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REVIEW ON LIQUISOLID COMPACTS

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ABSTRACT:

The "Liquid-solid" strategy is a cutting-edge and effective addition to such objectives for boosting solubility and dissolving, and so increasing bioavailability. This tactic can improve the rate of solubility and bioavailability of BCS class-II medications. Approximately 40–50% of drugs available are not soluble in water. Since liquid solid compact technology is the best alternative, industry must overcome a challenge by making unit dose forms more soluble. The Liquisolid system combines the Orodispersible and Liquisoild methodologies.

Utilising Liquisolid compact technology for oral drug delivery is an innovative strategy. The first to discuss liquidsolid compact technology was "Spireas et al" in 1998.

It is possible to transform acceptable nonvolatile liquid carriers, such as solutions or suspensions of water-insoluble medications, into flowable and compressible powders using the novel formulation process of liqui-solid compacts. Improving the oral bioavailability of poorly water-soluble drugs is one of the trickiest aspects of drug research. Using a more modern technique called as "powdered solution technology" or "Liquisolid technology," water-insoluble medications have been transformed into rapid-release solid dose forms.The industry has a challenging obstacle in the development of the ideal solid dosage form unit: drug solubility. In order to create powders that flow and compress properly, the procedure entails dissolving the insoluble drug in a nonvolatile solvent and mixing drug-loaded solutions with the right carrier and coating materials.

KEYWORDS*: liquid-solid systems, liquid load factor (Lo), liquisolid compacts, compressible liqui-solid system, appropriate quantities of carrier (Qo).*

INTRODUCTION : A key consideration in pharmaceutical formulation design is drug solubility, which has an impact on oral bioavailability.[1] A Liquisolid system is a powdered version of a liquid medication. It is created by mixing a liquid lipophilic substance, or a solution or suspension of a substance that is insoluble in water, in a non-volatile solvent, into a powder that is dry, non-adherent, freely flowing, and simple to compress.[8] The dissolution rate is the rate-limiting element in medicine absorption for class II (low solubility and high permeability) and class IV (low solubility and low permeability) medications, according to the Biopharmaceutics Classification System.[10] Dissolution is a crucial component of drug absorption, especially when the drug is either poorly or completely soluble in water. In many pharmaceutical formulations, the rate-limiting phase is dissolution.[2] The introduction of formulation techniques to enhance the dissolution of poorly soluble chemicals is ongoing. Bioavailability of chemicals that are poorly absorbed. Water-soluble medications have a restricted solubility and rate of dissolution. In order to increase the pace of disintegration, numerous investigations have been carried out.By reducing particle size, creating nanoparticles, and using other methods, microparticles, drugs can be made smaller.[7] Liquisolid compacts are powdered variations of fluid medicines, which are defined as fluid medications, arrangements, and suspensions of potent water-insoluble pharmaceuticals administered through fluid vehicles, which are unpredictable dissolvable frameworks. Using the liquisolid method, water-insoluble solid medications were transformed into non-volatile liquid carriers and powders suitable for

tableting or encapsulation.[14]

Liquisolid tablets are a result of "powdered solution technology," which can be used to create "liquid medication." "Liquid medicines" are solid pharmaceuticals that have been dissolved in suitable non-volatile liquid carriers. When the carrier's moisture content rises, the flowability of the powder decreases. A coating substance must be applied to the surface in order to maintain the powder's flowability. [7] Poorly soluble medications can release more readily when their surface area, solubility, or manufacture in a dissolved state are increased. Liquisolid tablets are the most innovative and promising of the various unique ways for promoting dissolving.[1] Mathematical model expressions are used to derive powder characteristics as well as the underlying ideas and mechanisms of pulverised solutions.[2] Micronization, lyohilization, solid dispersion, and other techniques have all been developed in the past few decades to improve the solubility and dissolution of poorly soluble compounds, with varied degrees of success.[15]

