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Review Article

A Review on Liquisolid Technique

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ABSTRACT

The majority of therapeutic agents have found oral medication administration to be most preferable and commonly usefull delivery technique. Because it is so convenient, easier to administer, and improves patient compliance, it is one of the most often utilized medication delivery methods. Dissolution rates, which are regulated by the effective surface area available for dissolution, restrict the bioavailability of several weakly water-soluble medications. One of the hardest parts of drug research is still making poorly water-soluble medications more oral bioavailable. The more modern "powdered solution technology" & "liquisolid technology" used in create rapid-release solid dosage forms from water-insoluble medications. When developing the perfect solid dosage form unit, industry faces a difficult problem: the restricted solubility of pharmaceuticals. The liquisolid method is a new and promising way to deal with this effect. The method's foundation is breakdown of non-volatile solvent for an insoluble drug, followed the addition in a suitable coating & carrier materials to drug-loaded solutions to create powders that flow and compress well. Individual chemical components have no bearing on the choice of the proportion of nontoxic hydrophilic solvent, carrier ingredient, and coating ingredient. Higher bioavailability can be attributed to either increased drug particle wettability, greater water solubility of drug, or enhanced drug surface area for accessible release

INTRODUCTION

The main determinant of a drug's potential for therapeutic benefit is its bioavailability, which is reliant on the drug's capacity to dissolve in gastrointestinal fluid. Improved disintegration rate will improve assimilation and bioavailability because the ability to dissolve is among the crucial thresholds for attaining the best possible centralization of the medicine for basic

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transmission of pharmacological reactions. Pharmaceuticals that are not sufficiently water-soluble will usually be administered at a moderate rate, as indicated by their limited ability to dissolve inside the GI substance; the rate at which this occurs is often the rate that determines the next step in the medication's assimilation.

Various are used to inhanced the solubility-

(a) Micronization
(b) Nanonisation
(c) Use of surfactants
(d) Use of salt form
(e) Supercritical fluid recrystalization
(f) Complex with cyclodextrine
(g) High pressure homonization
(h) Spray drying
(I) Co-precipitate method
(j) Liquisolid compact [1, 2]

Liquisolid Technique:

When certain transporters and materials covering fluid pharmaceuticals, drug suspensions, or medication arrangements are combined, they can transform from unpredictable liquid into powder mixes that are dry, non-following, freely streaming, and compressible. Mixtures of dry, non-following, free-streaming, and compressible powders containing unpredictable solvents. Liquisolid structure is produced by this method. The most promising liquisolid structure for quick dissolve. Fast distribution rate can be generated in liquisolid technique and they effectively using in water-insoluble medication, Lipophilic fluid drugs and potent water-insoluble drugs are separated into unstable dissolvable. Both free or non-free streaming are options for this fluid treatment. Dry-looking powders that compress quickly with a transporter and a covering substance. Water-insoluble drug liquisolid medications have improved disintegration profile and bioavailability. [3, 4].

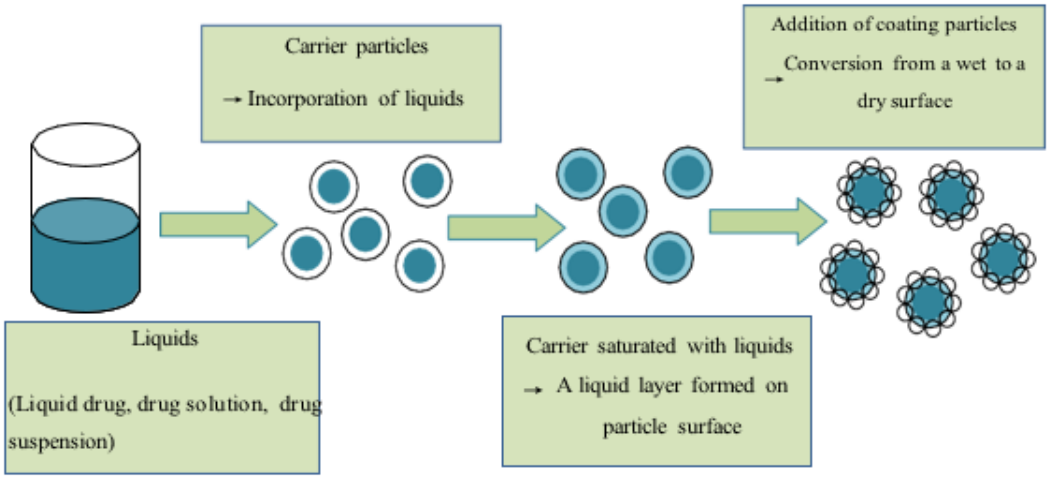

Fig. 1 – Mechanism of liquisolid system formation

Need of liquisolid techniques:

