Journal of Coastal Life Medicine
www.jclmm.com
ISSN: 2309-5288(Print)/2309-6152(Online)
Volume 10 No.1 (2022), Page No. 536 – 545
Article History: Received: 02 January 2022, Revised: 10 February 2022, Accepted: 21 February 2022, Publication: 31 March 2022

A Review on Liqui-Solid Compaction of Solid Dispersion

N. Madhavi[1] , O. Likitha[2] ,V.T. Iswariya[3], K. Mary swarnalatha[4], T. Rama rao[5]
1,2,3,4 - Department of pharmaceutics, CMR College of pharmacy, Telangana, Hyderabad
5- Professor & Principal, Department of pharmaceutics, CMR College of pharmacy, Telangana, Hyderabad
Email: nimmathota.madhavi@gmail.com

Abstract:
The poor dissolution rate of water-insoluble drugs is still a substantial problem confronting the pharmaceutical industry. There are several methods used to increase the solubility of drugs, of those liquid-solid compact technique is a new and promising addition towards such a novel aim, that the solubility of the insoluble drug moiety is increased by the aid of non- volatile solvents and hence increasing the dissolution and bioavailability. Oral drug administration has been one of the most convenient and widely accepted routes of delivery for most of the therapeutic agents. It is one of the most extensively used routes of administration because of its obvious advantages of ease of administration, improved patient compliance, and convenience. The enhancement of oral bioavailability of poorly water- soluble drugs remains one of the most challenging aspects of drug development. A simplest and easiest way of administering drug is through oral route.

Keywords*:* solubility, dissolution, solid dispersion, oral administration

INTRODUCTION

The oral dosage forms have many advantages over other types of dosage forms like greater stability, accurate dosage, smaller bulk and easy production is possible. The formulation of poorly soluble compounds for oral delivery at present is one of the most frequent and greatest challenges to formulation scientists in the pharmaceutical industry. Nearly 40% of identified potential new drug by pharmaceutical industry are poorly water soluble. Poor water-soluble compounds show decreased release rate & poor bioavailability. So large dose is required to produce desirable effect but that may lead to toxicity of the drug. So best option for increasing release rate is improvement of the solubility through formulation approaches. A variety of formulation strategies have been explored to overcome the poor aqueous solubility of drugs, including micronization, nano crystalization, cyclodextrin inclusion, co-crystallization, micelle solubilization, solid dispersion, liquisolid technique, and encapsulation in nanoparticles.[1,2]

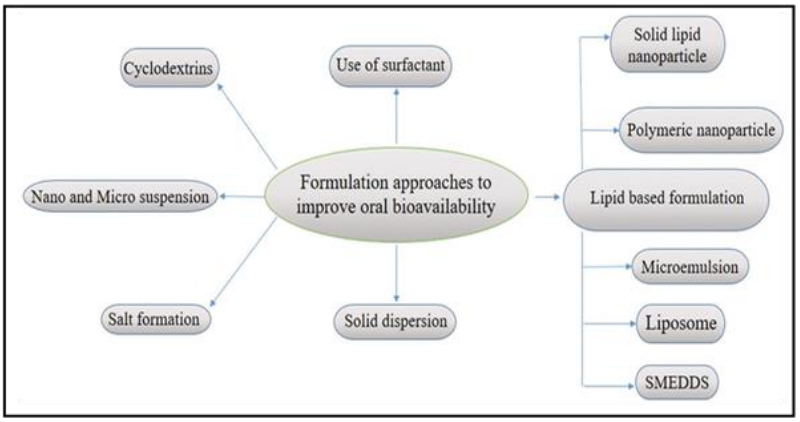

Figure1: various methods for enhancing solubility of poor water soluble drugs

Journal of Coastal Life Medicine
www.jclmm.com
ISSN: 2309-5288(Print)/2309-6152(Online)
Volume 10 No.1 (2022), Page No. 536 – 545
Article History: Received: 02 January 2022, Revised: 10 February 2022, Accepted: 21 February 2022, Publication: 31 March 2022

Pharmaceutical engineering involves all sorts of dispersion systems, including suspension system, colloidal system and solution system, in which a drug can be dispersed by itself or in a solid matter, a semisolid matter, a solvent or nanoparticles. Among these, solid dispersion, lipid-based dispersion and liquisolid dispersion are well-developed and more commonly used pharmaceutical dispersion techniques. Liquisolid system as a viable alternative to the conventionally used dispersion techniques for dissolution and bioavailability improvement has received considerable attention in recent years.[3]

