



Novel Approaches to Enhance Solubility Medicine

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Abstract: "The solubility enhancement of poorly aqueous soluble drugs presents a significant challenge in pharmaceutical formulation. Liquisolid technology, also known as powdered solution technology, has emerged as a promising approach to enhance the solubility and bioavailability of such drugs. This paper provides a detailed discussion of the novel approaches employed within the framework of Liquisolid technology to overcome solubility limitations. The study explores the principles, advantages, and applications of Liquisolid technology in drug formulation, highlighting its potential to revolutionize oral medication delivery. This research aims to investigate the effectiveness of Liquisolid technology in enhancing drug solubility, elucidate its underlying mechanisms, and evaluate its impact on drug dissolution, bioavailability, and therapeutic outcomes. The objectives are to review the background and challenges associated with poor solubility of drugs, introduce the concept of Liquisolid technology and its principles, discuss the advantages and benefits of Liquisolid technology in solubility enhancement, explore the formulation strategies and key components involved in Liquisolid formulations, evaluate the *in vitro* and *in vivo* performance of Liquisolid systems, and identify future research directions and potential applications of Liquisolid technology in pharmaceutical development. Through this comprehensive analysis, the study aims to provide valuable insights into the novel approaches based on Liquisolid technology for enhancing drug solubility, facilitating the development of effective and efficient drug delivery systems. Liquisolid technology, a novel approach to solubility enhancement, offers promising advantages over conventional techniques. It involves solubilizing poorly aqueous soluble drugs using surfactants, then incorporating these solubilized drugs into a carrier system or powdered solution. The powdered solution facilitates the conversion of the solubilized drug into solid residues, which can be further processed into different dosage forms."

Keywords: Liquisolid system; coating material; non-volatile solvents; carrier material; surfactant; solubilization/solubility enhancement

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I. INTRODUCTION

The most convenient doses form in the oral doses form; however, the major problem in the process of oral solid doses form in the poor drug's solubility candidates. Drug discovery involves the evaluation of many drug candidates, resulting in the accumulation of vast amounts of data regarding crystal structures, including physical and chemical properties. However, many active drug ingredients produced have poor water solubility, affecting their absorption and bioavailability. Solubility problems affect about 60% of drug medication chemically and 40% of newly developed drugs and manufactured substances. This is due to their classification as BCS II drugs, which have low solubility but high permeability. In vitro research has shown that drug dissolution is a significant component, particularly for not water-soluble drugs. Various methods have been developed to improve

drug solubility, including particle size reduction through micronization and nanonization, surface-active agents, cosolvent use, micro and micro and self-emulsification, incorporation of APIs into cyclomaltooses, drug derivatization, and the use of pro-drugs. However, these methods require complex and expensive equipment, resulting in high manufacturing costs.^{1,2} The liquisolid technique is an advanced method for enhancing drug dissolution and is a newly developed one that can overcome many barriers. This technique involves adding appropriate excipients to liquid pharmaceuticals, transforming them into powders that are non-adherent, compressible, free-flowing, and dry. Small particles develop once the liquid drug has been completely absorbed inside the carrier. A liquid drug is first absorbed into the carrier. This results in a free-flowing powdered combination that feels dry and can be compacted.^{3,4} Various part introductions are in Fig.1.

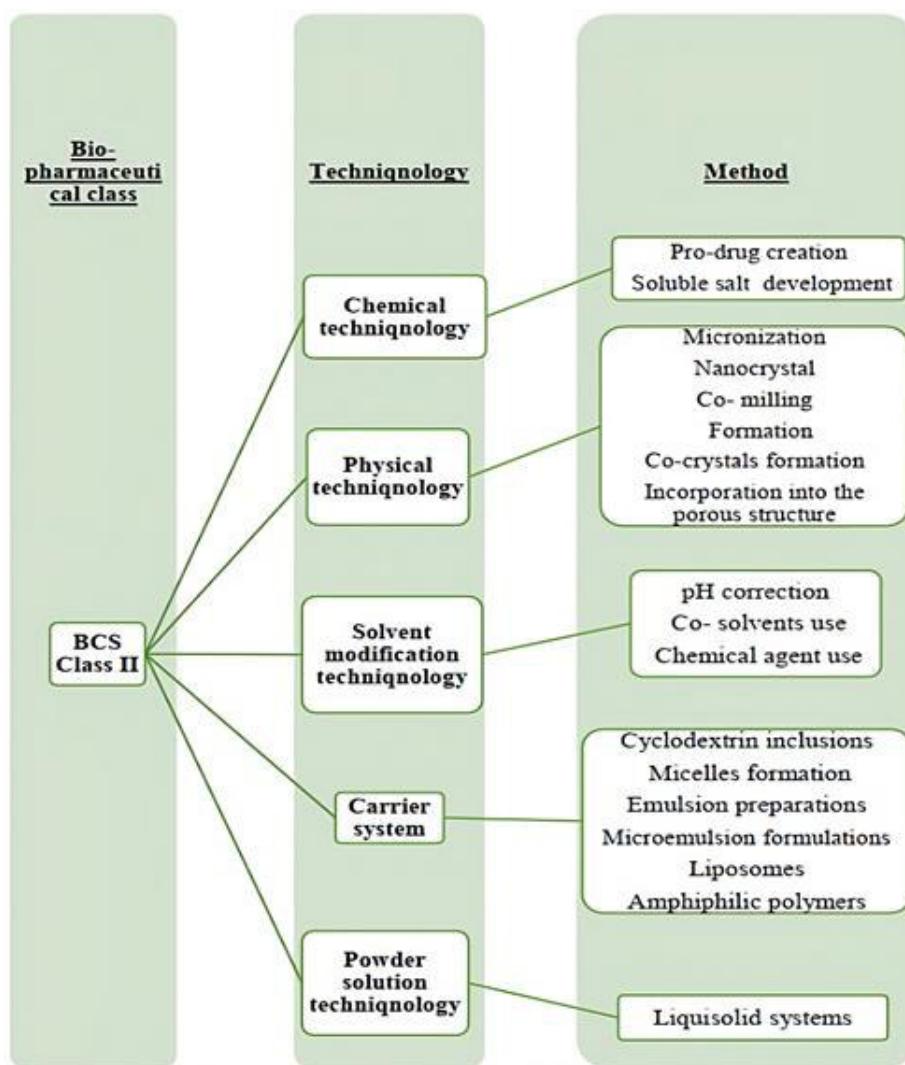


Fig 1: Techniques for Improving Drug Solubility and Dissolution.

The figure illustrates various chemical and physical technologies that improve drug solubility and dissolution, including pro-drug creation, micronization, co-crystal formation, pH correction cyclodextrin inclusions, microemulsion formulation, and liquisolid systems. These techniques are utilized in BCS Class II drugs to enhance their solubility and optimize drug delivery. Using this technology to manufacture tablets from liquisolid systems has proved useful in industrial production and brings low costs. Liquisolid technology can be utilized in drug formulation to improve the bioavailability and solubility of drugs with poor solubility. This

technology effectively enhances drug dissolution and absorption, improving patient therapeutic outcomes. This technique is easy to implement and can be used in industrial production, making it an effective strategy for enhancing the dissolution of the drug's properties.^{4,5}

1.1. Preparation of liquisolid

Preparing liquisolid systems involves several steps, including selecting appropriate coating and carrier materials, determining the drug and solvent ratios, and mixing the

components. The following is a general procedure for preparing liquisolid systems:⁶⁻⁸

1.1.1. Coating and carrier materials

Carrier material should be highly porous and have a large surface for high liquid absorption. Suitable carrier materials include microcrystalline cellulose, lactose, and silica. The coating material should be hydrophobic to prevent liquid penetration into the carrier material. Suitable coating materials include magnesium stearate, talc, and colloidal silicon dioxide.