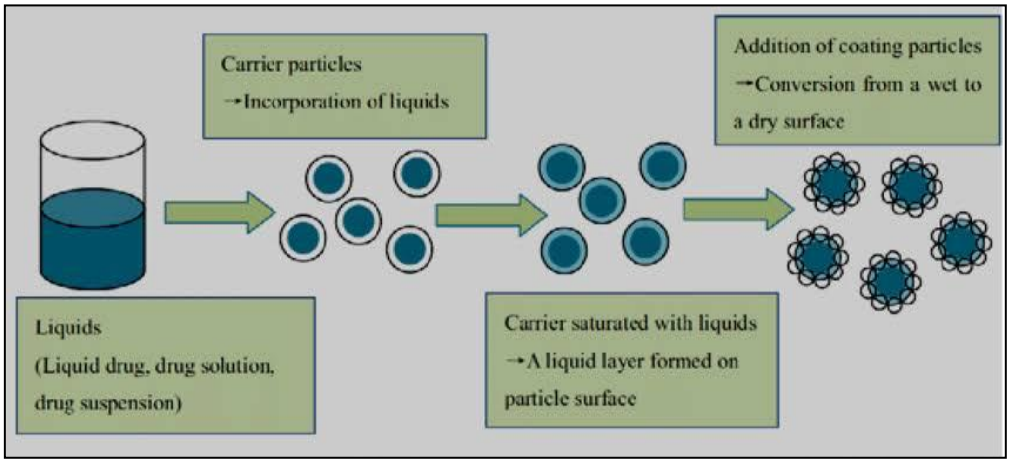

Fig:- Schematic representation of liquisolid systems.[10]

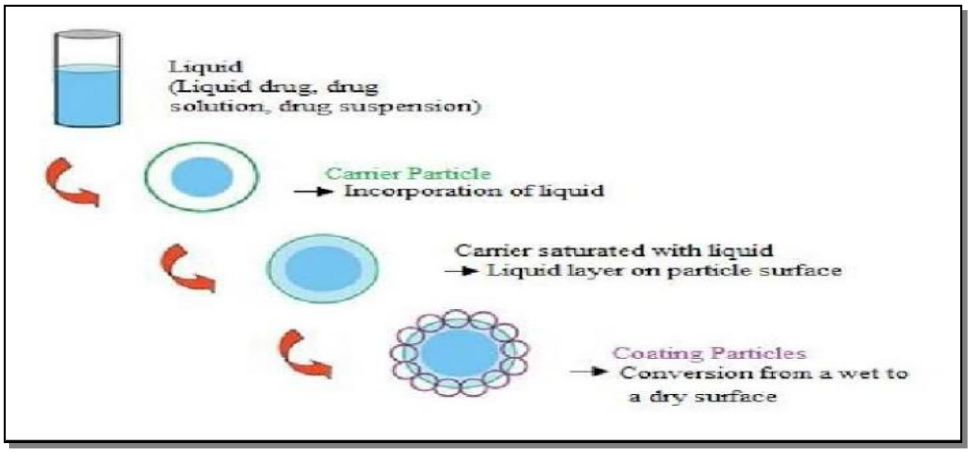

Fig :- Theoretical Concept of Liquisolid System [14]

A LIQUISOLID SYSTEM IS REQUIRED:

1)Liquid medications that are poorly soluble, insoluble, or lipophilic.
2)Powder admixtures with a low flowability.
3)To make direct compression easier.
4)To make tablet production more efficient.[10]

Historical development:

Liquisolid compacts are a direct descendant of "powdered solutions," an earlier method that included predominantly adsorbing a medicine solution in a nonvolatile solvent onto silicas with large specific surfaces to produce a dry-appearing, nonadherent powder.Additionally, the term "liquid medication" includes drug suspensions, emulsions, and liquid oily pharmaceuticals in

addition to powdered drug solutions. As opposed to "powdered solutions," the term "liquisolid compacts" is more general and can be used to describe four alternative formulation systems:
1) Powdered drug solutions