LIQUISOLID SYSTEM

Over the years, various solid dosage formulation techniques, to enhance the dissolution of poorly soluble substances, have been introduced with different degrees of success. Liquisolid technique is a new and promising method that can change the dissolution rate of drugs. It has been used to enhance dissolution rate of poorly water-soluble drugs especially those belonging to the biopharmaceutical classification system (BCS) class II and IV, dissolve slowly, poorly and irregularly, and hence pose serious delivery challenges, like incomplete release from the dosage form, poor bioavailability, increased food effect, and high inter- patient variability. The new ‘liquisolid’’ technique may be applied to formulate liquid medications (i.e., oily liquid drugs and solutions, suspensions or emulsions of water-insoluble solid drugs carried in non-volatile liquid vehicles) into powders suitable for tableting or encapsulation. Since, the liquisolid tablets contain a solution of the drug in suitable solvent; the drug surface available for dissolution is tremendously increased. Due to significantly increased wetting properties and surface area of drug available for dissolution, liquisolid compacts of water-insoluble substances may be expected to display enhanced drug release characteristics and, consequently, improved oral bioavailability. In this case, even though the drug is in a solid dosage form, it is held within the powder substrate in solution or, in a solubilized, almost molecularly dispersed state, which contributes to the enhanced drug dissolution properties. [4,5,6]

DEFINITION

Liquisolid technique is a new and promising method that can change the dissolution rate of drugs. Liquisolid systems is based on the principles of conversion of the drug in the liquid state into a free flowing, readily compressible and apparently dry powder by simple physical blending with selected excipients, which are termed as carriers and coating materials. Liquid drug could be also sprayed into the carrier material in fluidbed equipment for homogenous distribution of the active substance. Liquid drug is incorporated into the porous structure of a carrier material due to adsorption and absorption. Liquisolid technique it has been used to enhance dissolution rate of poorly water-soluble drugs. For poorly soluble (class II) and (class IV) drugs the rate of oral absorption is often controlled by the dissolution rate in the gastrointestinal tract. The new ‘liquisolid’’ technique may be applied to formulate liquid medications (i.e., oily liquid drugs and solutions, suspensions or emulsions of water-insoluble solid drugs carried in non-volatile liquid vehicles) into powders suitable for tableting or encapsulation. Since, the liquisolid tablets contain a solution of the drug in suitable solvent; the drug surface available for dissolution is tremendously increased. Due to

Journal of Coastal Life Medicine
www.jclmm.com
ISSN: 2309-5288(Print)/2309-6152(Online)
Volume 10 No.1 (2022), Page No. 536 – 545
Article History: Received: 02 January 2022, Revised: 10 February 2022, Accepted: 21 February 2022, Publication: 31 March 2022

significantly increased wetting properties and surface area of drug available for dissolution, liquisolid compacts of water insoluble substances may be expected to display enhanced drug release.[7,8]

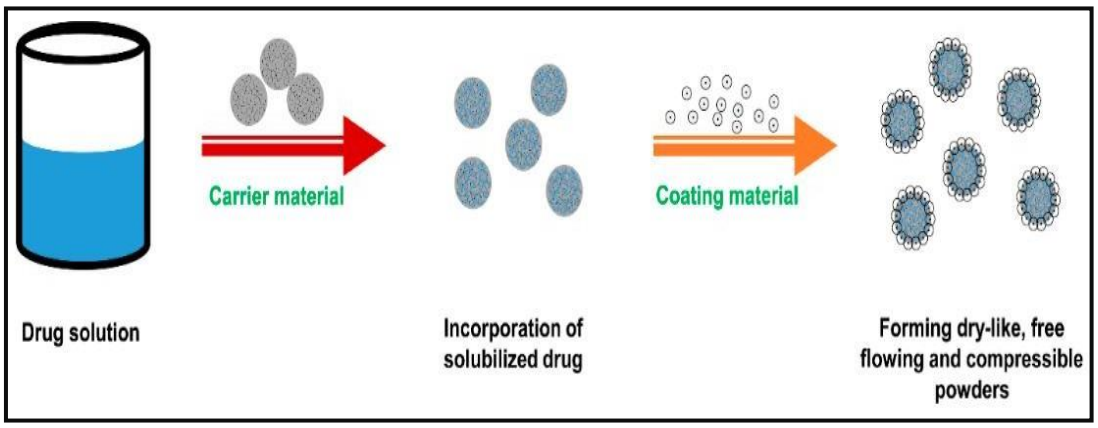

Figure 2: formation process of dry-looking freely flowing and compressible powders in the liquid solid system