1.1.2. Drug determination of solvent ratios

The amount of drug and solvent used in the liquisolid system is critical to optimal drug loading and release. As discussed in previous sections, the drug and solvent ratios are determined based on the liquid and drug loading factors.

1.1.3. Preparation of drug-solvent mixture

To achieve uniform drug distribution within a non-volatile solvent, the drug and solvent are typically combined in a beaker and heated until the drug has completely dissolved or dispersed within the solvent.

1.1.4. Addition of coating materials and carrier

The drug-solvent mixture is poured onto a mixture of coating materials and carrier pre-mixed using a pestle and mortar. The drug-solvent mixture is evenly distributed on the carrier material by mixing and kneading with a spatula or other suitable device.

1.1.5. Compression or encapsulation

The liquisolid mixture is compressed into tablets or encapsulated into capsules using standard tableting or encapsulation equipment.

1.1.6. Characterization

The liquisolid system is characterized using various analytical techniques to determine its physical and chemical properties, such as drug content, dissolution rate, and flowability.

1.2. Solubility enhancement liquisolid-⁹⁻¹³

Enhancing the solubility of poorly soluble drugs is crucial to improve their bioavailability and therapeutic effectiveness. Several classical and commonly employed approaches are utilized to enhance the aqueous solubility of such drugs, particularly those classified as BCS (Biopharmaceutics Classification System) Class II and Class IV. The following methods are commonly employed for solubility enhancement:

1.2.1. pH Adjustment

Altering the pH of the drug formulation can significantly influence its solubility. This approach involves adjusting the pH to create a favorable environment for drug dissolution. For example, ionizable drugs that exhibit poor solubility at their natural pH can be dissolved by adjusting the pH to a

level where the drug molecule is predominantly ionized, thus increasing its solubility.

1.2.2. Co-Solvency

Co-Solvency involves the addition of water-miscible organic solvents (cosolvents) to the drug formulation. These cosolvents can enhance drug solubility by disrupting the drug's crystal lattice structure and increasing its solubilization within the solvent system. Commonly used cosolvents include ethanol, propylene glycol, polyethylene glycols, and glycerin.

1.2.3. Micro-Emulsification

Microemulsions are clear, thermodynamically stable dispersions of oil and water, stabilized by surfactants and sometimes co-surfactants. Micro-Emulsification is an effective approach to enhance drug solubility by increasing the surface area available for drug dissolution. The small droplet size of microemulsions enhances drug solubility and bioavailability. Additionally, microemulsions can improve drug permeability through biological barriers.

1.2.4. Self-Emulsification

Self-emulsifying drug delivery systems (SEDDS) are formulations that rapidly disperse in aqueous media under gentle agitation, forming fine oil-in-water emulsions or microemulsions. SEDDS typically consist of oils, surfactants, and co-surfactants. Upon dispersion, these systems form colloidal structures that enhance drug solubilization. Self-emulsifying formulations can improve drug absorption and bioavailability.

1.2.5. Micelles

Micelles are self-assembled structures formed by surfactant molecules in aqueous solutions. Surfactants have hydrophobic and hydrophilic regions, allowing them to solubilize lipophilic drugs within their hydrophobic core. Micellar solubilization can enhance drug solubility and facilitate absorption by increasing drug concentration gradients.

1.2.6. Liposomes

Liposomes are spherical vesicles composed of lipid bilayers, which can encapsulate hydrophobic drugs within their lipid core or hydrophilic drugs within their aqueous compartments. Liposomes provide an aqueous environment for drug solubilization, improving drug stability and solubility. They can also enhance drug delivery to specific sites and exhibit controlled-release properties.

1.2.7. Emulsions

Emulsions consist of two immiscible liquids, typically oil and water, stabilized by surfactants. Emulsions can solubilize lipophilic drugs within the oil phase, improving drug solubility and bioavailability. Depending on the drug's characteristics and desired application, they can be formulated as oil-in-water (o/w) or water-in-oil (w/o) emulsions. Moreover, each solubility enhancement method has its own merits and demerits, and the selection of an appropriate method depends on various factors such as drug properties, target

application, dosage form, and stability requirements. A thorough understanding of these methods and their suitability for a particular drug is essential in the formulation process.

1.3. Concept

Liquisolid systems incorporate liquid medication into a porous carrier material, which is then absorbed onto the carrier particles' external and internal surfaces. This creates a highly absorbent coating material with a large specific surface area, which enhances the drug's wetting properties and improves its oral absorption. Compared to traditional solid dose forms, liquid drugs have superior solubility because they are already in solution and have a higher dissolution rate. This is especially effective for non-polar drugs, which may

have difficulty dissolving inside the gastrointestinal tract's aqueous environment. Soft elastic gelatine capsules are a good example of how liquid drugs can be delivered orally with better absorption, as they dissolve quickly and release the drug in solution form.^{14,15} Liquisolid compacts are a formulation technique aimed at improving the dissolution properties of drugs. This technique involves incorporating a liquid medication into a powder mixture of carrier materials, which is then compressed into a solid tablet form. The carrier particles absorb the liquid medication, creating a porous structure that facilitates the release and dissolution of the drug. Liquisolid compacts have demonstrated efficacy in enhancing the bioavailability of poorly soluble drugs, thereby improving their therapeutic efficacy in oral drug formulations Fig 2^{16,17}

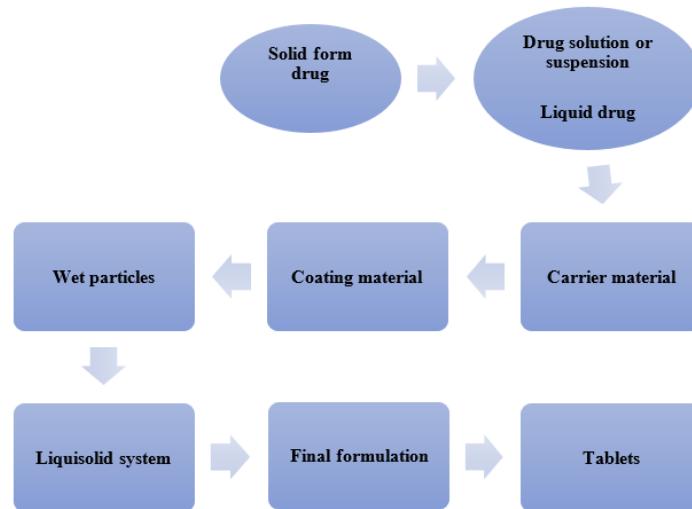


Fig 2: Production of Liquid Drug

Fig 2; The preparation of liquisolid tablets involves various components, including solid and liquid drugs (API) such as Ketoprofen, Indomethacin, Nifedipine, and Tadalafil. These drugs serve as the active pharmaceutical ingredients in the formulation. Carrier materials play a crucial role in liquisolid systems. Common carrier materials include Microcrystalline Cellulose (MCC) pH101 and MCC pH200, ethyl cellulose, and methylcellulose. These materials have high absorption capacity for the liquid vehicle and aid in maintaining the desired formulation characteristics. Coating materials coat the carrier particles, improving their flowability and compressibility. One commonly used coating material is Aerosil200, which is colloidal silicon dioxide. It helps in reducing particle weight and enhancing the formulation's flow properties. By incorporating the appropriate carrier and coating materials, liquisolid tablets can be formulated with improved dissolution properties, bioavailability, and tablet characteristics.