The oral route most commonly used method of medication administration because it's convenient, high patient acceptance, and low manufacturing expenses. After taken orally, a medication must dissolve into stomach acids in order to enter the bloodstream. It is estimated that 40% of all novel created medications are either insoluble & rarely soluble into water, making poor solubility among

the main issues facing the drug production business today. By reducing crystallinity, reduce particle size & increase surface area, these drugs can dissolve more quickly. Several studies have been conducted in order to generate micro particles and nanoparticles and micro particles and decrease the size of the particles in order to speed up the rate at which medications dissolve. However, smaller particles of drug have significant propensity to join together because of hydrophobicity. [4]

Classification:

A. Depending on the category of liquid drug: Three subgroups of liquisolid technique can be determined:

1. Drug solutions in powder form
2. Drug suspensions in powder form
3. Liquid medications in powder form

The initial two type created by converting medication solutions (for example, Solution of prednisolone in propylene glycol) and suspensions of drugs (for example, suspension of gemfibrozil in Polysorbate 80). Third type is created by forming liquid medications (for example, vitamins in liquid form) in liquisolid method. In the case of non-volatile solvents in the liquid medium, such as the medication suspension or solution, does not evaporate, enabling the medication to be transferred inside the liquid system and ultimately distributed over the finished product.

B. Depending on the formulation method: This method can be divided in two groups:

1. Compact of liquisolid
2. Liquisolid microsystems

When producing a sufficient flowing agent for encapsulation, the basis of liquisolid microsystems is a novel creativity that combines a similar approach with the addition of supplements, such as polyvinylpyrrolidone [PVP], in the drug liquid form that is included in the coating and carrier ingredients to create tablets or capsules, liquisolid compacts are made using the previously mentioned technique. This new technique has the advantage of potentially producing liquisolid microsystems with unit sizes up to five times smaller than liquisolid compacts. [5, 6, 7]

ADVANTAGES:

1) Liquisolid systems can be developed from liquid and solid medications that are almost completely insoluble in water and only very slightly soluble.
2) The medicine remains in a solubilized liquid condition even if it is in tablet or capsule form, which improves drug dissolving by increasing the drug wetting abilities.
3) Manufacturing costs are less expensive.
4) Can be used to create greasy liquid medicines and other liquid pharmaceutical products.
5) Improved availability of tablet. [8, 9]

DISADVANTAGES:

1) Not suitable for creating excessively high dosage insoluble medications.
2) More carrier are added to create free-flowing powder. flows freely, but this make tablet bulkier than 1 gram, result in harder to take in.
3) Since the Liquid drugs are possibly squeezed when compressed, from the liquisolid medicine, resulting in tablets with an unacceptable hardness, acceptable compression characteristics might not be obtained.
4) To get further challenges in combining diminutive volumes in sticky solution of liquid with numerous quantities of the carrier substance.[10]

Applications of liquisolid technique:

1) The liquisolid approach increases drug photostability in the solid dosage form.
2) Liquisolid formulations allow for immediate and sustained release of medications.
3) Water-insoluble solid medications or liquid lipophilic medications are the best alternatives for the liquisolid method.
4) Drug release is less impacted by pH variations when using the liquisolid method.
5) Liquisolid technique increases drug solubility and dissolution rate.[11]

Concept:

When absorb and adsorb happen when cellulose or another substance for carriers with strongly matted fibers and a porous within is combined with the medicine that has been dissolved in the liquid vehicle. This shows that the liquid is adhering to the porous carrier particles' exterior and interior surfaces after first being absorbed in the particles' interior and then being trapped by their internal structure. The liquisolid system thus has the desired flow characteristics due to the coating material's large specific surface area and high adsorptive qualities. (R. H. Fahmy and others, 2008). In liquisolid systems, the medicine is transported by the granules of powder (silica and MCC) while also being inside the liquid vehicle in solution. This liquisolid compounds may be anticipated as an exhibit superior drug release quality or, as a result, greater oral bioavailability because of the markedly increased in wetting qualities or as well as the surface area of the medication accessible to dissolve. Greater bioavailability of oral water-insoluble medicine is attained when the substance has already been resolved, exhibiting improved dissolution rate, because the rate-limiting stage of absorption through the gastrointestinal tract is often the breakdown of a non-polar drug. For this reason, as compared to traditional oral solid dose forms, capsules made of soft gelatin and elastic that hold solutions of drugs have better bioavailability. The method of medication administration from liquisolid compacts is based on a similar concept, which is also primarily in charge of the better dissolving profiles that these preparations display. The liquisolid compacts' rate is one of the hypothesized mechanisms for the increased dissolving rate and wettability of the compacts by the dissolution media. The non-volatile fluid in the liquisolid system helps to moisten the medication particles by lowering the tension caused by the interfacial contact between the tablet surface and the dissolving liquid. (Javadzadeh Y et al.., 2007). [12]

