EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 8
Issue: 6
256-261
Year: 2021

A REVIEW: LIQUISOLID TECHNIQUE

Roshani I. Sheikh*[1], Dr. Shrikant D. Pande[2], Pawan B. Tripathi[3], Jaya P. Madage[4], Minal S. Taywade[5] and Vivek S. Harbade[6]

[1,2,3,4,5,6]Department of Pharmaceutics, Vidyabharti College of Pharmacy, C.K, Naidu Road, Camp, Amravati, Maharashtra, India.

***Corresponding Author: Roshani I. Sheikh**

Department of Pharmaceutics, Vidyabharti College of Pharmacy, C.K, Naidu Road, Camp, Amravati, Maharashtra, India.

Article Received on 06/04/2021 **Article Revised on 26/04/2021** **Article Accepted on 16/05/2021**

ABSTRACT

Slow dissolution rate of poorly water soluble drugs plays a major challenge in the drug development. Drug dissolution and its release from the dosage form have basic impact on bioavailability. Bioavailability depends on solubility of drug. Liquisolid technology is the most latest and novel approach to overcoming the problem of poorly soluble drugs. This technique is an effective method for formulating water insoluble and water soluble drugs. It relies upon the admixture of drug loaded solutions with applicable carrier and coating materials. Liquisolid technique involves a preparation where the liquid drug present in the form of a solution or suspension is converted into a non-sticky, dry, compactable, free-flowing powders, this is accomplished by adding certain coating agents and carriers agents that are appropriate. Liquisolid technique is a promising alternative for formulation of water-insoluble solid drugs and liquid drugs and a novel approach for solubility enhancement.

KEYWORDS: Liquisolid technique, poorly water soluble drug, solubility enhancement, carrier and coating material.

INTRODUCTION[1,2,3]

Solubility of drug is one of the most important parameter for bioavailability of drug. In recent year, approximately 70% of new drugs and 40% of marketed new drugs in oral immediate release dosage form exhibits low aqueous solubility. Mainly oral route is preferred for administration of the drugs because of patient compliance, low cost factor and convenience. The drug must be presented in aqueous form for absorption through gastrointestinal tract (GIT) when given orally. The solubility and dissolution nature of a drug is the key determinants of its oral Bioavailability. Release improvement of poorly soluble drugs is rise can be achieved by a rise of the drug surface area, the drug solubility, or by formulating the drug in its dissolved state. Different techniques are employed to enhance the dissolution of poorly soluble drugs like use of water-soluble salts and solid dispersion, increasing surface area by reducing particle size, coprecipitation, lyophilization pH adjustment, microencapsulation, inclusion of drug solutions or liquid drug in to soft gelatin capsule, solubilisation in a surfactant system**.**

LIQUISOLID COMPACT TECHNIQUE[4]

The liquisolid technique is a novel and most effective technique for improving the dissolution rate of poorly water-soluble drugs. In this technique with the use of carrier and coating agents the liquid form of drug transformed into dry looking, non-adherent, free flowing, and directly compressible powder. In liquisolid technique, the liquid part is a drug suspension, liquid drug, or drug solution made in suitable non-volatile liquid vehicles.

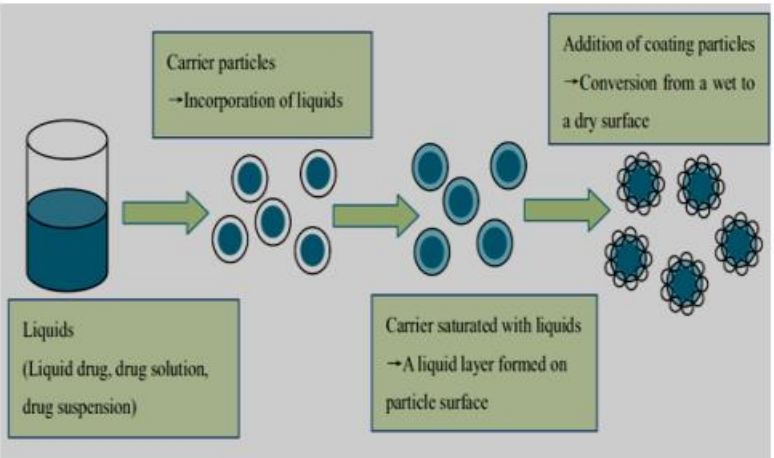

Fig. 2: Liquisolid compact formation.

