].

Sustained-release LS formulations are usually prepared with a higher content of the coating material, which contributes to slower drug release from these formulations. Liquid vehicles can play an important role in achieving prolonged drug release. In the case of prolonged release preparations, liquid vehicles with lower solubility are recommended. Polysorbate 80 also acts as a plasticizer, contributing to the flexibility of carrier chains and keeping the API entrapped more tightly within the polymer network [31,32].



4. Development of solid dosage forms with liquid herbal preparations:- LS technology was also used to prepare tablets with oleoresin-like crude extract of Curcuma comosa. The LS system showed better flowability and improved mechanical properties compared to freeze-dried extracts. It was also used to develop colon-targeted delivery tablets containing natural purple rice bran oil, which is used as a supplement in colorectal carcinoma treatment.
5. Towards the lower influence of the pH value variations on drug dissolution rate :- the application of Liquid Liquid Systems (LS) to reduce the influence of pH values on drug dissolution rates. They used Loratadine as a model, and LS tablets were prepared with propylene glycol, MCC, and colloidal silicon dioxide. Dissolution studies showed that LS systems could enhance loratadine dissolution in the stomach, regardless of the fed or fasted state. Liquisolid techniques also improved dissolution and pH-independent release of telmisartan, attributed to improvedwetting and increased surface area [34].
6. Improvement of drug photostability in solid dosage forms :- A study evaluating the potential of LS technology to improve drug photostability, using amlodipine as a model substance, found that admixtures with nanometer-sized silicon dioxide and titanium dioxide, either alone or in combinations, had a photoprotective effect. The content of API in LS admixtures was approximately 97% higher than conventional film tablets, indicating that LS could be a suitable alternative for improving photostability [33].

Advancements in Liquidsolid compact technology :-

1. liquisolid pellets :- An interesting liquisolid-based concept, "liquisolid pellets," was first proposed by Pezzini et al. as a new preparation method for multiparticulate systems using a combination of LS technique and extrusion-spheronization method. LS pellets were smaller in size, with larger pore diameter and volume compared to conventional pellets. They showed an improved dissolution rate compared to conventional pellets [35].
2. liqui-mass technology :- which combines LS technology and extrusion-spheronization to improve the dissolution of poorly soluble APIs while allowing high liquid loads in liqui-pellets or liqui-tablets as dosage forms. This system can be used to obtain pellets or tablets with immediate or sustained drug release [36].

CONCLUSION :

Liquidsolid compact technology has gained considerably increased research attention during the last decade. Liquidsolid technique is a promising tool to improve the solubility, wettability of water insoluble drug and ensures the molecular dispersion of a drug in the formulation by blending the pure drug with non-volatile solvent, carrier and coating material modification of formulation. By use of certain agents also causes sustained release of drugs from the liquid solid compacts. The addition of disintegrants may further accelerate drug release from liquisolid compacts. The liquisolid technology may also be used for the preparation of sustained release formulations with zero order release pattern. Thus, a constant plasma level will be reached, which is maintained throughout the dosing interval. For sustained release liquisolid compacts, the selection and the concentration of the excipients such as liquid vehicle, retarding agent (matrix forming material) as well as carrier and coating material play an important role.

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