CLASSIFICATION OF LIQUISOLID SYSTEM [4,9]

A. Based on the type of liquid medication contained therein, liquisolid systems may be Classified into three subgroups:

1. Powdered drug solutions
2. Powdered drug suspensions
3. Powdered liquid drugs

B. Based on the formulation technique used, liquisolid systems may be classified into two Categories:

1. Liquisolid compacts:

Refers to immediate sustained-release tablets or capsules that are described under “liquisolid systems”.

2. Liquisolid Microsystems:

Refers to capsules prepared by “liquisolid systems” plus the Inclusion of an additive resulting in a unit size that may be as much as five times less than that of a liquisolid compact.

Journal of Coastal Life Medicine
www.jclmm.com
ISSN: 2309-5288(Print)/2309-6152(Online)
Volume 10 No.1 (2022), Page No. 536 – 545
Article History: Received: 02 January 2022, Revised: 10 February 2022, Accepted: 21 February 2022, Publication: 31 March 2022

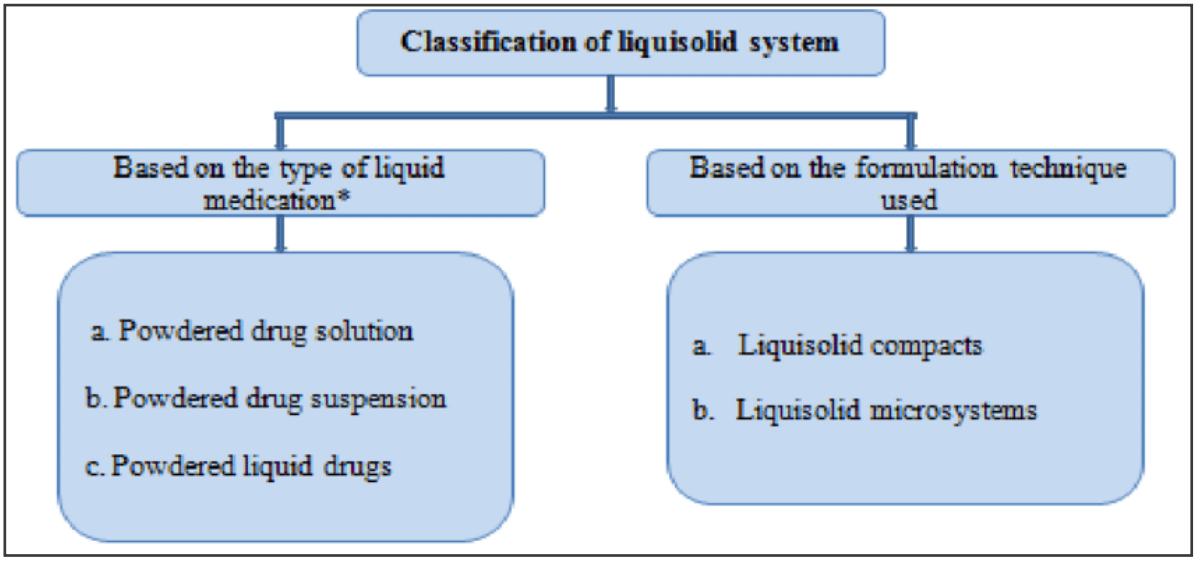

Figure3: classification of liquisolid system

HISTORICAL DEVELOPMENT

Historically, liquisolid compacts are descendants of 'powdered solutions, an older technique which was based on the conversion of a solution of a drug in a non-volatile solvent into a dry- looking, no adherent powder by mainly adsorbing the liquid onto silicas of large specific surfaces. Such preparations, however, have been investigated for their dissolution profiles while being in a powder dispersion form and not as compressed entities, simply because they could not be compressed into tablets. In later studies on powdered solutions, compression enhancers such as microcrystalline cellulose were added in such dispersions in order to increase the compressibility of the systems. In these studies, however, large quantities of silicas were still being used, and the flow and compression properties of the products were never validated and standardized to industrial specifications and requirements. Specifically, when such modified powdered solutions were compressed into tablets, they presented significant 'liquid squeezing out' phenomena and unacceptably soft tablets, thereby hampering the industrial application of such systems.[9,10]