Theory of liquid solid systems[4,5]

A powder can retain only limited amounts of liquid while maintaining acceptable compression and flow properties. To calculate the required amounts of powder excipients (carrier and coating materials) a mathematical approach for the formulation of liquid-solid systems has been formulated by Spireas. This approach is based on the compressible (Ψ-number) and flowable (Φ- value) and liquid retention potential introducing constants for each powder or liquid combination. The φ-number of a powder is defined as maximum amount of non-volatile liquid the powder can retain inside its bulk while maintaining acceptable compatibility resulting in compacts of sufficient hardness during compression. It can be measured as the maximum crushing strength of one gram tablet compacted at sufficiently high compression forces.

MECHANISMS OF ENHANCED DRUG RELEASE FROM LIQUISOLID SYSTEMS[6]

Various mechanisms of enhanced drug release have been suggest for liquisolid technique. The three main mechanisms include as, an increased surface area of drug available for release, an increased aqueous solubility of the drug, and an improved wet ability of the drug particles. Formation of a complex between the drug and excipients or any changes in crystalline of the drug could be ruled out using XRPD and DSC measurements.

a. Increased drug surface area: If the drug within the liquisolid technique is completely soluble in the liquid vehicle it is located in the powder substrate still in a solubilized, molecularly dispersed state. Therefore, the surface area of drug available for release is greater than that of drug particles within directly compressed.

b. Increased aqueous solubility of the drug: In addition to the first mechanism of drug release enhancement it is expected that *Cs*, which is the solubility of the drug, might be enhanced with liquidsolid technique. As the adequately very small amount of liquid vehicle in a liquidsolid compact is not enough to increase the overall solubility of the drug in the aqueous dissolution medium. However, at the liquid or solid interface between an individual liquisolid primary particle and the release medium it is possible that in this microenvironment the amount of liquid vehicle get diffusing out of a single liquisolid particle together with the drug molecules might be sufficient to enhance the aqueous solubility of the drug if the liquid vehicle acts as a cosolvent.

c. Improved wetting properties: Due to the fact that the liquid vehicle can either has a low surface tension or act as surface active agent, the wetting of the liquisolid primary particles is improved. Wettability of these systems has been demonstrated by measurement of contact angles and water rising times44.Several poorly soluble drugs have been formulated as liquisolid technique showing enhanced drug release. Different liquid vehicles, carrier and coating agents were used to formulate these drug delivery systems.

ADVANTAGES OF LIQUISOLID TECHNOLOGY:[7]

- In liquisolid systems, a number of water-insoluble solid drugs can be formulated. Also can be applied to formulate liquid medications such as oily liquid drugs.
- Better availability of an orally administered water insoluble drug can be achieved.
- There is lower production cost than that of soft gelatin capsules.
- Production of liquisolid systems is very similar to that of conventional tablets.
- Exhibits enhanced in-vivo and in-vitro drug release as compared to commercial counterparts, including soft gelatin capsule preparations.
- Can be used in controlled drug delivery system.
- Drug release can be modified using suitable formulation ingredients.
- The drug can be molecularly dispersed in the formulation.
- Capability of industrial production is also possible by this technique.

- Enhanced bioavailability can also be obtained as compared to conventional tablets.

DIS ADVANTAGES:[8]

1. Liquid solid systems requires low drug loading capacities.
2. Higher amounts of carriers and coating materials are required.
3. Requires more efficient excipients should provide faster drug release with the smaller tablet size.
4. Requirement of high solubility of drug in nonvolatile liquid vehicle.

APPLICATIONS[9]

- Liquisolid compact technology is a powerful tool to improve bioavailability of water insoluble drugs. Many water insoluble drugs on dissolving in different non-volatile solvents have been formulated into Liquisolid compacts.
- Literature cites different drugs successfully incorporated into Liquisolid compacts systems.
- Rapid release rates are achieved in Liquisolid formulations.
- These can be efficiently used for liquid lipophilic drugs or water insoluble solid drugs.
- Sustained Release of drugs which are water soluble drugs such as propranolol HCL has been obtained by the use of this technique.
- Solubility and dissolution improvement achieved.
- Good Flowability and compressibility achieved
- Designing of Controlled Release Tablet.

CLASSIFICATION OF LIQUI-SOLID SYSTEMS (10)

A. Based on the type of liquid medication contained therein, liquid-solid systems may be classified into three subgroups:

- Powdered drug solutions
- Powdered drug suspensions
- Powdered liquid drugs

The first two may be produced from the conversion of drug solutions or drug suspensions and the latter from the formulation of liquid drugs into liquid-solid systems. Since non-volatile solvents are used to prepare the suspension or drug solution, the liquid vehicle does not evaporate and thus, the drug is carried within the liquid system which in turn is dispersed throughout the final product.

