POWDER SOLUTION TECHNOLOGY REVIEW

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ABSTRACT
Bioavailability and Solubility are the challenges for the formulation of highly lipophilic drugs. Oral routes of administration is one of the acceptable route due to improved patient compliance and convenience. Regularly newly advanced drug candidates are lipophilic, BCS Class II and IV drugs. Among various methods to improve the solubility of these drugs, liquid-solid technology or Powdered solution technology change the liquid drug into non-sticky, dry free-flowing, rapid release powder. This technique involves mixing of insoluble drug with nonvolatile solvent, admixing of drug-loaded excipients change into loose powder. This technique enhances major challenges like bioavailability with low production cost and a simple manufacturing process.

Keywords: Liquisolid technology, Bioavailability, Dissolution enhancement, Lipophilic drugs, Solubility

INTRODUCTION
Mostly newly developed drugs are Lipophilic which generally faces challenges like solubility and bioavailability. Numerous methods like salt formation, [1] cosolvency, [2] complexation, [3] micrornization, [4] melts onocrystallization, [5, 6] lyophilization, [7], solubilization by surfactants [8] solid solution [9], drug solution incorporation in soft gelatin capsule [10] liposomes, nanoparticles, SEEDS, [11] improves the dissolution of the drugs of low solubility. These techniques have some limitations such as hygroscopicity, creating solubility problem [12, 13]. The word liquid medicine means oily liquid drug solutions or suspensions held as liquid vehicles in appropriate nonvolatile solvent systems. “Liquisolid Tablets” or “Liquisolid Compacts” not involve drying and evaporation [14]. In tabletted and capsulated form drug is embedded in liquid so this technique is known as “Powder Solution Technology”. Greater surface area and adsorption of carrier material to adsorb adequate space in liquid medicine. Usually Carrier adsorb liquid on its surface with a very large surface area and coating material forms the layer on carrier particles represented [16] [fig. 1.

Classification
A. Liquid medication within the systems: Powdered drug solutions and suspensions have the concept of changing them into liquisolid systems with its formulation. Liquid drug is circulate all over the final product.
B. Formulation technique-. Liquisolid compacts-Immediate sustained-release tablets or capsules whereas the microsystems-Liquid medication is integrated towards excipients and give free-running powder for encapsulation [17].

Mechanism
Surface area of drug increased
Molecular dispersed state-Region of the product which is accessible to discharge is beyond rather product molecules in the strictly constricted state [18].

Poarity enhanced
Liquid vehicle scatter in a single liquisolid particle jointly with the drug molecules is acceptable to improve the water solubility of the drug at the solid/liquid intersection among distinct liquisolid primary particle and the release medium [19].

Improved wetting properties
Wet ability is an indication of calculating contact angles and water rising times [20]. It will increase the drug release of many poorly soluble drugs.

Theory
Compressible liquid retention potential (ѱ-value): Uttermost of liquid that a powder can maintain within its bulk (w/w) while keeping reasonable compatibility, produces cylindrical compacts of adequate crushing strengths liquid loading capacity of powders: A mathematical approach is used to enumerate the amount of carrier and coating materials for the management of Liquisolid systems [21, 22, 27, 28]. With the help of angle of repose, flowability can be determined.

Liquid load factor (Lf) Refers to scale among the weights of liquid formulation (W) and the carrier material (Q): W/Q, R means equation among the weights of the carrier (Q) and coating (q) material Q/q [23]. The techniques for increasing solubility are enclosed in fig. 1.

Preparation of Liquisolid powder which can be incorporated in capsules and punched into tablets are enclosed in given fig. 2

Formulation components
Components such as Nonvolatile solvent, Carrier and Coating materials, Disintegrating agents and lubricants are used in the
formulation of Liquisolid compact non-volatile solvent: Non toxic, great boiling point, good solubilization power and also work as binder. E.g; Polyethylene glycol 200 and 400, Glycerine. Polarity and lipophilicity are important parameters on drug release profiles [21]. It is a good binder in low concentration for compactness of liquisolid tablets. Lower tablet weight is achieved with more solubility of drug in the solvent. The fragment of the molecularly diffused drug will confirm the enhancement of the dissolution rate [24, 25].

Carrier Materials: Compression-enhancing, relatively large, porous surface and high liquid adsorption function. E.g; Cellulose, starch and glucose. Coating material influences the carrier material like polarity and viscosity [26]. MCC PH 101 is a worthy carrier amid all the grades of MCC (i.e., PH 101, 102, and 200) in liquisolid system concerning flowability, compressibility, and dissolution profile [27].

Coating Material: It will make a film that surrounds the carrier material which stops the gathering of particles and also decrease the inter-particulate friction. By adsorbing an excess liquid it enhances flowability and gives a dry-looking appearance [28]. e.g. Various grades of colloidal silica

Disintegrating Agents: They splits the solid into little particles and the incorporation of super disintegrants is encouraged for solubility enhancement studies. e.g sodium starch glycolate Various excipients used in the preparation of Liquisolid powder are enclosed in table 1.