COMPONENTS GENERALLY USED IN LIQUID SOLID SYSTEM

Formulation of liquisolid compacts a carrier, coating material, non-volatile solvent, disintegrants, lubricants and binding agents. Carrier material used should be spongy in nature, should have satisfactory absorption properties for a liquid vehicle, both carrier as well as coating materials should hold a limited quantity of liquid, at the same time it should maintain flowability and compressibility.[11]

Journal of Coastal Life Medicine
www.jclmm.com
ISSN: 2309-5288(Print)/2309-6152(Online)
Volume 10 No.1 (2022), Page No. 536 – 545
Article History: Received: 02 January 2022, Revised: 10 February 2022, Accepted: 21 February 2022, Publication: 31 March 2022

Coating material
Coating materials are usually coarsely powdered particles which provide covering to the particles that are wet by adsorbing the excess of liquid, results in a dry free-flowing powder.[12]

Non-volatile solvent
Solvents used are non-volatile, water-miscible, inert and not extremely viscous. They should have a high boiling point, possess good solubilization power for drugs used. Binding action can also be provided within the formulation with the help of non-volatile liquids.[12]

Disintegrating agents (disintegrants)
These are agents which take up water, increases wettability, water solubility and the rate of drug release. The breakup of compacts into smaller particles can be achieved by the use of disintegrants. E. g sodium starch glycolate and cross-povidone, explotab and pregelatinized starch.

Carrier material
Carrier material the carrier used should be spongy in nature, should poses satisfactory absorption properties for a liquid vehicle, both carrier as well as coating materials should hold a limited quantity of liquid, at the same time it should maintain flowability and compressibility. E.g. microcrystalline cellulose (MCC) (avicel200 and avicel102)

Drug candidate
BCS class II and IV drugs are generally choosen as a drug candidate for the liquisolid system. This results in increased water solubility of such candidates. E.g. Naproxen, Digitoxin, Prednisolone, Hydrocortisone, Ketoprofen, Haloperidol. [13,14,15]

Table1: Components generally involved in a liquisolid formulation,[16]

Excipients Type	**Characteristics**	**Examples**
ɔn-volatile solvent	Inert water-miscible,, compatible with drug candidate.	glycerin, propylene glycol, polysorbate
Carrier material	Porous, large specific surface area, sufficient adsorption ability, good flowability and compressibility.	MCC, Avicel Celous, vivapurMagnesium Aluminometa silicate Dibasic calciumphosphat anhydrous
Coating material	Ultrafine and highly adsorptive particles, good flow-aided effect.	Colloidal silicon dioxide (e.g.,Aerosil/ Cab-O-Sil) Neusilin CalciumSilicate

Journal of Coastal Life Medicine
www.jclmm.com
ISSN: 2309-5288(Print)/2309-6152(Online)
Volume 10 No.1 (2022), Page No. 536 – 545
Article History: Received: 02 January 2022, Revised: 10 February 2022, Accepted: 21 February 2022, Publication: 31 March 2022

CONCEPT OF LIQUISOLID SYSTEM

When the drug dissolved in the liquid vehicle is incorporated into a carrier material which has a porous surface and closely matted fibers in its interior as cellulose, both absorption and adsorption take place; i.e., the liquid initially absorbed in the interior of the particles is captured by its internal structure, and after the saturation of this process, adsorption of the liquid onto the internal and external surfaces of the porous carrier particles occur. Then, the coating material having high adsorptive properties and large specific surface area gives the liquisolid system the desirable flow characteristics. In liquisolid systems the drug is already in solution in liquid vehicle, while at the same time, it is carried by the powder particles (microcrystalline cellulose and silica). Thus, due to significantly increased wetting properties and surface area of drug available for dissolution, liquisolid compacts of water-insoluble substances may be expected to display enhanced drug release characteristics and consequently, improved oral bioavailability. Since dissolution of a non-polar drug is often the rate limiting step in gastrointestinal absorption, better bioavailability of an orally administered water-insoluble drug is achieved when the drug is already in solution, thereby displaying enhanced dissolution rates. That is why soft gelatin capsules containing solutions of such medications demonstrate higher bioavailability when compared to conventional oral solid dosage forms. A similar principle underlies the mechanism of drug delivery from liquisolid compacts and is chiefly responsible for the improved dissolution profiles exhibited by these preparations. [16,17]