B. Based on the formulation technique used, liquid-solid systems may be classified into two categories:

- Liquid-solid compacts
- Liquid-solid Microsystems.

Liquid-solid compacts are prepared using the previously outlined method to produce capsules or tablets, whereas the liquidsolid microsystems are based on a new concept which employs similar methodology combined with the inclusion of an additive, e.g., Polyvinylpyrrolidone (PVP), in the liquid medication which is incorporated into the coating and carrier materials to produce an acceptably flowing admixture for encapsulation.

FORMULATION OF LIQUISOLID COMPACTS[11]

Carriers, binding agents, non-volatile solvents, disintegrants, coating materials, lubricants are used in the formulation of liquisolid compacts.

Carrier materials The carrier materials should maintain flowability and compressibility, should be spongy in nature and must have required absorption properties both carrier and coating material should posses only a limited water quantity. Eg: microcrystalline cellulose (MCC).

Coating Materials

They are generally coarse powdered materials which help in covering the particles which have been wet by adsorbing of the liquid in excess amounts thereby producing a dry free flowing powder.

Non-Volatile Solvents

Nonvolatile, inert and not extremely viscous solvents are used in the formulation, they must also posses high boiling point and good solubilisation power. These liquids also provide binding action. Eg: glycine, polysorbate 80, propylene glycol, polyethylene glycol200 and 400.

Disintegrating Agents

Use of these agents increases wet ability, drug release rate and water solubility as they take in water. They play a role in breaking the compacts into smaller particles. Eg: sodium starch glycolate and cross povidene, explotab and pregelatinized starch.

Drug Candidate

Less soluble drugs like BSC class II drugs and class-IV drugs used as drug candidates for this technique this provides increased water solubility of these drugs. Eg: g-naproxen, digitoxin, bednisolone, hydrocortisone, ketoprofen.

METHODOLOGY[12]

The required quantities of the drug and stated quantity of nonvolatile solvent is weighed, mixed and heated (if required) results in a solution of the drug. Carrier and coating materials is incorporated into the drug solution. The process of mixing is to be done as three stages according to Spireas et al. (fig. 5)

First stage: The weighed ingredients are to be combined at an estimated mixing rate of one rotation/second or minute, which will aid the liquid medication to contribute its role in the powder.

Second stage: The above mixture should be spread uniformly on a mortar surface for about 5 min. This results in complete absorption of drug solution into the voids of powder particles.

Third stage: The above blend is to be mixed with a super disintegrant for 30 sec at a blending speed, which will results in the final blend ready for compression.

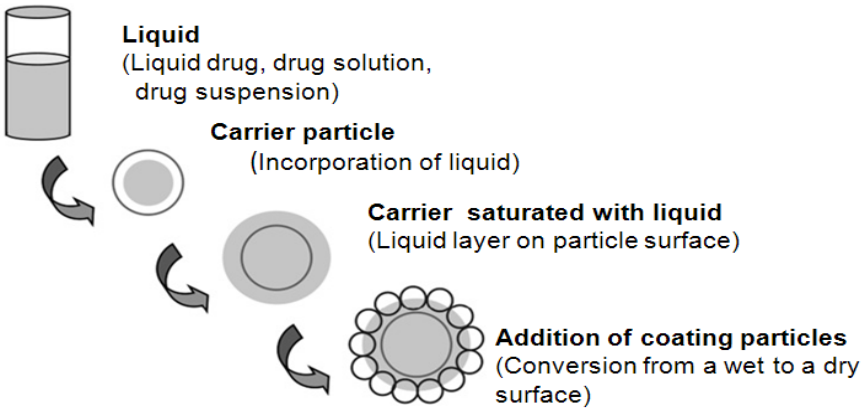

Fig. 5: Schematic representation of liquisolid preparation.

PRECOMPRESSION STUDIES OF LIQUIDSOLID SYSYTEM:

Flow Properties of liquid solid system[13]

Flow behaviour

The flowability of a powder is very importance in the production of pharmaceutical dosage forms in order to reduce high dose variations. Angle of repose, Hausner's ratio, Carr's index were used in order to ensure the flow properties of the liquisolid systems.

Angle of repose

This is the maximum angle possible between the horizontal plane and the surface of a pile of powder. 10 gm of powder was allowed to flow by funnel from 4 cm of height from the base. The diameter of the base and the height of pile was measured and calculate the angle of repose by the following the formula:

$\tan \theta = h/r$

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

Where = angle of repose,

h = Height of the heap,

r = Radius of the heap.