2. Powdered drug suspensions

3. Powdered drug emulsions

4. Powdered liquid drugs

Liquid pharmaceuticals (oily liquid pharmaceuticals and solutions, suspensions, or emulsions of water-insoluble solid pharmaceuticals delivered in nonvolatile liquid vehicles) can be converted into tabletable or encapsulable powders using the novel "liquisolid" technique.[7]

Content:-

A powder can only hold a little volume of liquid while yet maintaining good flow and compression characteristics. Spireas developed a mathematical method for liqui-solid system formulation in order to determine the necessary quantities of powder excipients and coating components.This method is based on the liquid retention potential for flowable (-value) and compressible (-number) media, which introduces constants for each powder/liquid mixture. The powder's -value indicates how much non-volatile liquid can be stored in its bulk (w/w) while still maintaining appropriate flowability.To assess the flow capacities, either the particle flow or the angle of repose may be used. The greatest quantity of liquid that a powder can store inside its bulk [w/w] while maintaining enough compact ability is known as the powder's "-number," which produces compacts that are sufficiently rigid and don't leak liquid during compression.[2] An adequate flowing and compressible liquid-solid system can only be produced if a maximum liquid load on the carrier material is not exceeded, dependent on the excipient ratio (R) of the powder substrate. The liquid load factor Lf [w/w] is the weight ratio of the liquid formulation (W) and the carrier material (Q) in the system.
W/Q = Lf. (1)
The ratio of the carrier's weights is denoted by the letter 'R.'
(Q) In addition, there is a coating (q) material in the formulation:
Q/q = R. (2)
The liquid load factor that assures that the flow ability is appropriate.
Lf =+ can be used to calculate
Φ+ φ. (1/R) = Lf (3)
Where Φ and φ are the Φ-values of the carrier and coating material, respectively.Similarly, the liquid load factor is important for producing liquid-solid systems with good compactability.
(ΨLf) can be determined by:
Ψ + ψ.(1/R =Ψ Lf (4)
Where Ψ and ψ are the Ψ-numbers of the carrier and coating material's -numbers, respectively.
Therefore, the optimal liquid load factor (Lo) needed to produce compressible and flowable liquid-solid systems is equal to the smaller of LforLf or LforLf. The appropriate amounts of carrier (Qo) and coating (qo) material necessary to convert a specific amount of liquid formulation (W) into a flowable and compressible liqui-solid system can then be estimated after the determination of the optimal liquid load factor:
W/Lo=Q0 (5) and
Q0/R=q0 (6)
By generating liquisolid compacts with appropriate flow and compaction properties, the validity and applicability of the above described principles have been evaluated and verified.[1]

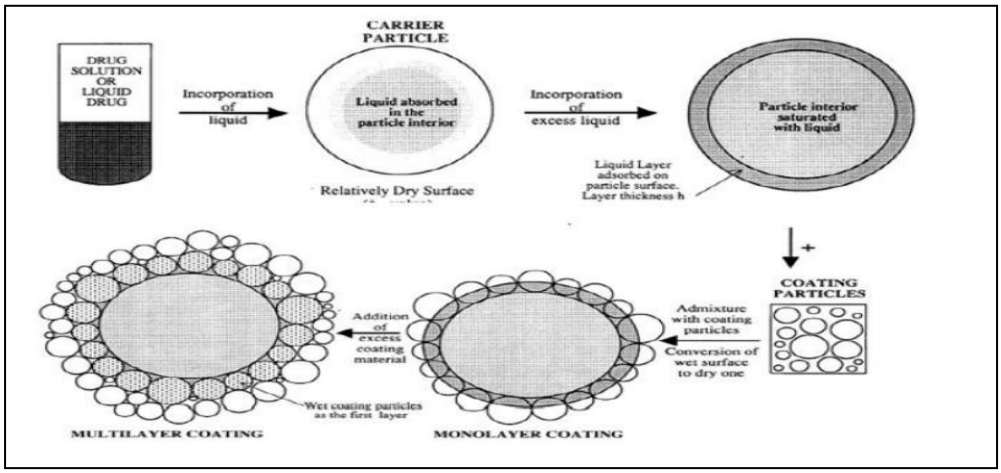

Fig :- Concept of liquisolid compacts .[9]

