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Review Article

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, Lipophyllic drugs, Solubility

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INTRODUCTION

Mostly newly developed drugs are Lipophyllic which generally faces challenges like solubility and bioavailability. Numerous methods like saltformation, [1] cosolvancy, [2] complexation, [3]micronization, [4] melts onocrystallization, [5, 6] lyophilization, [7], solubilization bysurfactants [8] solid solution [9], drug solution incorporation in soft gelatin capsule [10] liposomes, nanoparticles, SEEDS, [11] imroves the dissolution of the drugs of low solubility These techniques have some limitations such as hygroscopicity, creating solubilityproblem [12, 13]. The word liquid medicine means oily liquid drugsolution or suspensio n 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 [15] so this technique is known as "PowderSolution Technology". Greater surface area and adsorption of carrier materialto adsorb adequate space in liqyidmedicine. 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 incresed

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 (ψ-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.

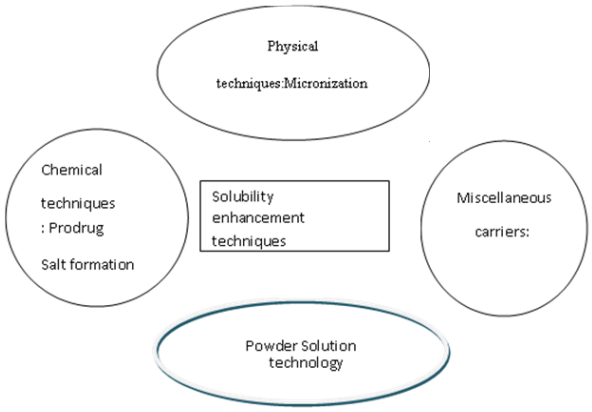

Fig. 1: Techniques for increasing solubility

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. Eg: 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 confirms the enhancement of the dissolution rate [24, 25].

Carrier Materials: Compression-enhancing, relatively large, porous surface and high liquid adsorption function. eg. 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. eg sodium starch glycolate Various excipients used in the preparation of Liquisolid powder are enclosed in table 1

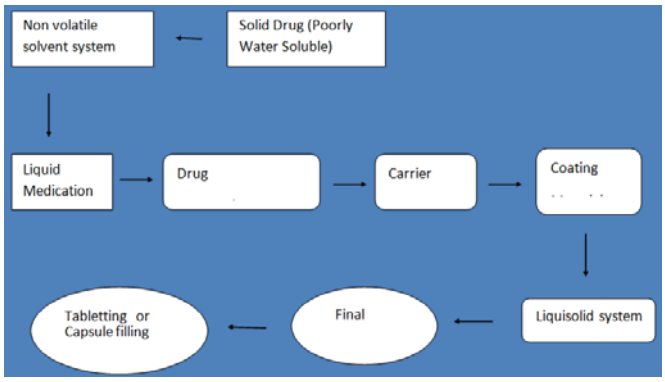

Fig. 2: General steps to prepare liquisolid formulation

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)	Polyvinylpyrrrolidine
2.	Propylene Glycol(PG)	Fujicalin (Dibasic Calcium Phosphate)	HPMC-E4M	Sodium Starch Glycolate (SSG) (Explotab)
3	Polyethlene Glycol PEG 200,300,400,600	Neusilin (Magnesium aluminometasilicate)	Fused Silica (Cab-o-Sil M5)	Cross Sodium carboxymethyl cellullose (Croscarmellose Sodium)
4	Polysorbate 20,40,60,80	Eudragit RL	Syloid 244FP	Pregelatized Starch
5	Tween 80	Eudragit RS	Colloidal Silicon dioxide	
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		

Preformulation studies

Solubility study of drug in non-volatile sovent: Pure drug liquefy in distinct non-volatile solvents and extreme, pure drug were joined shift 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 (h) [30].

Determination of Flowable Liquid Retention Potential (Φ value)

Φ–value= weight of liquid/weight of solid ….

Liquid Load Factor (L_f)

L_f = 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 20:1to 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 Haunsers 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 loss. 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

II,900 ml 0.1N HCl at constant temperature of 37 °C±2 and at speed of 50 to 200 rmp [32]. *In vivo* Evaluation of Liqisolid Tablets: Relative bioavailability and Area under plasma concentration display mobile differences among the liquisolid compact and a commercial tablet [33]. Outcomes of Liquisolid technology are enclosed in given table 2

Table 2: Workout and results of liquisolid technology

S. No.	LST concept (Year wise)	Investigation reported or significance [34]
1	2007	Initiation of concept: Liquisolid tabletslike Prednisolone, methylclothiazide, Hydrochlorothiazide and piroxicamboost up the dissolution profiles as related to Direct compressible tablet.
2	2008	Tablete prepared by Liquisolid technology of Carbamazepine, Famotidine, 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 used in Indomethacin 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 Aceclofenac and Rofecoxib Liquisolid tablet as compared to commercial product.
5.	2011	Fujicalin (Dibasic Calcium Phosphte) and Neusilin (Magnesium alumino metasilicate) are more effective carrier materials than Avicel(Microcryatalline cellulose) compared. Dissolution rate and bioavailability of Glipizide, Indomethacin, Lansoprazole, 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, Candesartancilextil, Mefanamicacid,Rosuvastatin, SpirinolactoneLiquisolid Tablets showed better release retardation Trimetazidine dihydrochloride sustained releae tablet by using Liquisolid technology proves show that polysorbate 80 also used ad liquid vehicle in sustaining the release of drug from liquisolid matrices [35]
8	2014	,Physicochemical characteristic among all Clonazepam, Candesartan,Lamotrigine and nateglimide Liquisolid Tabletes. Solubility and dissolution rate of piroxicam is increased by Span 20, Tween 80, PEG 400,Labrosol.[36]
9	2015	Hydrochlorthiazide and Domperidone maleate LSC showed improvement in dissolution rate and solubility
10	2016	Liquisolid pellets of Felodipine (101) and Curcumin loaded Liquisolid systems using different vechicles in different concentration enhances the drug dissolution
11	2017	LSC of Clinidipine 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 statein Curcumin Liquisolid tablets exhibited improvement in dissolution rates as well as apparent solubility was obtained [39]
14	2020	Proves difference between Liquisolid pellet and liquipellet 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 hydrophyllicpolymers. Polymer network surrounds the drug as leaching is not possible so easy to sutain 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-Masstechnology). 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,29% Non-volatile organic solvent, Aerosil 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 performanusing felodipine as a model drug using copovidone in water (1%) granulating liquid, 5% Non-volatile organic solvent, crospovidone (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 bioavailbilty of highly lipophllic 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 grabby 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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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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