Tapped bulk density (TBD)[14]

About 5 gm of powder sample was poured gently through a glass funnel into a 10 ml graduated cylinder. The cylinder was tapped from height of two inches until a constant volume was obtained. Volume occupied by the sample after 100 tapping were recorded and tapped density was calculated as follows:

Tapped density = Mass/ Tapped volume.

Bulk density (BD)

Bulk density of the powder was determined by pouring gently 5 gm of sample through a glass funnel into a 10 ml measuring cylinder. The volume occupied by sample was recorded. The bulk density was calculated as given below:

Bulk density = Mass / Bulk volume.

Percentage compressibility or Carr's index[15]

Based on the poured density and tapped density, the percentage compressibility of the agglomerates was computed using the Carr's compressibility index by the formula:

Carr's index (%) = tapped density x poured density /tapped density x 100.

Hausner's ratio: Hausner's ratio was calculated using the formula, as given below:

Hausner's ratio = tapped density/ poured density.

POST COMPRESSION STUDIES OF LIQUI-SOLID COMPACTS

Hardness[16]

Monsanto Hardness tester used to measure hardness expressed in Kg/cm2.

Weight variation[16, 2]

20 Tablets are selected weight variations of individual tablets were determined with respect to average weight and % weight variation. The average weight and standard deviation of three batches were calculated. It passes the test for weight variation test if less than two of the individual tablet weights deviate from the everyday weight by quite than the allowed proportion deviation and none deviate by more than twice the proportion shown. It was calculated by an electronic weighing balance.

Thickness[17]

Ten tablets were randomly selected picked from all formulations and thickness was measured by using Vernier caliper and average thickness was calculated.

Friability Test[18]

The friability of the prepared liquisolid tablets was measured by a Roche type apparatus, and the % loss in weight was calculated.

% Friability = (Loss in weight / Initial weight) × 100

Maximum weight loss = Less than 1%.

Differential Scanning Calorimetry (DSC)[19]
It is important to determine any possible interaction between excipients used in the formulation. This will also show success of stability studies. If the characteristic peak for the drug is not present in the DSC thermogram, there is an indication that the drug is in the form of solution in liquisolid formulation and hence it get molecularly dispersed within the system.

X-ray diffraction (XRD)[19]
Generally, disappearance of characteristic peaks of drug in the liquisolid formulation and retaining peaks of carrier material is notice. This indicates that drug gets transformed to amorphous form or in solubilized form in the liquisolid formulation.

FTIR[20]
FTIR studies are performed to determine the chemical interaction between the excipients and drug used in the formulation. The presence of drug peaks in the formulation and absence of extra peaks shows there is no chemical interaction.

Estimation of drug content[20]
The liquisolid compacts are powdered well and powder equivalent to 10 mg of the drug is accurately weighed and suitably diluted using suitable solution. The drug content is calculated by at wavelength using UV-Visible spectrophotometer.

In vitro release studies of the liquisolid tablets [21]: It is performed using USP dissolution apparatus type II. The studies are carried out in 900 ml 0.1 N HCl maintained at a constant temperature 37 °C±2 °C at a stirring speed of 50 to 200 rpm. After adding a known amount of drug equal formulation into the media, the percentage (%) of drug dissolved is determined by withdrawing the samples at regular intervals and sink conditions are maintained by replacing with fresh buffer. The concentration of drug can be determined spectro-photometrically.

The disintegration test[19]
The disintegration was carried out on six tablets in distilled water at 37 ± 2 ºC using the USP disintegration apparatus.

CONCLUSION

The liquid solid technique is capable method the formulation of water insoluble solid drugs and liquid liphophilic drugs. This technique gives to enhance absorption, dissolution rate and bio-availability of poorly soluble, insoluble or liphophilic drugs and these are formulated into immediate release sustained control release by selection of suitable solvent and carrier. This technique is found to be truly promising as the solubility and dissolution related problems of drugs, especially BCS class II and IV which leads to poor bioavailability. The technique is also used to design sustained release systems by using hydrophobic carriers instead of hydrophilic carries in liquisolid method. Therefore, this formulation of the drug has the potential to be considered for human study in order to be manufactured on large scale.