2. MECHANISMS OF ENHANCED DRUG RELEASE FROM LIQUISOLID TECHNIQUES^{18,19}

The enhanced drug release from liquisolid compacts can be attributed to several mechanisms. These mechanisms include increased wetting properties, improved dispersibility, increased surface area, and reduced drug particle size. Each mechanism in more detail:

➤ **Increased Wetting Properties:** Liquisolid compacts contain liquid medication that is adsorbed onto a carrier material and coated with a coating material. The liquid medication enhances the wetting properties of the powder mixture. When the liquisolid compact comes into contact with the dissolution medium, the liquid medication quickly wets the surrounding solid particles, facilitating the dissolution process.

➤ **Improved Dispersibility:** The carrier and coating materials used in liquisolid compacts are typically highly porous, allowing for increased dispersibility of the liquid medication within the powder matrix. The porous structure provides numerous interstitial spaces that accommodate the liquid medication, promoting its uniform distribution throughout the compact. This enhanced dispersibility ensures a higher drug release rate.

➤ **Increased Surface Area:** Liquisolid compacts possess a significantly higher specific surface area than conventional solid dosage forms. The liquid medication coats the carrier material, which results in the formation of a thin liquid film around the solid particles. This liquid film increases the effective surface area of the drug available for dissolution. Consequently, the dissolution medium has better access to the drug molecules, leading to enhanced drug release.

➤ **Reduced Drug Particle Size:** The liquisolid technique can reduce the particle size of the drug within the

compact. The liquid medication acts as a solvent, dissolving the drug and reducing it to a molecular or submicron level. The reduced drug particle size facilitates faster dissolution and improves drug release. The smaller drug particles exhibit increased solubility due to the increased surface area available for interaction with the dissolution medium. Moreover, these mechanisms collectively contribute to the enhanced drug release from liquisolid compacts. The increased wetting properties, improved dispersibility, increased surface area, and reduced drug particle size are crucial in promoting rapid and efficient drug dissolution and release.

2.1. Advantages

The liquisolid technique is a formulation approach that transforms liquid drugs into a compressible, dry, and free-flowing powder by blending them with a carrier material. The use of liquisolid techniques provides several benefits, which include:²⁰⁻²⁵

- The liquisolid approach increases poorly water-soluble drug dissolving rate, enhancing bioavailability.
- Including liquid drugs in a carrier material can improve their solubility by increasing the surface area accessible for dissolution.
- Liquisolid formulations can allow for a lower dose frequency than conventional dosage forms, resulting in better patient compliance.
- Liquisolid formulations provide increased stability for the drug by protecting it from environmental factors such as humidity, oxidation, and light.
- Liquisolid formulations are generally more cost-effective than other drug delivery systems since they require fewer excipients and simpler manufacturing processes.
- Liquisolid technology allows for flexibility in the choice of carrier materials, making it possible to develop formulations with customized release profiles.
- The enhanced dissolution rate of drugs and solubility of drugs in liquisolid systems can result in improved bioavailability, which means that a higher percentage of the drug is held in the bloodstream and can utilize its therapeutic effects.
- The liquisolid technique is relatively simple and easy to manufacture, making it suitable for mass production.

2.2. Disadvantages

Here are some disadvantages of using liquisolid techniques

- Liquisolid systems rely on the non-volatile liquid in the drug solubility. However, some drugs may have limited solubility in the chosen liquid, making it challenging to do optimal drug loading.²⁶
- Formulating a suitable liquisolid system requires a good knowledge of the physicochemical properties of the drug, the excipients used, and the liquid vehicle. This complexity can lead to increased development time and cost.²⁷
- The dissolution behavior of liquisolid systems may be impacted by several variables, such as the ratio of solid components to liquid, the carrier's particle size, and the preparation method. This can lead to variability in drug release and affect the consistency of therapeutic outcomes.²⁸
- Liquisolid systems are prone to moisture uptake and may have limited stability over time, especially if not stored

properly. This can impact the drug's effectiveness and lead to potential safety issues.²⁹

- Some drugs may not be compatible with certain excipients used in liquisolid formulations, which can affect the stability and efficacy of the final product.³⁰
- Regulatory agencies may not accept liquisolid systems in some countries due to their relatively new status and lack of established guidelines for their use.³¹
- The preparation of liquisolid systems can be complex and require specialized equipment, which may be limited in some manufacturing facilities.³²

3. APPLICATION

Liquisolid techniques, also known as powdered or liquid loadable formulations, are innovative approaches to formulating solid dosage forms. They involve the conversion of liquid drug formulations into dry, free-flowing powders, which can be further processed into tablets or capsules. This technique offers several advantages, such as improved drug dissolution, enhanced bioavailability, and increased stability.³³

A. Improved dissolution and bioavailability:

Liquisolid systems have been successfully employed to enhance the dissolution and bioavailability of poorly soluble drugs. By dispersing the drug in a suitable non-volatile solvent and then adsorbing it onto a carrier material (such as microcrystalline cellulose), the resulting liquisolid powder exhibits increased surface area, leading to improved drug release and absorption. This approach has been demonstrated for various drugs, including simvastatin (Al-Saidan et al., 2018) and ibuprofen (Khames et al., 2019).³⁴

B. Taste masking: Liquisolid techniques can mask the unpleasant taste of bitter drugs, thus improving patient acceptability. The drug's taste can be effectively masked by incorporating the drug into a liquisolid powder, which is subsequently formulated into tablets or capsules. For example, a study by Kulkarni et al. (2019) demonstrated the successful taste masking of a bitter drug, azithromycin, using the liquisolid approach.³⁵

C. Sustained-release formulations: Liquisolid techniques can be employed to develop sustained-release dosage forms by modulating the drug release characteristics. By adjusting the composition of the liquisolid formulation, including the carrier material and coating agents, sustained drug release profiles can be achieved. A study by Jain et al. (2020) investigated the use of the liquisolid approach to developing sustained-release tablets of metoprolol succinate.³⁶

D. Self-emulsifying drug delivery systems (SEDDS):

Liquisolid techniques can also convert self-emulsifying drug delivery systems into solid dosage forms. SEDDS typically consist of liquid or lipophilic drug formulations dispersed in a self-emulsifying vehicle. By converting the liquid SEDDS into a solid liquisolid powder, the formulation becomes more convenient to handle, store, and administer. Patel et al. (2017) demonstrated the conversion of a liquid SEDDS formulation of lovastatin into a solid dosage form using the liquisolid technique.³⁷

4. COMPONENTS

- Non-volatile solvent

- Drug candidate
- Coating material
- Carrier material
- Disintegrant
- Non-volatile solvent