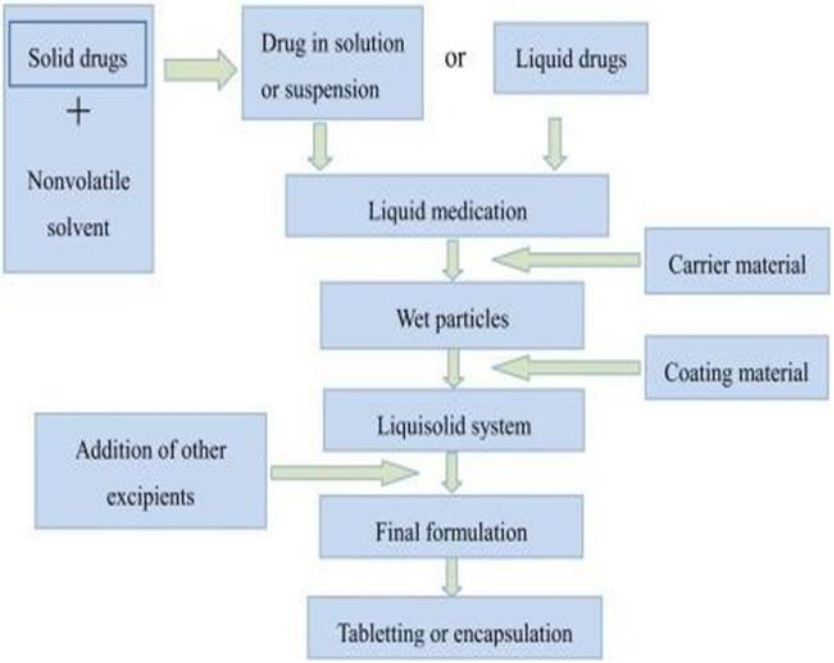

Figure4: steps involved in liquisolid system

Journal of Coastal Life Medicine
www.jclmm.com
ISSN: 2309-5288(Print)/2309-6152(Online)
Volume 10 No.1 (2022), Page No. 525 – 535
Article History: Received: 02 January 2022, Revised: 10 February 2022, Accepted: 21 February 2022, Publication: 31 March 2022

MECHANISMS OF ENHANCED DRUG RELEASE FROM LIQUISOLID SYSTEMS

Several mechanisms of enhanced drug release have been postulated for liquisolid systems. The three main suggested mechanisms include an increased surface area of drug available for release, an increased aqueous solubility of the drug, and an improved wettability of the drug particles.[18]

1. Increased drug surface area

If the drug within the liquisolid system is completely dissolved 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 much greater than that of drug particles within directly compressed tablets.

2. Increased aqueous solubility of the drug

In addition to the first mechanism of drug release enhancement it is expected that Cs the solubility of the drug, might be increased with liquisolid systems. In fact, the relatively small amount of liquid vehicle in a liquisolid compact is not sufficient to increase the overall solubility of the drug in the aqueous dissolution medium. However, at the solid/liquid interface between an individual liquisolid primary particle and the release medium it is together with the drug molecules might be sufficient to increase the aqueous solubility of the drug if the liquid vehicle acts as a co solvent.

