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Review Article

Overview On The Novel Medication Of Liquisolid Technology For Improving Solubility And Bioavailability

Desai Avni P.[1], Krishna P. Vairagi[2], Dhruvi B. Parmar[3], Heli H. Desai[4]

[1]*Assistant Professor, Department of Pharmaceutics, Smt. B.N.B Swaminarayan Pharmacy, Salvav-Vapi*
[2]*Assistant Professor, Department of Pharmaceutical Quality Assurance, Smt. B.N.B Swaminarayan Pharmacy, Salvav-Vapi*
[3]*Assistant Professor, Department of Pharmaceutical Quality Assurance, Smt. B.N.B Swaminarayan Pharmacy, Salvav-Vapi*
[4]*Assistant Professor, Department of Pharmaceutical Quality Assurance, Smt. B.N.B Swaminarayan Pharmacy, Salvav-Vapi*

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ABSTRACT

The majority of the novel medication candidates are lipophilic and water-insoluble. The pharmaceutical industry has a tremendous difficulty in improving the solubility and bioavailability of these medications. The Liquisolid technique, which involves converting a liquid medicine into a seemingly dry, non-adherent, free-flowing, and compressible powder, is an innovative and sophisticated method for dealing with the problem. The purpose of this article is to provide an overview of the Liquisolid technology as well as a summary of its advancement in pharmaceutics. The key advantages of this technology are its low cost, easy processing, and large industrial production capacity. This approach is a relatively recent technique for efficiently retarding drug release, in addition to improving the dissolving rate of weakly water-soluble medicines. In addition, the Liquisolid approach has been examined as a tool for reducing the impact of pH variations on drug release and as a possible alternative to traditional coating for improving drug photostability in solid dosage forms. Overall, the Liquisolid approach is a new and promising tool for improving drug dissolving and extending drug release, and its pharmaceutics applications are currently being explored.

INTRODUCTION

The molecular weight and Lipophilicity of pharmaceuticals rose as a result of the use of combinatorial science and high data screening for the testing of novel compound substances, reducing the solubility of new chemical entities in water. Actives that are very permeable and

***Corresponding Author:** Avni Desai
Address: *Assistant Professor, Department of Pharmaceutics, Smt. B.N.B Swaminarayan Pharmacy, Salvav-Vapi*
Email ✉: avnidesai1308@gmail.com

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ineffectively soluble pharmaceutical ingredients (BCS Class II medicines) are a novel type of medication. Poor water quality is the sole reason of their low bioavailability. Low medicine absorption due to dissolvability.

New advancements that increase the solubility release of a medicine are sought in this manner. Dissolution augmentation of poorly soluble pharmaceuticals can be achieved by increasing the drug's solubility, increasing the drug's surface area, or planning the drug in its dissolved state. Over 40% of new pharmaceutical candidates are ineffectively water-dissolvable, indicating a significant issue in drug formulation. (3)

Various methodologies for improving the dissolution of hydrophobic drugs have been developed, including polymorphic forms or water-soluble salts, solubilisation, solvency, complexation, and micro encapsulation, pro-drugs, particle size reduction, and incorporation of liquid drugs or solution of drugs into soft gelatin capsules or extraordinarily fixed hard-shell capsules; and development of self-emulsifying drug delivery systems have been presented. (1)

The above-mentioned strategies have certain practical constraints. Salt production may enhance hygroscopicity, causing stability issues. The palatability of salts of strong bases and acids must also be considered. When a medicine that has been dissolved with co-solvents is diluted, it may precipitate. The use of co-solvents and surface-active agents to solubilize drugs in aqueous media or organic solvents results in liquid formulations that are often unsuitable for patient acceptance and commercialization.

The resulting tiny particles may not provide the predicted faster breakdown and absorption as a result of particle size reduction. This is mostly due to the possibility of fine particle collection and agglomeration as a result of their increased surface liveliness and, as a result, more grounded vanderwaal's attraction between nonpolar molecules. (2)

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If the complexing specialist has a large molecular size, increase the dosage form size because of complexation. There is a chance of fatality if the proportion of medication and complexing ingredient increases. The release of a medicine from a complexing substance is also a problem. If the surfactant concentration is higher, it may cause palatability concerns and negative effects due to micellar solubilization. There is a chance of interaction between the preservative and the surface-active agent; solid dispersion has shown promise in improving wettability, solubility, and the rate of drug dissolution, and hence its bioavailability. (1)

- **Liquisolid method is a concept**.

A liquid may be turned into a dry, non-adherent, free-flowing, and readily compressible powder using the Liquisolid method, as depicted by Spireas15, by simple physical mixing with specified excipients referred to as the carrier and coating material. The liquid component is a liquid drug, a drug suspension, or a drug solution in a non-volatile co-solvent.