A non-volatile solvent has a high boiling point and does not easily evaporate at room temperature. Non-volatile solvents are often utilized as binding agents, which dissolve the drug and create a uniform liquid mixture. It is important to ensure that the non-volatile solvent is compatible with the drug and does not interfere with its therapeutic properties.³⁸ Examples of commonly used non-volatile solvents in liquisolid formulations include glycerine, PEG (polyethylene glycol) 200 and 400, polysorbate (Tween 80), and PG (propylene glycol). These solvents are highly miscible in water and have low viscosity, making them suitable for organic solvents. The water-soluble polymer is PEG (Polyethylene glycol), commonly used as a liquisolid formulation in the non-volatile solvent. PEG 200 and PEG 400 are the most frequently used types, as they have a low viscosity and high solubility in water. Glycerine is another common non-volatile solvent used in liquisolid formulations due to its high solubility in water and ability to act as a plasticizer.³⁹ Polysorbate 80 is an emulsifier widely used in the industry to increase the solubility of weakly soluble drugs. In liquisolid formulations, it is employed as a non-volatile solvent owing to its capacity to dissolve both hydrophilic and lipophilic drugs. Propylene glycol (PG) is another commonly used non-volatile solvent in liquisolid formulations. It has low toxicity and can solubilize a wide variety of drugs.⁴⁰ Non-volatile solvents are an essential component of liquisolid formulations, serving as a binding agent that dissolves the drug and produces a uniform liquid mixture. The non-volatile solvent must be compatible with the drug and have a high boiling point, making it appropriate for organic solvents.⁴¹

4.1. Drug candidate

The liquisolid approach has shown promising results in treating BCS class II (Low-solubility and high-permeability) drugs and BCS class IV (Low-solubility and low-permeability) drugs with a slow dissolution rate. This approach involves using a binding agent as a non-volatile solvent to dissolve the drug and create a uniform liquid mixture, which is then adsorbed onto a porous carrier material. The resulting liquisolid formulation has a large surface, which enhances the drug's bioavailability and rate of dissolution. Some drugs effectively treated using the liquisolid approach includes hydrocortisone, naproxen, prednisolone, piroxicam, famotidine, carbamazepine, and piroxicam⁴². Other drugs that have shown improved solubility and dissolution rates when formulated as liquisolid systems include liquid drugs such chlorpheniramine, water-insoluble vitamins, and fish oil, as well as digoxin, digitoxin, spironolactone, hydrochlorothiazide, and polythiazide. The efficacy of the liquisolid technique in enhancing the drug rate of dissolution and solubility has been established in various studies. For example, a study demonstrated that the liquisolid approach significantly increased the rate of disintegration of carbamazepine, a drug with poor solubility, by up to 98%.⁴³ Similarly, the liquisolid approach improved the rate of disintegration of famotidine, a Low-solubility and high-permeability drug, by up to 22-fold.⁴⁴ The liquisolid approach has shown promise to increase the dissolution rate and weakly soluble solubility drugs, particularly those with slow

dissolution kinetics. This approach has shown effectiveness for various drug candidates, including those classified under Biopharmaceutics Classification System (BCS) classes II and BCS IV class drugs. These findings suggest that the liquisolid approach holds significant implications for developing effective and efficient drug delivery systems.^{45,46}

4.2. Coating material

The coating substance must assist in absorbing the extra liquid and give the wet carrier particles a dry look. The coating material should include highly absorbent microscopic particles covering the particles and preserving the powder's flow characteristics. Examples of coating substances using the liquisolid systems include colloidal silicon dioxide (silica), Aerosil200 (hydrophilic fumed silica), SYLOID® G silica, and others⁴⁷. These materials are highly absorbent and can effectively trap the liquid and maintain the dryness of the carrier particles. Colloidal silicon dioxide (silica). Silica is a highly absorbent and hydrophilic material often used as an anti-caking and glidant agent in pharmaceutical formulations⁴⁸. Its high surface area and porosity allow it to absorb large amounts of liquid, making it an effective coating material in liquisolid systems. Aerosil200, which is a hydrophilic fumed silica. It is known for its high surface area and excellent absorption properties, making it ideal for drug delivery systems⁴⁹. Its unique structure and properties enable it to absorb large amounts of liquid and provide a dry appearance to the carrier particles. SYLOID® G silica is a coating material used in liquisolid systems. It is a highly absorbent and porous material used as a glidant and flow aid in pharmaceutical formulations⁵⁰. Its high surface area and porosity allow it to absorb any extra liquid in the liquisolid system and maintain a dry appearance.

4.3. Carrier materials

Carrier materials are used to provide a suitable matrix for the drug substance, such as to enhance the pharmacokinetic properties and bioavailability of that drug. Porous materials are commonly used as carrier materials due to their ability to absorb liquids, maintain flow and compressive characteristics, and control drug release over time.⁵¹ Avicel pH102 and Avicel pH200 are porous polymers widely used as carriers in pharmaceutical formulations. Avicel pH102 is a microcrystalline cellulose produced by treating alpha-cellulose with mineral acids. It has a high surface area and porosity, which makes it an ideal carrier material for drugs that need to be delivered in a controlled manner. Avicel pH200 is another type of microcrystalline cellulose similar to Avicel pH102 but has a higher degree of crystallinity.^{52,53} Eudragit RL and Eudragit RS12 are polymers used as carrier materials in sustained drug delivery systems. These polymers are insoluble in water but can be dissolved in organic solvents. When a drug is encapsulated in these polymers, it is released slowly over time, providing a sustained release profile. Eudragit RL is methacrylic acid, and ethyl acrylate and copolymer, while Eudragit RS12 is a copolymer of methacrylic acid, methyl methacrylate, and a low concentration of trimethylammonioethyl methacrylate chloride.^{54,55}

4.4. Disintegrant

Disintegrants are important in pharmaceutical formulations, especially for oral solid dosage forms. They help to break

down the tablet or capsule into smaller particles, allowing for efficient dissolution and absorption of the active ingredient. Super disintegrants are a type of disintegrant that can rapidly disintegrate the tablet or capsule, leading to an increased drug release rate. This is particularly useful for drugs with poor solubility or low bioavailability, as it can improve their effectiveness.⁵⁶ Cross povidone and sodium starch glycolate (GLYCOLYS®) are two examples of commonly used super disintegrants. Cross povidone is a cross-linked polymer of N-vinyl-2-pyrrolidone that is highly effective in rapidly disintegrating tablets and capsules. It has a high swelling capacity and can rapidly absorb water, leading to rapid disintegration.⁵⁷ SSG (Sodium starch glycolate) is a sodium salt of a carboxymethyl ether of starch. It is also highly effective in rapidly disintegrating tablets and capsules and has a high swelling capacity. It is often used in combination with other disintegrants to enhance their effectiveness.⁵⁸ In addition to cross povidone and sodium starch glycolate, other super disintegrants that are commonly used in pharmaceutical formulations include crospovidone, croscarmellose sodium, and CMC (sodium carboxymethylcellulose). Disintegrants can greatly enhance the performance of dosing formulations for oral solids forms by increasing the rate of release of drugs and improving bioavailability.^{59,60}

4.5. Essential properties of components to develop liquid solids

Liqui-solid techniques are an advanced powder solution used in technology. To ensure that the formulation has the necessary flow and compression properties, mathematical formulae are used to determine the appropriate ratios of actives and excipients^{61,62}. Formulators need to be familiar with the theoretical concepts underlying this technology.