3. Improved wetting properties

Due to the fact that the liquid vehicle can either act as surface active agent or has a low surface tension, wetting of the liquisolid primary particles is improved Wettability of these systems has been demonstrated by measurement of contact angles and water rising times. possible that in this microenvironment the amount of liquid vehicle diffusing out of a single liquisolid particle[19]

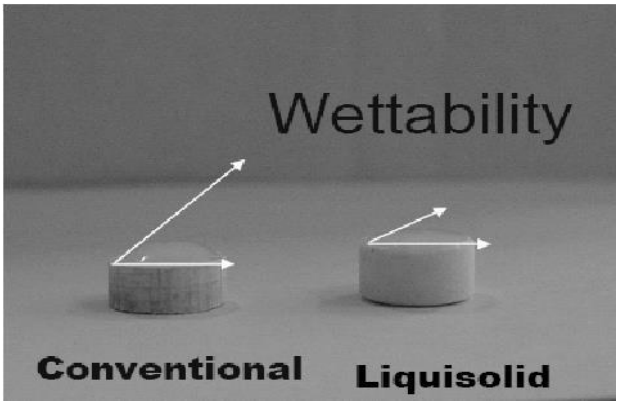

Figure5: wetting property of liquisolid system

ADVANTAGES[20]

- Liquisolid tables have many advantages. which include:
- Liquisolid systems are low cost formulations than soft gelatin capsules.
- Drug release can be modified using suitable formulation ingredients

Journal of Coastal Life Medicine
www.jclmm.com
ISSN: 2309-5288(Print)/2309-6152(Online)
Volume 10 No.1 (2022), Page No. 525 – 535
Article History: Received: 02 January 2022, Revised: 10 February 2022, Accepted: 21 February 2022, Publication: 31 March 2022

- Drug can be molecularly dispersed in the formulation.
- Capability of industrial production is also possible.
- Enhanced bioavailability can be obtained as compared to conventional tablets.
- Several slightly and very slightly water-soluble and practically water-insoluble liquid and solid drugs can be formulated into liquisolid systems.
- Even though the drug is in a tablet or capsule form, it is held in a solubilized liquid state, which contributes to increased drug wetting properties, thereby enhancing drug dissolution

LIMITATIONS

- This methodology cannot be used to prepare high dose water-Insoluble drugs.
- It is observed that there is an increase in weight of tablet due to Presence of carrier material and coating materials in larger levels.
- Application of mathematical calculations are required.
- Faster drug release can be achieved by ingredients with high Absorption capacity which provide smaller tablet size.
- The inadequate hardness of liquisolid tablets results when Acceptable compression is not achieved.
- Dissolution rate and bioavailability depends on the solubility of Drugs in non-volatile liquids.[21]

APPLICATIONS

- Liquisolid compact technology is a powerful tool to improve bioavailability of water insoluble drugs. Several 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.
- Rapid release rates are obtained in liquisolid formulations.
- These can be efficiently used for water insoluble solid drugs or liquid lipophilic drugs.
- Sustained Release of drugs which are water soluble drugs such as propranolol hydrochloride has been obtained by the use of this technique.[22]

CONCLUSION:

liquisolid technique can be an enticing approach for improving the dissolution profile of drugs having high dose requirements and low water solubility. Liquisolid technique is a new and promising method used to enhance dissolution rate of poorly water-soluble drugs (BCS Class II and IV Drugs). Since, the liquisolid tablets contain a solution of the drug in suitable solvent, the drug surface available for dissolution and wetting property of the drug tremendously increases. So the liquisolid tablets shows an enhanced drug release characteristics and, consequently, improved oral bioavailability.

Journal of Coastal Life Medicine
www.jclmm.com
ISSN: 2309-5288(Print)/2309-6152(Online)
Volume 10 No.1 (2022), Page No. 525 – 535
Article History: Received: 02 January 2022, Revised: 10 February 2022, Accepted: 21 February 2022, Publication: 31 March 2022

REFERENCES

[1]. ferences Alonzo, D.E., Zhang, G.G., Zhou, D., Gao, Y., Taylor, L.S., 2010. Understanding the behavior of amorphous pharmaceutical systems during dissolution. Pharm. Res. 27, 608–618.

[2]. Avachat, A.M., Parpani, S.S., 2015. Formulation and development of bicontinuous nanostructured liquid crystalline particles of efavirenz. Colloids Surf., B 126, 87– 97..

[3]. Burra, S., Yamsani, M., Vobalaboina, V., 2011. The liquisolid technique: an overview. Brazil. J. Pharm. Sci. 47, 475–482.

[4]. Kulkarni, A. S., Aloorkar, N. H., Mane, M. S. &Gaja, J. B. Liquisolid Systems : A review. International Journal of Pharmaceutical Sciences and Nanotechnology : 3, 795–802 (2010).