Liquid vehicles should be inert, ideally water-miscible organic solvent systems with high boiling points, such as liquid polyethylene glycols, glycerine, and propylene glycol. When the liquid formulation saturates the carrier, a liquid layer forms on the molecular surface, which is immediately absorbed by the thin coating particles. As a result, a powder that is free-flowing,

compressible, and superficially dry is obtained. (1,4)

MCC is commonly utilised as the carrier material, with colloidal silica as the coating material.

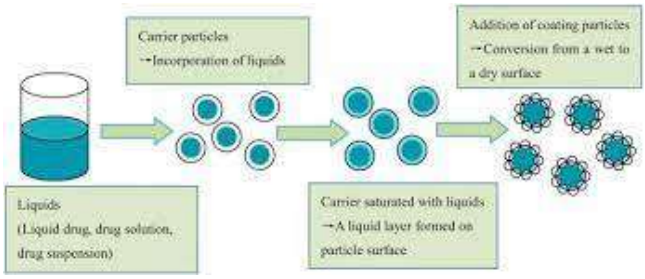

Figure 1: Liquisolid systems are depicted as a diagram.

To make Liquisolid compacts, a few additional compounds, such as disintegrates and lubricants (rapid release) or matrix shaping additives (sustained release), might be added to the Liquisolid system.

- **Definitions:**

Liquid formulations are made up of liquid lipophilic medicines, suspensions, or solutions of water-insoluble solid pharmaceuticals in non-volatile solvent systems.

"Liquisolid systems" refers to powdered versions of liquid pharmaceuticals created by mixing liquid lipophilic drugs, drug suspensions, or solutions of water - insoluble solid compounds in appropriate non-volatile solvent systems into dry, non-adherent, free-flowing, and easily compressible powder admixtures.

Carrier material refers to porous materials with good absorption properties, such as amorphous cellulose and microcrystalline cellulose that absorb liquid.

Coating material refers to a substance with extremely adsorptive and small particles, such as various forms of silica that is used to coat wet carrier particles and demonstrate a dry powder by adsorbing any of the abundant liquids.

General preparation procedures of Liquisolid system

To thoroughly solubilize or uniformly blend, calculated quantities of medication and liquid carrier are combined, then heated or sonicated. The liquid drug is then mixed with the other excipients in the Liquisolid formulation in three phases. To allow a homogeneous distribution of liquid medicine throughout the carrier powder, the resultant liquid medication is poured onto a determined quantity of carrier material and mixed at an approximate mixing rate of one rotation per second for one minute. The coating substance is next applied in a calculated amount and homogeneously blended.

The resulting powder combination is distributed as a homogeneous layer on the surface of a mortar and left to stand for 5 minutes to promote complete absorption of the drug medicine into the internal framework of the carrier and coating materials in the second step. In the third stage, disintegrant is added to the aforesaid powder combination and properly mixed, yielding a final Liquisolid system. The Liquisolid system that has been developed can be squeezed or encapsulated further. It should be noted that the mixing speed, mixing duration, and standing time may all be adjusted to suit the circumstances. (5)

- **In pharmaceutics, the Liquisolid method is used:**

The Liquisolid approach as a means of improving drug solubility.

According to the literature, the Liquisolid approach has been widely utilised to increase the dissolving rate of low-dose insoluble pharmaceuticals such prednisolone, famotidine, valsartan, ketoprofen, raloxifene hydrochloride, clonazepam, and clofibrate, among others.

The practicality of the Liquisolid approach has also been considered in the situation of high dosage water insoluble medicines (such as carbamazepine). Javadzadeh et al. suggested that by adding some additives (such as PVP, HPMC, and polyethylene glycol 35000), it is possible to

use the Liquisolid technique to incorporate high dose water-insoluble drugs into Liquisolid systems. These additives have the ability to increase the liquid absorption capacity of carrier and coating materials. Hentzschel et al. have demonstrated another method for loading high doses of weakly water-soluble medicines into Liquisolid systems, namely the use of contemporary carriers (such as Ensiling®) with greater SSA values and absorption capacities. (3,4)

Pezzini et al. recently looked into the possibilities of employing this technology to make Liquisolid pellets for felodipine dissolving improvement. It was discovered that a Liquisolid microenvironment with soft structures and high porosity was produced, which encouraged felodipine Liquisolid pellet disintegration and dissolution. The findings showed that using Liquisolid pellets as a new drug delivery technology to increase the dissolution rate of poorly water-soluble medicines is viable.

Khan et al. conducted a comparative research to confirm the viability of the Liquisolid approach, in which the Liquisolid technique was used to increase the dissolving rate of hydrochlorothiazide in contrast to the solid dispersion technique. The results indicated that Liquisolid systems raised the medication dissolving rate to 95%, whereas solid dispersions only increased to 88 percent. As a result, the Liquisolid approach was shown to be more successful than solid dispersion in terms of increasing the rate and amount of drug release.