- Liquid drug
- Flowable liquid retention capacity (φ)

$$\text{Flowable liquid } \varphi = \frac{\text{liquid}}{\text{solid}}$$

When the carrier particles are approached with a flowable liquid capacity (φ), the liquid on the inside of the nanoparticles is properly mixed, which keeps the surface dry and results in a powder flow with adequate properties. However, if the φ value exceeds the nanoparticles' visible surface, carriers on the water phase form as the inner half of the particles becomes saturated.⁷⁰ This technique is important to produce liquid drugs, as it ensures that the drug can be effectively contained within the powder material, allowing for proper absorption and administration to the patient. By accurately determining the flowable liquid retention capacity, manufacturers can ensure that the medication is delivered to the patient safely and effectively.^{71,72}

4.5.3. Determining the slide angle (θ)

Determining powders' slide angle (θ) is a widely used method for evaluating their flow properties. The slide angle is the angle of the plane at which a powder starts sliding down due to gravity. The measurement is carried out using an angle of repose apparatus. The apparatus typically consists of a flat plate with a polished surface, a funnel mounted above the plate to deliver the powder onto the plate, and a mechanical device that can gradually lift one end of the plate. A method for determining the slide angle of a powder involves carefully pouring the powder onto one end of a plate and gradually raising the plate until the powder begins to slide. The angle of the plate is then measured, which is considered the slide angle of the powder.⁷³ The slide angle is an important parameter that can be used to predict the flow characteristics of powders and granules. It is closely related to the frictional properties of the powder. Powders with low

- Determining the slide's angle (θ)
- Retention capacity (ψ)
- Liquid load factor (L_f)

4.5.1. Liquid drugs

Liquid drugs refer to medications that are in a liquid form, which may include drug suspensions, lipid-soluble drugs, or crystalloids of drugs that are not soluble in water or non-volatile solvents. These medications may be administered via intramuscular injections or through other routes of administration.^{63,64} The development of liquisolid solutions involves using non-volatile solvents such as polyethylene 200, 400, glycerol, Glycol (polysorbate 80), or polyoxymethylene. These solvents help to dissolve the drug and create a homogenous liquid solution. Liquisolid solutions have been developed to improve the solubility and bioavailability of poorly soluble drugs.^{65,66} Examples of liquid drugs include glycosides, cortisol, 1,2-dehydrohydrocortisone, spironolactone, lisinopril, refusal, chlorpheniramine, water-insoluble minerals, and fatty fish. Case studies have explored the potential use of liquid drugs for various medical conditions.⁶⁷

4.5.2. Flowable liquid retention capacity (φ)

The flowable liquid retention capacity (φ) is a measurement used to determine the amount of liquid that can be contained per unit weight of powder material. This measurement is important in producing solvent combinations that flow, as it ensures that the maximum weight of the liquid can be contained within the powder material. The carrier particle reaches its maximum absorption capacity as the liquid is absorbed.^{68,69} At this point, the flowable liquid capacity (φ) is calculated using the formula:

slide angles flow more easily and are less likely to become compacted or stick together. On the other hand, powders that have a high slide angle typically have poor flow properties and may require additional processing steps, such as milling or granulation, to improve their flowability.⁷⁴

4.5.4. Retention capacity (ψ)

The retention capacity (ψ) of a compressed fluid absorption material refers to the maximum amount of compressed liquid or powder that the material per unit weight can absorb without causing any leakage or compromising the compressive strength of the final product. This is an important parameter in determining the suitability of a material for compressed fluid absorption applications. Various methods can be used to determine a material's retention capacity. One common method involves mixing a known quantity of the compressed liquid or powder with the

solid material and compressing the mixture into tablets. The tablets are then subjected to various tests, such as dissolution studies and compressive strength tests, to evaluate the material's performance.⁷⁵ In the case of liquisolid formulations, the retention capacity refers to the amount of liquid that can be absorbed by the solid carrier material without any leakage or compromising the final product's performance. Liquisolid formulations are a compressed fluid absorption system in which a powdered carrier material absorbs a liquid drug or active ingredient to form a solid dosage.⁷⁶ The retention capacity of a liquisolid formulation is influenced by various factors, such as the properties of the liquid and solid materials, the type and amount of excipients used, and the preparation method. A high retention capacity is desirable for liquisolid formulations as it allows for higher loading of the liquid drug or active ingredient, which can improve the bioavailability and therapeutic efficacy of the final product.⁷⁷

4.5.5. Liquid load factor (Lf)

The liquid load factor (Lf) is also an important parameter in pharmaceutical processes that involve packed beds, such as tablet coating, granulation, and chromatography. In tablet coating, for example, the load factor of liquid determines the amount of coating solution that can be sprayed onto the tablets without over-wetting or under-coating them. In granulation, Lf affects the granules' size, shape, and porosity, as well as their compressibility and flowability. In chromatography, Lf determines the efficiency and selectivity

of the separation process, as well as the pressure drop and flow rate through columns^{78,79}. The selection of an appropriate liquid load factor in pharmaceutical processes depends on several factors, such as the desired product quality, manufacturing efficiency, and regulatory requirements. In tablet coating, it is important to strike a balance between a high enough liquid load factor to ensure uniform and complete coating and avoiding an excessive load factor that can result in over-coating. Over-coating can lead to various issues, such as delayed dissolution, disintegration problems, and poor bioavailability. Such as granulation, the liquid load factor should be carefully optimized to achieve the desired granule properties, such as size, shape, and porosity. Minimizing the use of binder and solvent is crucial to ensure product stability and safety. The liquid load factor selection should consider the trade-off between separation efficiency and pressure drop when chromatography. An optimal liquid load factor can balance these factors and enhance the process's throughput, resolution, and cost-effectiveness.^{80,81} The determination of Lf is typically done using experimental methods, and its selection depends on several factors, such as the desired product quality, manufacturing efficiency, and regulatory requirements. Optimization of Lf can lead to improved process performance, product quality, and cost-effectiveness. The liquid load factor is a metric that quantifies the maximum amount of liquid that a specific carrier material can absorb. It is typically represented as a ratio of the weight of the liquid to the weight of the carrier material.

The liquid load factor (Lf) formula is:

$$\text{Liquid load factor (Lf)} = \frac{\text{Liquid medication (W)}}{\text{Weight of carrier material (Q)}}$$

5. CLASSIFICATION

Classification of liquisolid system is divided into two different parts one is a liquid-solid system, and another is formulation liquisolid techniques. They are classified in Fig. 3.