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**Table 1: List of major excipient used to prepare suitable liquisolid formulation**

| S. No. | Nonvolatile solvent | Carrier materials | Coating materials | Disintegrants |
|--------|---------------------|------------------|------------------|---------------|
| 1      | Glycerine           | MCC Avicel pH 101,102,105,200 | Colloidal Silica (Aerosil200) | Polyvinylpyrrolidone |
| 2      | Propylene Glycol(PG) | Pujiholin (Dibasic Calcium Phosphate) | HPMC-E4M | Sodium Starch Glycolate (SSG) |
| 3      | Polyethylene Glycol PEG 200,300,400,600 | Neusilin (Magnesium aluminometaslicate) | Fused Silica (Cab-o-Sil M5) | Cross Sodium carboxymethyl cellulose |
| 4      | Polysorbate 20,40,60,80 | Eudragit RL | Syloid 244FP | (Croscarmellose Sodium) |
| 5      | Tween 80            | Eudragit RS | Colloidal Silicon dioxide | Pregelatized Starch |
| 6      | Olive Oil           | HPMC-E15 |                |               |
| 7      | Castor oil derivatives | Guargum |                |               |
| 8      | Soyabean oil        | Xanthum Gum |                |               |
| 9      | Liquid paraffin     | Ethyl cellulose |                |               |
| 10     | Poloxamer 181       | Methyl cellulose |                |               |

**Preformation studies**

Solubility study of drug in non-volatile solvent: Pure drug liquefy in distinct non-volatile solvents and extreme, pure drug were joined to a rotatory shaker at 25 °C under constant vibration for 48 h, 0.45 μm Millipore filter used for refining the saturated solution then analyzed [29].

Determination of angle of slide: In polished metal plates, liquid/powder admixtures were settled and plate tilted. The inclination set up in middle of the plate and horizontal surface [30].

Determination of Flowable Liquid Retention Potential (Φ value)

Φ-value= weight of liquid/weight of solid ....

Liquid Load Factor (Lt)

Lt = W/Q  ………..W = weight of liquid medication, Q = weight of carrier material

R = Q/q  R (ratio of the weight of carrier and coating material present in the formulation) [31]

**Formulation Steps to prepare liquisolid compact**

This preparation is mainly for Lipophyllic drugs. Drug liquefy in non volatile solvent to make drug solution. Mixing should be such that one rotation per second till one minute. Liquid medication extent as a uniform layer on the surface for 5 min to allow the drug solution to be absorbed inside the powder particles. Carrier and coating material is incorporated in the ratio of 20:1 to this mixture and blended. Final formulation can compress into tablet or filled into a capsule.

**Characterization of liquisolid system**

The evaluation of liquisolid powder like bulk density, tapped density, % Compressibility Index and Hausers ratio which exhibits the powder with low interparticle is required. In Differential Scanning Calorimetry drug (3 to 5 mg) evacuated in aluminium pans bares the temperature range of 30 to 300 °C. Thermal behavior is examined and in X-Ray Diffraction Studies the machine usually serves at an angle 5 to 70° and counting rate of 0.45/step, use a 30mA current and a copper target of voltage 40Kv. Peak pattern explains change of crystalline state to amorphous. Scanning Electron Microscopy estimates the surface behaviour of the drug. Due to the dissolving nature of the drug, molecular forms can get lost. Fourier Transform Infrared spectroscopy gives information that there is compatibility among drugs and excipients the absence of chemical interaction shown by the peaks. Post compression parameters include weight variation, Friability and Disintegration test In vitro Drug Release Studies which involves USP dissolution apparatus type.
Relative bioavailability and Area under plasma concentration technique has the capacity to be optimized for the reduction of drug. Therapeutic concentration of drug is maintained in the blood throughout of 50 to 200 rpm [32]. In vivo Evaluation of Liquisolid Tablets: Relative bioavailability and Area under plasma concentration of 50 to 200 rpm [32].