[5]. Pathak, A., Goyal, R., Agrawal, P., Rajput, S. &Tiwari, G. a review on liquisolid technology.World Journal of Pharmaceutical research. 1, 500–512 (2012).

[6]. Vijaykumar Nagabandi,T.Ramarao.,K.N.Jayaveera. LIQUISOLID Compacts: A Novel Approach to Enhance Bioavailability of Poorly Soluble Drugs. International Journal of Pharmacy and Biological Sciences1,89-102 (2011).

[7]. K. Rajesh., R. Rajalakshmi., J. Umamaheswari&C.K. Ashok Kumar. liquisolid technique a novel approach to enhancesolubility and bioavailability.International Journal of Biopharmaceutics2, 8– 13 (2011).

[8]. Dokoumetzidis, A. & Macheras, P. A century of dissolution research: from Noyes and Whitney to the biopharmaceutics classification system. International journal of pharmaceutics321, 1– 11 (2006).

[9]. Akinlade, B., Elkordy, A. a, Essa, E. a & Elhagar, S. Liquisolid systems to improve the dissolution of furosemide. Scientia pharmaceutica78, 325–44 (2010).

[10]. Shashidher Burra., Sandeep Kumar Galipelly. Enhancement of solubility and dissolution rate of Frusemidethrough liquisolid technique.Scholars Research Library. 2, 321–328 (2010).

[11]. Gordon MS et al. Effect of the mode of super disintegrant incorporation on dissolution in wet granulated tablets. J Pharm Sci 1993; 82: 220–226.

[12]. Lachman L, Libermann HA, Kaning. The Theory& Practice of Industrial Pharmacy, Lea Febiger, Philadelphia, 1976; 101pp.

[13]. Indian Pharmacopoeia, 4th Ed. Vol. I: Controller of Publications, Ministryof Health & Family Welfare, Govt. of India, Delhi; 1996: 511-13.

[14]. Pradeep yala., S. Srinivasan., k. Mahalingan., siddalingappa zalaki .solubility enhancement of a model etoricoxib drug using liquisolid compacts International Journal of Biological & Pharmaceutical Research. 3, 577–585 (2012).

[15]. Hong, D.S.; Banerji, U.; Tavana, B.; George, G.C.; Aaron, J.; Kurzrock, R. Targeting the molecular chaperone heat shock protein 90 (HSP90): Lessons learned and future directions. Cancer Treat. Rev. 2013, 39, 375–387.

[16]. Vogt, M.; Kunath, K.; Dressman, J.B. Dissolution enhancement of fenofibrate by micronization, cogrinding and spray-drying: Comparison with commercial preparations. Eur. J. Pharm. Biopharm. 2008, 68, 283–288.

[17]. Barmpalexis, P.; Grypioti, A.; Eleftheriadis, G.K.; Fatouros, D.G. Development of a new aprepitant liquisolid formulation with the aid of artificial neural networks and genetic programming. AAPS PharmSciTech 2018, 19, 741–752.

[18]. Kamalakkannan, V.; Puratchikody, A.; Masilamani, K.; Senthilnathan, B. Solubility enhancement of poorly soluble drugs by solid dispersion technique—A review. J. Pharm. Res. 2010, 3, 2314–2321.

[19]. Bandari S, Mittapalli RK, Gannu R, Rao YM. Orodispersible tablets: An overview. Asian journal of pharmaceutics, Jan 2008, 2-11.

Journal of Coastal Life Medicine
www.jclmm.com
ISSN: 2309-5288(Print)/2309-6152(Online)
Volume 10 No.1 (2022), Page No. 525 – 535
Article History: Received: 02 January 2022, Revised: 10 February 2022, Accepted: 21 February 2022, Publication: 31 March 2022

[20]. Bi YX, Sunada H, Yonezawa Y, Danjo K. Evaluation of rapidly disintegrating tablets by direct compression method. Drug Develop Ind Pharm, 1999, 25, 571-81.

[21]. Gohel MC, Jogani PD. A review of co-processed directly compressible excipients. J Pharm Pharm Sci, 2005, 8, 76-93.

[22]. Hardman JG, Limbird LE. Goodman and Gilman's the pharmacological basis of therapeutics. McGraw Hill Medical Publishing Division, New Delhi, 10th edition, 2001, 496.