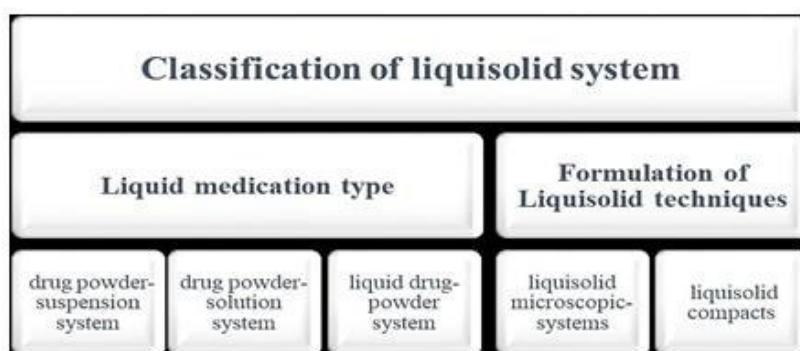


Fig 3: Classification of Liquisolid Systems

Figure 3. The classification of liquisolid systems covers various aspects of these formulations. It includes different types of liquid medications and various techniques for creating liquisolid formulations. These techniques involve a drug powder-suspension system, a drug powder-solution system, and a liquid drug-powder system. Additionally, there are classifications known as liquisolid microscopic systems and liquisolid compacts. These classifications help us understand the different ways liquisolid systems.

5.1. Type of liquid medication

5.1.1. Drug Powder-Suspension System

When a drug is suspended in a powdered form, it can be considered a drug delivery system known as powdered drug suspension. The drug is finely ground and mixed with a powder carrier material, such as lactose or microcrystalline cellulose, to form a homogeneous powder mixture. The mixture is then suspended in a liquid medium, such as water,

to form a suspension.⁸² The suspended particles in the powdered drug suspension are large and settle down over time. To prevent this, suspending agents, such as sodium carboxymethyl cellulose or xanthan gum, are added to the liquid medium to increase viscosity reading increase in

sedimentation time. Other ingredients, such as preservatives, flavorings, and sweeteners, may also be added to better the taste and stability of the suspension.^{83,84} Some examples of drugs that are commonly formulated as powdered drug suspensions are mentioned in Table 1

Table 1 Drug powder suspension systems.

No.	Drug Class	Examples	Uses	References
1	Antibiotics	Amoxicillin, Azithromycin, Cefixime	Treat bacterial infections	85
2	Anti-inflammatory agents	Ibuprofen, Naproxen, Diclofenac	Reduce inflammation and pain	86
3	Antihistamines	Loratadine, Diphenhydramine, Chlorpheniramine	Treat allergic reactions and symptoms	87
4	Antipsychotics	Risperidone, Olanzapine, Quetiapine	Treat schizophrenia and bipolar disorder	88
5	Antidiabetic	Metformin, Glipizide, Pioglitazone	Manage blood sugar levels in diabetes	89
6	Antidepressants	Fluoxetine, Sertraline, Paroxetine	Treat depression, anxiety, and other mood disorders	90

Table 1 Provides examples of drug powder suspension systems. The includes different drug classes such as antibiotics (e.g., Amoxicillin, Azithromycin), anti-inflammatory agents (e.g., Ibuprofen, Naproxen), antihistamines (e.g., Loratadine, Diphenhydramine), antipsychotics (e.g., Risperidone, Olanzapine), antidiabetic drugs (e.g., Metformin, Glipizide), and antidepressants (e.g., Fluoxetine, Sertraline). These medications are used for various purposes, from treating bacterial infections to managing blood sugar levels in diabetes. Liquid medium for drug delivery can depend on various factors, including the specific drug being administered, the target site, the patient's medical history, and other relevant parameters. It is essential to consider these factors carefully to ensure optimal drug delivery and patient safety. For instance, researchers have explored using biodegradable polymers like chitosan and polylactic-co-glycolic acid (PLGA) as carrier materials for drug delivery systems. These materials have been shown to offer several advantages, including sustained drug release, biocompatibility, and low toxicity.^{91,92} The choice of liquid medium can also affect drug delivery systems' performance. Researchers have investigated using various liquid media, including water, ethanol, and oils, to optimize drug delivery. For example, some studies have shown that adding surfactants can enhance drug solubility and increase the bioavailability of drugs in the body.^{93,94} In addition, selecting carrier materials and liquid media for drug delivery systems should consider patient-specific factors such as age, weight, and medical history. For instance, pediatric patients may require different carrier materials and liquid media than adult patients due to differences in drug absorption and metabolism.⁹⁵ Similarly, patients with pre-existing medical conditions may require different drug delivery systems to avoid adverse reactions.

5.1.2. Drug Powder-Solution System

The drug powder solution in the liquisolid system refers to the expansion of the carrier material, a drug-powdered. The carrier material, such as microcrystalline cellulose or lactose, is typically porous with a high surface area. The powdered drug is adsorbed by carrier stuff, and the resulting powder has a high drug content.^{96,97} The liquisolid system in the coating material maintains the integrity of the drug-carrier matrix and prevents the drug from interacting with the environment. The coating material can be hydrophilic, such as hydroxypropyl cellulose or polyethylene glycol, or hydrophobic, such as magnesium stearate or stearic acid.⁹⁸ The methodology of drug powder solution systems involves placing the drug in a liquid solvent to create a homogenous solution. The answer is administered to the patient orally or through injection.^{99,100} To develop an effective drug powder solution system, several factors must be considered, including the drug's solubility, physicochemical characteristics in the selected solvent, or compatibility of the drug with the solvent. These factors' stability impacted and efficacy of the drug delivery system.^{100,101} Developing a drug powder solution system is the use of cosolvents. Cosolvents are mixtures of two or more solvents that can enhance drug solubility and improve drug delivery. Ethanol, PG, and PEG have commonly used cosolvents.¹⁰² Another approach is the use of surfactants. Surfactants are amphiphilic molecules that can reduce the surface tension of a solution, enhance drug solubility, and improve the absorption of drugs in the body. Commonly used surfactants include Tween 80, sodium lauryl sulfate, and polysorbate 80.¹⁰³ several techniques can be employed to enhance the homogeneity of drug powder solution systems, including sonication, magnetic stirring, and vortexing. These techniques can help ensure the drug is uniformly dispersed throughout the solution and enhance drug delivery efficacy.¹⁰⁴ Some examples of drugs commonly formulated as powdered drug solutions are mentioned in Table 2.

Table 2. Drug powder-solution systems.^{105,106}

No.	Drug Class	Examples	Uses
1.	Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)	Ibuprofen, Naproxen	Treatment of pain, fever, and inflammation
2	Antidepressants	Amitriptyline, Imipramine	Treatment of depression, anxiety disorders, and neuropathic pain
3.	Antipsychotics	Haloperidol, Risperidone	Treatment of schizophrenia, bipolar disorder, and severe anxiety

4.	Antibiotics	Amoxicillin, Ciprofloxacin	Treatment of bacterial infections
5.	Antifungals	Fluconazole, Ketoconazole	Treatment of fungal infections

Table no 2 Provides examples of a drug powder solution system of commonly used drugs within each drug class. It is important to note that this is not an exhaustive list, and other drugs are available in each class with different uses and mechanisms of action. It is always recommended to consult a healthcare professional for accurate information and appropriate use of medications.