For designing of sustain release tablet:

Providing the best possible treatment regarding effectiveness, patient compliance and safety, sustained release oral dose formulations are being developed. A controlled release dosage form should ideally offer a therapeutic blood concentration of the medication that is sustained over the course of the dosing interval. Because of its ease of use and affordability, one of the greatest and most efficient methods for developing prolonged release formulations is to regulate medication dissolution. Numerous techniques have been created for achieving this goal, including coating with specific materials, preparing pharmaceuticals in salt form, and incorporating medications into hydrophobic carriers. A new and exciting technology called the liquisolid method can change how quickly drugs dissolve. According to certain theories, hydrophilic carriers in liquisolid systems could be used to create sustained release systems in place of hydrophobic ones like Eudragit RL and RS. Consequently, it is proposed that the technique may be improved to lower the rate of drug

disintegration and create sustained release systems. [12]

Components in Liquisolid Formulation:

1. **Carrier material:** Carrier material having sufficient ingestion properties. carrier material having a adsorbing properties.

Example- Avicel PH 102, Avicel PH 200, Lactose, Eudragit RL, Eudragit RS etc.

2. **Coating material:** The coating material having a fine and profoundly adsorptive particles, for example different forms of silica, which helps in covering the wet transporter particles and showing a dry looking powder by adsorbing any overabundance fluids. The fluid parcel, which can be a fluid medication, a medication suspension or a medication arrangement in suitable non volatile fluid vehicles, is considerated into the permeable coating material.

3. **Non-volatile solvents:** Different Non-volatile solvents are used in liquisolid medication.

Examples- PEG 200, PEG 400, Glycerine, Polysorbate 80, Propylene Glycol, Tween 20, Tween 80 etc.

4. **Disintegrant:** The most common used disinterant is sodium stach glycolate or crosspovidone etc.

Examples of medications that are suitable for use in liquisolid systems: Hydrochlorothiazide, methyclothiazide, carbamazepine, digoxine, clofibrate, nifedipine, spironolactone, ibuprofen etc.

Necessary equipment use in liquisolid systems: Weighing balance, uv spectrophotometer, tablet punching machine, friability tester, thickness tester, dissolution and disintegration machine, water bath, etc. [13]

Preparation of Liquisolid Tablet:

A 20 ml glass beaker containing accurately calculated amount of drug and non-volatile solvent are heated until the drug dissolves in the solvent. Calculated amounts of coating and carrier components are mixed with the resultant hot medicine. Three steps are involved in the mixing process:

1. Initially, the system are combined for approximately one minute at a rate of one revolution per second in order to evenly distribute the liquid medication throughout the powder.
2. The second stage entails evenly covering the mortar's surfaces with the liquid/powder admixture and letting it stand for around five minutes to enable the drug solution to seep into the interior of the powder particle. The third step involves removing the powder from the mortar surfaces with an aluminum spatula. Then, for another 30 seconds, it is mixed with sodium starch glycolate, as in the first step. This signifies the creation of the final Liquisolid tablet formulation. [14]