REFERENCES

1. Anand D. Savkare, Malavi R. Bhavsar, Vishal D. Gholap and Pooja M. Kukkar. (Liquisolid Technique: A Review). Int J Pharm Science and Res, 2017; 8(7): 2768-2775.
2. Pawar et al. Liquisolid Compacts: A Promising Approach for Solubility Enhancement. J Drug Deliv and Therap, 2017; 7(4): 6-11.
3. Athira T Vijayan, K Krishnakumar, B Dineshkumar, Smitha K Nair. Liquisolid Compact Technique for Improvement of the Dissolution Rate: A Review. Sch. Acad. J. Pharm. (SAJP), 2018; 7(3): 148-154.
4. Satyajit Panda, R. Varaprasad, K. Priyanka, Ranjit P. Swain, Liquisolid Technique: A Novel Approach for Dosage Form Design. Int J Applied P'ceutics, 2017; 3.
5. Urvashi B. Patel et al. Liquisolid Compacts: A Review. Int J Adv P'ceutics, 2017, 06(07): 110-113.
6. Pusuluri et al, Review on Liquisolid Compact Technology. World J Pharmaceut Res, 2015; 2.
7. Bhumi B. Patel and Chainesh N. Shah. Recent Research on Liquisolid Technology for Solubility Enhancement: A review. Int J Adv P'ceutics, 2016; 1.
8. K. Kranthikumar, M. Shirisha and D. Bhagyalakshmi. Solubility Enhancement of Poorly Soluble BCS Class 2 and Class 4 drugs by Liquid Solid Technique. World J Pharm & Pharm Sci, 2018; 2: 1212-1225.
9. J. Hamsanandini, S. Parthiban, A.Vikneswari, T. Tamiz Mani. Dissolution Enhancement Techniques of Poorly Soluble Drugs by Liquisolid Compacts. Int J Res Pharmaceut & Nano Sci, 2014; 3(4): 298 - 304.
10. Sirisha V.N.L. et al. A Review on Liquid Solid Compacts. Int.J Pharm Phytopharmacol Res, 2012, 2(2): 116-121.
11. R. Santosh Kumar and Jampana Divija Sai. Liquisolid Compacts: A Review. J Drug Deliv & Therap, 2019; 9(4-A): 880-883.
12. Anjana Anil, Litha Thomas, Preethi Sudheer. Liquisolid Compacts: An Innovative Approach for Dissolution Enhancement. Int j Pharm & Pharm Sci, 2018; 6.
13. Manisha Rokade, Pradnya Khandagale, Dipti Phadtare, Liquisolid Compact Techniques: A Review. Int J Current Pharmaceut Res, 2018; 4.
14. G. Y. Srawan Kumar, R. B. Desireddy, P. Kasi Reddy, S. Saikrishna Reddy, S. Durga Prasad and U. Naga Ravi. Enhancement of Solubility of Poorly Soluble Drugs by Liquisolid Compact Technique. World J Pharmcet Res, 2020; 4: 459-473.
15. Dhananjay Ahir, Rajeshree Panigrahi, Prasanta Kumar Choudhury and Ajit Kumar Acharya.

16. Formulation and Evaluation of Telmisartan Liquisolid Compact Tablets. Int J Pharma Chem Res, 2018; 3.
17. Vinod Valjibhai Siju1, Moinuddin Soniwala, Swati Nagar. A Novel Technique to Enhance Dissolution Rate of Cilnidipine Using Liquisolid Compact & Wet Granulation. Int. J. Pharm. Sci. Drug Res, July-August, 2017.
18. Sunitha R, Venugopal K and Satyanarayana SV**.** Formulation and Development Studies on Enhancement of Dissolution Rate of BCS Class II Antidiabetic Drug. Int J Drug Dev & Res, 2018; 10(3): 1-6.
19. Purushottam R. Patil, Paresh R. Mahaparale and Khalid U. Shaikh. Formulation development and evaluation of Atorvastatin Calcium liquisolid tablets. Int J Pharm Sci Res, 2021; 12(3): 1849-1859.
20. Sahil M. Gavali, Sharad S. Pacharane, Shirish V. Sankpal, Kisan R. Jadhav and Vilasrao J. Kadam. Liquisolid Compact: A New Technique for Enhancement of Drug Dissolution. Int J Res Pharm and Chem, 2011; 1(3).
21. Kishor S. Gavhane, Dr. F. J. Sayyad, Liquisolid Compact A Review. Int J Pharmaceut & Bio Res (IJPBR), 2013; 2.
22. Snehal P. Patil, N. A. Gujrathi, B. R. Rane. Liquisolid Compact A Review. Pharm Sci Monitor, 2014; 5(2): 59-68.