5.1.3. Liquid drug- Powder system

A liquid drug-powder system is a drug formulation in which a liquid drug is mixed with a powder to create a homogeneous and stable mixture that can be conveniently reconstituted with a liquid for administration. To improve the stability and flowability of the mixture, the liquid drug is typically added to

a powder carrier such as lactose or mannitol. This type of drug formulation is commonly used when a drug is more soluble in a liquid than in a solid form, and it offers a more precise dosing option for drugs with a narrow therapeutic window. The liquid drug-powder system can also enhance the bioavailability of the drug since the liquid form is more easily absorbed by the body.¹⁰⁷ However, this system has some drawbacks. The stability of the mixture can be affected by factors such as humidity and temperature, which can cause the powder to clump or the liquid to evaporate, leading to a loss of potency and reduced efficacy of the drug. Moreover, the mixing process can be time-consuming and require specialized equipment, increasing production costs. Some examples of drugs that are commonly formulated as liquid drug-powder systems are mentioned in Table 3

Table 3. Liquid drug-powder systems.¹⁰⁸⁻¹¹⁰

S.no	Drug Class	Drug Name Example	Uses in Liquisolid Form
1.	Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)	Ibuprofen	Used for pain relief and reducing inflammation
2.	Antihypertensives	Amlodipine	Treatment of high blood pressure
3.	Anticonvulsants	Gabapentin	Treatment of seizures and epilepsy
4.	Antipsychotics	Risperidone	Treatment of psychotic disorders such as schizophrenia
5.	Antihistamines	Loratadine	Treatment of allergies and allergic reactions

Table no 3 Provides examples of drug classes, specific drug examples, and their uses when formulated using the liquisolid technology approach. It is important to note that the use of drugs in liquisolid form should be based on appropriate formulation development and regulatory considerations. Always consult a healthcare professional for accurate information and guidance on drug usage and formulation suitability. Moreover, the liquisolid formulation is a promising approach to improving weekly soluble drugs' bioavailability and dissolution rate. It has the potential to revolutionize drug delivery systems and provide better treatment options for patients.¹¹¹

5.2. Liquisolid formulation techniques

5.2.1. Liquisolid microscopic system

The term "liquisolid microscopic system" describes the microstructure of the liquisolid formulations, where the drug suspension and the solution are absorbed into the porous carrier particles, and the coating ingredient forms a continuous solid layer on the carrier surface¹¹². The

microscopic composition of liquisolid formulations is essential in deciding the drug release rate and bioavailability. The high surface area of the porous carrier particles enhances the drug dissolution rate, while the coating material regulates the drug release by controlling the water penetration into the formulation¹¹³. The liquisolid technique offers several advantages over conventional formulation methods, such as improved drug solubility, dissolution rate, bioavailability, and reduced dose and side effects.¹¹⁴

5.2.2. Liquisolid compacts

Liquisolid compacts a solid dosage form consisting of a drug in a liquid state, typically dissolved or dispersed in a non-volatile liquid, mixed with a powdered carrier material to create a dry powder. The resulting mixture is then compressed into tablets or capsules.^{115,116} Researchers prepared liquisolid compacts of valsartan using MCC (Microcrystalline cellulose) as the carrier material and polyethylene glycol 400 as the non-volatile liquid. The resulting tablets showed significantly improved bioavailability and dissolution rate compared to the pure drug.¹¹⁷

Table 4: Components of Liquisolid Technique

Components	Example
Drug Candidates	Telmisartan, Fenofibrate, Griseofulvin, Celecoxib, Ibuprofen, Carbamazepine, Ketoprofen, Indomethacin, Nifedipine, Tadalafil, Glibenclamide.
Non-Volatile Liquid	PEG(Poly Ethylene Glycol) 200, 300, 400, Propylene Glycol, Glycerine
Carrier Material	MCC (Microcrystalline Cellulose)pH101, 200, ethyl cellulose, methylcellulose, Hydroxy Propyl Methyl Cellulose K4M, K100M, Lactose,

Coating Material	Aerosil200, Cab-O-Sil M5(Silica), Colloidal Silicon Dioxide.
Disintegrant	Croscarmellose Sodium, Cross Polyvinyl Pyrrolidine, Sodium Starch Glycolate, Pregelatinized Starch.
Glidant	Talc
Lubricant	Magnesium Stearate

Table 4 Presents various components used in Liquisolid technology with corresponding examples. These components play specific roles in the formulation of liquisolid systems. It is important to note that this is not an exhaustive list, and some other components and excipients can be utilized in liquisolid formulations. The information provides a general overview and should be validated with appropriate references and formulation guidelines for specific applications.

6. PRE-COMPRESSION OF LIQUISOLID

These Are Granules of Many Types

- Flow behavior
- The angle of Repose
- Volumetric density
- Tapped Density
- Compressibility Index [Carr's Index]
- Hausner's Ratio

6.1. Flow behavior

In pharmaceutical formulation, it is crucial to ensure that the powders used in the dosage forms have suitable flow properties to prevent significant dosage fluctuations. Several factors can influence the flowability of powder, including particle size, shape, density, surface area, and moisture content. Inadequate flow properties can lead to poor content

The angle of repose, the formula for calculating, is

$$\theta = \frac{\text{Height } (h)}{\text{Radius } (r)}$$

6.3. Bulk density

Bulk density describes the packing efficiency of powders and granules. It is expressed as the mass of a material per unit volume. To measure the bulk density of a powder, a standardized amount of the powder is sifted through a #40

Using the following formula to determine the bulk density

$$\text{bulk density} = \frac{\text{weight of powder}}{\text{bulk volume}}$$

The determination to create solid dosage forms and bulk density is crucial. It can affect tablets' and capsules' weight variation, uniformity, and dissolution characteristics. In addition, it can influence the flowability and compressibility of powders and granules, impacting manufacturing processes' efficiency and accuracy.

6.4. Tapped density

The pharmaceutical industry constantly uses tapped density, a physical characteristic of powders and granules, to assess the

uniformity, segregation, and difficulty filling the dosage forms.¹¹⁸ Improving the flow properties of powders is crucial for ensuring the uniform distribution of drugs in the final dosage form. One strategy is using liquisolid systems, which involve converting liquid drugs into free-flowing or dry powders by adsorbing them onto suitable carrier particles. Various techniques can be utilized to evaluate powders' flow properties, such as the angle of repose, Compressibility index, and Hausner's ratio. The angle of repose calculates the angle created by the powder pile while at rest and indicates how easily the powder will flow. Measures of powder compressibility, like the Carr index and Hausner's ratio, can reveal whether or not the powder will clump or cling together.¹¹⁹ The flow properties of powders play an important part in the uniform distribution of drug dosage forms. Liquisolid systems can enhance the flow properties of powders, and evaluating these properties using techniques like the compressibility index, angle of repose, and Hausner's ratio can help ensure suitable flow characteristics.¹²⁰

6.2. Angle of repose

The packing and flowability characteristics of powders and granules are measured using an important measurement in the pharmaceutical industry called the angle of repose. The angle of repose refers to the steepest angle that can be formed between the horizontal plane and the surface of a pile of powder or granules.¹²¹⁻¹²³

[USP] sieve, which helps to achieve a uniform particle size. The powder is then carefully added to a graduated cylinder and leveled without causing any disturbance. The volume of the powder in the cylinder is calculated consequently using on the cylinder, the graduation marker in milliliters (ml); it is known as the bulk volume.^{124,125}

material's compressibility and packing efficiency. It is described as the mass of the material's volume-to-weight ratio following compaction or tapping.¹²⁶ The measurement of tapped density is important in the formulation, such as capsules and tablets, which are solid dose forms. It can impact these products' uniformity, weight variation, and dissolution characteristics. In addition, the flowability and compressibility of powders and granules can be influenced by their tapped density, which can impact the efficiency and accuracy of manufacturing processes.¹²⁷ Then, the following formula is used to get the tapped density.

$$\text{Tapped density} = \frac{\text{Weight of powder}}{\text{Tapped Volume}}$$

The determination of tapped density is typically performed using a tapped density apparatus, which consists of a graduated cylinder, a tapping mechanism, and a timer. Depending on the material being tested, the cylinder is usually tapped for a specified time, such as 100 or 500 taps.