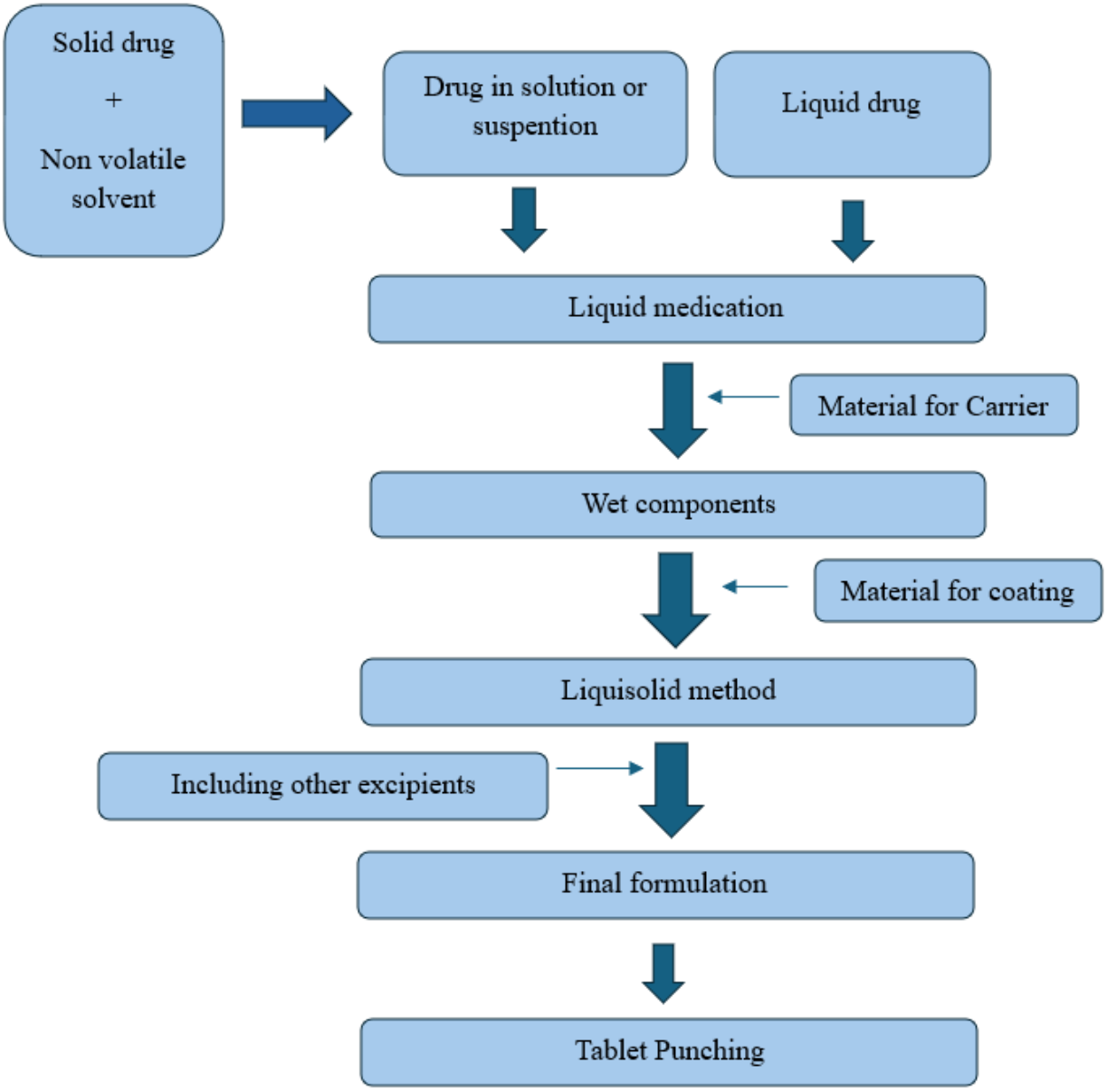

Fig: Preparation process of liquisolid system [5]

Pre-compression studies:

- **Flow property:** The formulation and industrial production of tablet dosage forms depend heavily on their flow properties. The angle of repose, tapped density, compressibility index, Carr's index, and other measurements are necessary.
- **Differential scanning colorimetry (DSC):** It assists in figuring out when the drug and excipients interact, which indicates that stability testing are working. When the drug's characteristic peak is missing from the DSC thermogram, it indicates that the drug is in liquid form as a solution and is dispersed molecularly throughout the body.
- **Fourier transform infrared spectroscopy (FTIR):** The chemical interaction between the medication and the formulation's excipients is ascertained using FTIR analyses. There is no

chemical interaction if the formulation has medication peaks and no additional peaks are present.

- **X-ray diffraction (XRD):** The drug's solubility or amorphous state can be ascertained by XRD tests. It is seen that the drug's distinctive peaks vanish and that peaks belonging to the carrier appear instead.
- **In vitro release studies (USP 2005):** Numerous studies have shown that the Liquisolid formulation exhibits an improvement in the rate of dissolving. It was also demonstrated that faster release rates are seen in liquid medications with lower drug concentrations. This can be the result of drug precipitation at high drug concentrations inside silica pores. The designed Liquisolid tablets and direct compression tablets were compared in the in vitro release investigations, which were carried out using the dissolving device. The medication release % was calculated.
- **Scanning electron microscopy (SEM):** The crystallinity of the medication in the Liquisolid system was ascertained by SEM examination. Drug solubilisation in the system is indicated by the drug's loss of its crystalline form. [15, 16]

CONCLUSION:

The liquisolid technique is a promising approach that uses simple manufacturing process and lower production costs than other standard tablets to enhance the rate of dissolution and solubility, consequently boosting the amount of absorption and bioavailability of water-insoluble medications. It is also utilized to create instant release and sustained release medications employing hydrophilic and hydrophobic carriers. When disintegrant is used in conjunction with liquisolid compacts medication release from coating agents and carriers is significantly improved. Additionally, the majority of water-insoluble medications now have much improved solubility, bioavailability, and dissolution thanks to this technology, particularly for BCS class II and class IV medications.

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