Advantages:

- A large number of biopharmaceutical classes II and IV exist.
- It is possible to improve the bioavailability of an orally delivered water insoluble medication.
- This liquisolid device is designed to work with powdered liquid pharmaceuticals.
- Flowability and compressibility are excellent.
- The release of a drug can be manipulated by utilising the right formulation elements.
- Release rates that are quick.
- Used for solid medicines that are insoluble in water or liquid lipophilic medicines.
- Improvements in solubility and dissolution.
- Enhancement of bioavailability.
- It's used in drug delivery systems that are controlled.
- It is a feasible method for drugs with a high penetrability and a water solvent that is ineffective.[14 ,10]

Disadvantages:

- High-dose oleophilic drug formulation One of the limitations of this technology is the liquid-solid tablet.
- The method works well for low-dose water-insoluble medications, but it has a major drawback when it comes to high-dose water-insoluble medications in liquisolid systems.
- To construct liquid solid systems, a high solubility of the medication in the liquid vehicle is necessary.[2, 3]

CLASSIFICATION OF LIQUISOLID SYSTEMS:

A)Liquisolid systems can be divided into three categories based on the type of liquid medicines they contain:
1)Powdered drug solutions
2) Powdered drug suspensions
3) Powdered liquid drugs [6]

B) Depending on the method of formulation:
1) Liquisolid compacts.
2) Liquisolid Microsystems.

MATERIALS AND METHODS:

Method of preparation:

The non-volatile solvent is heated after precise amounts of the medication have been introduced to aid in the drug's dissolution. This liquid medicinal solution is mixed with the carrier and coating components before being thoroughly combined. Simply adding and mixing coating material produces a wet slurry that is turned into a dry, non-adherent, freely flowing, and easily compressible powder. Excipients with small, highly adsorptive particles are best for this phase. Liquisolid compacts are made by adding various adjuvants, such as lubricants and super-disintegrants, to the final liquisolid system before compression or encapsulation. According to Spireas et al., the mixing procedure is divided into three parts.

To disperse the drug throughout the liquid equally, the system is mixed for about a minute at a speed of one revolution per second.
After being evenly distributed on the motor surface, the medicine in this admixture is allowed to soak into the powder particle for five minutes.
After scraping the powder away, the process is repeated for a further 30 seconds with the extra excipients. This is the liquisolid tablet's final formulation..[13,14]

Componants of liquisolid compact:

1. Non-volatile solvent
2. Disintegrant
3. Carrier material
4. Coating Materials

Non-volatile solvent:
It should be inert, have a high boiling point, be water soluble, not very viscous, and be able to solubilize the medication. In the liquisolid formulation, the nonvolatile solvent acts as a binding agent.
Propylene glycol, liquid synthetic resin glycols, polysorbates, glycerin, N, N-dimethylacetamide, fixed oils, and other similar substances are ideal for use as vehicles.e.g., PEG 200 and 400, glycerin, polysorbate 80 and propylene glycol, Tween-80.[2,16]

Disintegrant:
The most often used disintegrant is starch glycolate (atomic number 11). Superdisintigrants increase the water solubility, wetability, and rate of drug release of liquisolid granules.Disintegrants like crospovidone and sodium starch glycolate are frequently used.for instance, sodium cross-carmellose, cross-povidone, and SSG.[1,2]

Carrier material:-

To help with liquid absorption, the carrier material should be a porous substance with sufficient absorption properties. Raising the carrier's moisture content decreases the powder's ability to flow since the carrier and coating materials can only hold so much liquid before losing their ability to flow and compress.
MCC grade, granular amorphous cellulose, starch, and lactose are a few examples.[1,10]

Coating Materials:
Small, highly adsorptive particles in the coating material should aid to cover the wet carrier particles and create an appearance of dry powder by adsorbing any excess moisture. You'll need a coating substance to protect the surface and keep the powder moving.
silicas (Cab-O-Sil), aerosil, etc. .[2,10]