6.5. Compressibility index

The compressibility index calculates the bulk and tapped densities of a powder or granular material. It is used to assess flow properties of powders and granules and is a crucial component for the solid dosage forms and their manufacturing.¹²⁸ The compressibility index is defined as how much of a difference there is between the bulk density and tapped density ratio expressed as a percentage.¹²⁹ The formula used to compute it is as follows:

$$\text{Carr's index} = \frac{\rho_T(\text{Tapped density}) - \rho_B(\text{Bulk density})}{\rho_T(\text{Tapped density})} \times 100$$

The compressibility index measures a powder or granular material's capacity to flow and compress. It is commonly used to assess the quality of powders and granules and can help predict problems such as capping, segregation, and bridging during manufacturing. Generally, a stable flow is indicated by a compressibility index of less than 15% flow properties, while if it is higher than 25%, it is poor flow properties. Values between 15% and 25% indicate moderate flow nature.

6.6. Hausner's ratio

Hausner's ratio provides information about the ability of a powder to be compressed and its potential to exhibit flow problems during manufacturing. A higher ratio indicates lower flowability and increased potential for issues such as segregation and bridging. A lower ratio indicates better flowability and a decreased likelihood of these problems occurring.^{130,131} The following formula is used to determine Hausner's ratio:

$$\text{Hausner's ratio} = \frac{\text{Tapped density}(\rho_T)}{\text{bulk density}(\rho_B)}$$

Good flowability is indicated by Hausner's ratio of less than 1.25, while a ratio of more than 1.25 suggests poor flowability. Values between 1.25 and 1.5 indicate moderate flowability.

7. POST COMPRESSION OF LIQUID COMPART

Tablets are a common solid dosage form frequently employed for drug delivery. Evaluating tablets is important to ensure their uniformity, quality, and efficacy. Various tests evaluate different aspects of tablets, including their physical and chemical properties. The following tests are commonly used to evaluate tablets.

7.1. Weight Variation

The weight variation test is critical to assess tablet weight consistency within a batch. To conduct this examination, a sample of 20 tablets is randomly selected from the batch, and their weights are measured and recorded. The weight on the average and standard deviation is then calculated, and the weight variation of every tablet has been determined. The weight percentage for each tablet should be within the predetermined limits set by the pharmacopeial standards. The US Pharmacopeia (USP) **<905>** specifies that for tablets weighing less than 324 mg, the weight variation should be within $\pm 5\%$ of the average weight, and for tablets weighing more than 324 mg, it should be within $\pm 1.5\%$.¹³²

7.2. Hardness

Tablet hardness is crucial in assessing a tablet's capability to endure mechanical stress during transportation, packaging, and handling. Determining tablet hardness involves utilizing a tablet hardness tester to measure the force needed to break a tablet, followed by calculating the tablet hardness based on

the recorded force measurement. The acceptable range for tablet hardness is determined based on the type of tablet and its intended use, as per the USP **<1217>** guidelines, which suggest a hardness range of 4-10 kg/cm² for uncoated tablets and 6-20 kg/cm² for coated tablets. It also highlights the inverse association between a tablet's mechanical strength and fragility.¹³³

7.3. Friability

Their friability measures the capacity of tablets to endure mechanical stress during handling and packing. This test selects six tablets from the batch and is weighted precisely. The tablets are then tested for friability, such as the Roche friability, and subjected to 100 revolutions at 25 rpm. The weight loss due to mechanical stress is calculated, and the weight loss percentage is determined. The tablet's friability should be acceptable range as per the pharmacopeial standards. According to the USP **<1216>**, the friability of tablets should be less than 1% for uncoated tablets and less than 0.8% for coated tablets¹³⁴

7.4. In vitro Dissolution Studies

Dissolution testing in evaluating the range release and rate of drug tablets. The testing is performed using a dissolution apparatus, such as the USP apparatus, in which the tablets are placed in a dissolution medium, and the drug release is monitored over time. The pharmacopeial standards mention the specifications that the tablet profile of the dissolution should meet. The specific monograph for the tablet

formulation provides information on the drug and dissolution medium used in the test.¹³⁵

7.5. Thickness

Tablet thickness is an important parameter determining tablets' ease of swallowing and packaging. In this test, the thickness of a sample of tablets is measured using vernier calipers. The thickness of the tablets should be within the acceptable range per the pharmacopeial standards. The tablet thickness should be between 2 and 4 mm for uncoated tablets and 2.5 and 5 mm for coated tablets.¹³⁶

7.6. Controlled drug delivery using a liquisolid system

Sustained release formulations are a great option for effective, safe, and convenient therapy. Controlling the solubility of a drug is one of the most effective ways to create a continuous-release formulation that is stable over time. There are various techniques and methods available to develop sustained-release formulations. One of the techniques to achieve sustained release is the liquid-solid method, where a liquid carrier is used to dissolve the drug and then adsorbed onto a carrier material, followed by drying to produce a solid form. Optimizing this process to account for drug depletion and dissolving rates is important. An alternative approach to creating controlled-release formulations in liquisolid systems is to use hydrophobic carriers, such as PEG (Polyethylene glycol) RL and RS, instead of hydrophilic ones. This method is believed to improve the drug particle encapsulation by hydrophobic polymers, leading to the formation of a low-porous matrix, a fine network, and high curvature at temperatures above the glass transition temperature, thus prolonging the release of the drug. Compared to traditional immediate-release formulations, sustained-release formulations provide a range of benefits, including improved efficacy, safety, and patient compliance.

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The development of sustained-release formulations can be achieved through various techniques and methods, which should be chosen based on the specific characteristics of the drug and the desired release profile.¹³⁷⁻¹³⁹

8. CONCLUSION

A constant search for ways to improve the solubility and dissolution of drugs that are not easily soluble in water led to the developing of one promising technology with a liquisolid approach. This method is effective in manufacturing sustained-release, quick-release formulations or with an increased dissolution rate for poorly soluble drugs. It has also been found to reduce the impact of pH fluctuations on drug release and enhance drug stability in solid dosage forms. Overall, the liquisolid approach shows great potential for the solubility and dissolution profile of various drug candidates with compromised bioavailability. Moreover, various other excipients could be explored for their potential in developing liquisolid formulations with more effective outcomes; future research will continue to explore its various applications in pharmaceuticals.

9. AUTHORS CONTRIBUTION STATEMENT

Anurag Kumar Yadav The author has created initial draft of the manuscript, designed the table and figures, explained the novel technique of solubility enhancement developing liquisolid, and covered the potential ingredients. Dr. Aditya Shiven Conceptualizing discussed the methodology, designed the manuscript, and significantly contributed to the editing process discussed and finalized manuscript formats.

10. CONFLICT OF INTEREST

Conflict of interest declared none.

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