| S. No. | LST concept (Year wise) | Investigation reported or significance [34] |
|-------|-------------------------|------------------------------------------|
| 1     | 2007                    | Initiation of concept: Liquisolid tabletike Prednisolone, methylclothiazide, Hydrochlorothiazide and piroxicam boost up the dissolution profiles as related to Direct compressible tablet. |
| 2     | 2008                    | Tablete prepared by Liquisolid technology of Carbamazepine, Fomotidine, Propranolol HCL and Bromhexine prove that drug release not only depend on solubility in non volatile solvent but also depend on surface of carrier material, physiochemical properties |
| 3     | 2009                    | Numerous grades of MCC, Propylene Glycol, Silica in I ndomethacin Liquisolid tablets, dissolution was improved by MCC. |
| 4     | 2010                    | Drug release rate, dissolution profile and Bioavailability of Liquisolid compact is higher as compared to DCT. Significant enhancement in Acelofenac and Rofecoxib Liquisolid tablet as compared to commercial product. |
| 5     | 2011                    | Fujicain (Dibasic Calcium Phosphte) and Neusslin (Magnesium alumino metabolisate) are more effective carrier materials than Avicel (Microcrystalline cellulose) compared. Dissolution rate and bioavailability of Glipizide, Indomethacin, Lamsoprazole, is enhanced and dissolution profile of simvastatin Liquisolid tablet show 90% release with 45 min. |
| 6     | 2012                    | From all carrier material used MCC shows higher dissolution among all developed liquisolid tablet such as Nimesulide, Loratidine, Ketoprofen and Griseofulvin and also proves PEG 400 is better than PG. |
| 7     | 2013                    | Amlodipine, CandesartanClext,B, Mefamicacid,Rosuvastatin, SpiroinactoU.Liquisolid Tablets showed better release retardation Trimeazidine ditydrochloride sustained release tablet by using Liquisolid technology proves show that polysorbate 80 also used as liquid vehicle in sustaining the release of drug from liquisolid matrices [35]. |
| 8     | 2014                    | Physiochemical characteristic among all Conzaepam, Candesartan,Lamotrigine and nateglimide Liquisolid Tablets. Solubility and dissolution rate of piroxicam is increased by Span 20, Tween 80, PEG 400, Labrosol. |
| 9     | 2015                    | Hydrochlorthiazide and Dopmeridone maleate LSC showed improvement in dissolution rate and solubility. |
| 10    | 2016                    | Liquisolid pellets of Felodipine (101) and Curcum loaded Liquisolid systems using different vehicles in different concentration enhances the drug dissolution. |
| 11    | 2017                    | LSC of Ginkipine in Tween 80 boost up the dissolution rate than marketed tablet based upon solubility. [37] |
| 12    | 2018                    | LST enhance solubility of BCS class II and IV (Loperamide, Furosemide) as compared to pure drug [38]. |
| 13    | 2019                    | Crystalline state of drug is changed to amorphous state in Curcum Liquisolid tablets exhibited improvement in dissolution rates as well as apparent solubility was obtained [39]. |
| 14    | 2020                    | Proves difference between Liquisolid pellet and lipippet Liquisolidpellet uses liquisolid system and Liqui-Pellet uses liqui-mass system [40]. |

**Liquisolid system for controlled drug delivery**

Therapeutic concentration of drug is maintained in the blood throughout the dosing interval with the help of this controlled drug delivery, this technique has the capacity to be optimized for the reduction of drug dissolution rate and thereby production of sustained release systems. Sustained release systems can be obtained by using hydrophobic carriers. Encapsulation of drug particles by hydrophobic polymers are more efficient than hydrophilic polymers. Polymer network surrounds the drug as leaching is not possible so easy to sustain the release of drug from Liquisolid matrices [41]. Efficacy, Patient Compliance and safety in formation of sustained-release oral dosage form.

**Advantages**

Low production cost. The Bioavailability of BCS class II and IV drugs can be improved manufacturing cost of formulations is lowest as compared to soft gelatin capsules drug release modification is achieved with the help of suitable ingredients. They are very ductile. Improves the drug release by using certain hydrophobic carriers and surface-active agents thus enhances the dissolution profile. The manufacturing capability can be increased. The extent of absorption is better than conventional tablets.

**Limitations**

Inadequate hardness achieved if the acceptable compression is not achieved This results in a decreased tablet size by the substances with greater absorption rate.

**Applications**

This system act as a weapon to increase drug dissolution: Felodipine Liquisolid pellet can be prepared with the help of this technique. Hydrochlorothiazide Liquisolid tablets by in vivo studies proves significant bioavailability rather commercial oral dosage forms, Sustain drug release: Venlafaxine Hydrochloride Liquisolid tablet having larger retardation effect contrast to DCT. Minimize the influence of pH variation on drug release: Minimizes the influence of pH in release of Loratidine Liquisolid tablet. It increases solubility and dissolution rate in drugs Sustained-release tablets can be formulated with hydrophobic Current reports Liqui-mass system is a fundamental difference between liquisolid technology and liquid-Pellet technology (also referred to as Liqui- Mass technology). There is a strategy to increase the ritonavir dissolution rate.[42] Liqui pellet (Liqui mass System) the emerging next-generation oral dosage form which stems from liquisolid concept incombination with pelletisation technology using deionized water granulating liquid, 25% Non-volatile organic solvent, Aerosol 300 as coating material, liquid load factor 1 by oven drying method. Liquisolid technology (Liquisolid system) applied to pellets: evaluation of the feasibility and dissolution performance by feldipine as a model drug using copovidone in water (1%) granulating liquid, 5% Non-volatile organic solvent, crosspovidone (also disintegrant) as coating material, liquid load factor 0.1 by Fluid bed dryer [43, 44].

**CONCLUSION**

This present review shows that numerous techniques are used to increase solubility and bioavailability of highly lipophilic drugs among all liquisolid technique act as a favourable technique for crushing these challenges. These tasks are enhanced as rise in wetting properties and surface area of the drug usable for dissolution medium. Drug release, can be modified by suitable disintegrating agents, carrier and coating materials. It has good production capability and formulations are of lower cost. Patient compliance in oral route grab by the technology will be high. This study proves that Liquisolid technology can be used effectively for the poorly soluble drugs and this technique is truly favorable for BCS class II and class IV drugs.

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CONFLICT OF INTERESTS
Declared none

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