Several researches have also looked at the in vivo characteristics of Liquisolid pills. Khaled et al., for example, used a two-way crossover strategy to assess the in vivo performance of hydrochlorothiazide Liquisolid pills in six male Beagle dogs. (3,5)

The bioavailability of hydrochlorothiazide Liquisolid tablets was found to be 15% higher than that of the commercial oral dose form. Badawy et al. recently conducted another trial in which they evaluated mosapride citrate Liquisolid tablets in six healthy male volunteers aged twenty to forty years. The trial employed a randomised, single-dose, two-way crossover open-label design. When compared to commercial alternatives, the authors found that mosapride citrate Liquisolid tablets increased oral bioavailability and had considerably enhanced pharmacokinetic characteristics (i.e., Cmax, Tmax, and AUC (0–12)).

Higher drug surface area, increased drug solubility, and increased wetting qualities are three plausible methods of dissolution enhancement for Liquisolid systems that have been postulated in the literature. Despite the fact that the medicine is in a solid dose form, it is either solubilized or disseminated. As a result, the amount of drug surface area accessible for disintegration is significantly enhanced. In addition to the previously mentioned process, medication solubility in the aqueous diffusion layer might be improved. It is acknowledged that the Liquisolid system's very small volume of liquid vehicle may be insufficient to boost total medication solubility in the dissolving medium.

However, in the microenvironment of the diffusion layer between the individual Liquisolid primary particle and the dissolving medium, the liquid vehicle may function as a co-solvent and diffuse out of the primary particle with the drug, which may be sufficient to boost drug solubility. Furthermore, the interfacial tension between the tablet surface and the dissolving media can be lowered due to the surface activity of liquid carriers, resulting in better wettability of the hydrophobic medication. (3)

Using the Liquisolid approach, we have increased the solubility of tadalafil, a weakly water-soluble medication. In the meanwhile, the mechanism of increased dissolution was studied. The findings revealed that the key reasons for tadalafil's increased dissolving rate were a reduction in

particle size and crystallinity, as well as an increase in wettability.

- **Application of Liquisolid:**
  - Liquisolid compositions provide rapid release rates.
  - These can be used for both solid and liquid lipophilic medicines that are insoluble in water.
  - The adoption of this approach has resulted in the sustained release of water-soluble medicines such as propranolol hydrochloride.
  - Enhancement of solubility and dissolution.
  - Controlled-release tablet development.
  - Probiotics application.
- **Advantages:**
  - Liquisolid systems may be used to create a large variety of BCS class II pharmaceuticals with somewhat or very little water solubility, as well as virtually insoluble solid and liquid medications with good permeability.
  - It is possible to improve the bioavailability of a water-insoluble medication taken by mouth.
  - This concept guides or governs the process of drug distribution from Liquisolid systems of powdered drug solutions, and it is principally responsible for the formulations' improved dissolving properties.
  - In comparison to soft gelatine capsules, the production budget for this technology is modest.
  - The drug is prepared in encapsulated dosage form or tablet dosage form and is kept in the solubilized liquid state, which confers improved drug wetting properties thereby improving drug dissolution characteristics.
  - The dissolving media is exposed to a larger surface area of the drug particle.
  - The Liquisolid technology can be used to create IR (immediate release) or SR (sustained release) dosage forms.
- **Disadvantage:**
  - The formulation of high-dose lipophilic medicines in Liquisolid tablets is one of the technique's limitations.
  - High amounts of carrier and coating ingredients should be incorporated in Liquisolid powder formulations to provide appropriate flow ability and compatibility. This push to make tablets heavier than one gram, which makes them difficult to swallow. As a result, converting a high dosage to a Liquisolid tablet with a tablet weight of less than 50mg using the traditional tablet method is challenging. When there are minimal quantities of hydrophilic carrier present and the coating material is not considerable, the dissolution properties improve.
  - Because liquid medication may be pushed out of the Liquisolid tablet during compression, acceptable compression characteristics may not be attained, resulting in tablets of unacceptable hardness.
  - It may not be possible to use this technology on an industrial scale and overcome the challenges of combining tiny volumes of viscous liquid solutions onto huge amounts of carrier material.

CONCLUSION

Pharmaceutical experts are still concerned with improving the solubility and dissolution of poorly water-soluble medicines. According to an examination of vast literature, the development of the Liquisolid technology has accelerated dramatically in recent years. The Liquisolid approach is not only a valuable tool for improving

the dissolving rate of poorly water-soluble pharmaceuticals, but it's also a unique and effective way to make sustained release tablets with a zero-order release pattern.

Furthermore, the approach has shown promise in minimising the impact of pH on drug release and enhancing drug photostability in solid dosage forms. In the future, more pharmaceutics uses of this technology will be investigated. More research into the creation of superior solvents, as well as contemporary carrier and coating materials for loading high-dose pharmaceuticals, is ongoing. Much of today's research is still focused on Liquisolid system formulation development and in vitro drug release profile evaluation. Future work on loading high-dose water-insoluble pharmaceuticals and in vivo assessment of Liquisolid systems should be investigated and reinforced.

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