Some medications that can be used in liquisolid systems are listed below.[1]
1. Chlorpheniramine
2. Digoxin
3. Nifedipine
4. Clofibrate
5.Carbamazepine
6. Hydrochlorothiazide
7.Methyclothiazide
8. Hydrocortisone

9. Indomethacin
10. Ibuprofen

Evaluation of liquisolid compact:-

1) Precompression Studies:-
   - Angle of Repose
   - Compressibility Index
   - Hausner'sRatio

2) Post Compression Evaluation:-
   - Thickness
   - Weight variation
   - Hardness
   - Friability
   - Disintegration

1) Precompression Studies:-

1. **Angle of Repose**:-

This is the most extreme angle that a pile of powder can make with the horizontal plane. A funnel was used to allow 10 gramme of powder to pour from a height of 4 cm above the base. The height of the pile and the diameter of the base were measured, and the angle of repose was calculated using the formula.

$\tan \theta = h/r$

$\theta = \tan^{-1} h/r$

Where θ is the angle of repose, h is the height of pile, and r is the radius of the powder pile's base.[7]

2. **Compressibility Index:-**

The compressibility index of a powder blend is mostly determined using Carr's compressibility index methods. Carr's index is calculated using the formula below.

Carr's index (%) = [(Tapped density − Bulk density) × 100] /Tapped density

Powders with a compressibility index of less than 15% have acceptable flow characteristics, while powders with a compressibility index of more than 25% have poor flow characteristics.[5,16]

3**. Hausner'sRatio**:-

The Hausner's ratio is a key factor in determining the flow properties of powders and granules. The following formula can be used to compute this:

Hausner's ratio = Tapped density/Bulk density.

A number of less than 1.25 suggests good flow behaviour, while values more than 1.5 indicate poor flowability. Because Hausner's ratio varies depending on the method used to calculate it, it is not considered an essential metric in flow behaviour.[5,7]

2) Post Compression Evaluation:-

1. **Thickness**:-

A digital micrometre was used to measure the thickness of liquid-solid tablets. The results were averaged from ten individual tablets from each batch.[1]

2. **Weight variation**:-

From each batch, twenty tablets were chosen at random and weighed separately. Three batches had their average weight and standard deviation calculated. If no more than two of the individual tablet weights differ from the average weight by more than the permissible percentage deviation and none by more than twice the percentage stated, it passes the weight variation test. An electronic weighing balance was used to calculate it.Only two of the individual weights differ more than 5% from the average weight.[1,16]

3. **Hardness**:-

Tablets are strong enough to withstand typical handling and breakdown properly after swallowing. It is used to determine the mechanical strength of an object. A Monsanto hardness tester was used to assess the hardness of the liquisolid compacts. It is measured in kilogrammes per square metre.[16]

4. **Friability:-**

The tablets' friability was tested using the Roche friabilator.
After that, the percent friability was computed using the following formula:

% friability = Initial Weight – Final Weight / Initial Weight × 100

The Roche friabilizer was filled with 20 tablets, which were weighed and spun at 25 rpm for 4 minutes. The tablets were taken away and weighed once more after revolutions.[13,16]

5. **Disintegration**:-

Six pills from each batch were chosen at random and placed in USP disintegration device baskets. After running the apparatus for 10 minutes and removing the basket from the fluid, check to see if all of the tablets have crumbled.[1]

CONCLUSION:

The liquisolid technique is one of the most promising ways for improving water solubility and medication release. Liquisolid technique uses a liquid portion as a suspension or solution of poorly soluble pharmaceuticals in a suitable nonvolatile liquid vehicle, which is subsequently transformed into easily smooth and compactable powders through simple physical blending with specific chemicals such as carrier and coating agent. This method has been proven to be extremely promising in terms of addressing medication solubility and dissolving issues, particularly in BCS class II and IV medicines with low bioavailability. Due to the good flow and compaction qualities of liquisolid formulations, the liquisolid method is a promising technology due to its simple manufacturing process, low production costs, and industrial manufacturing potential.

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