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Review paper

An In-Depth Review of Liquisolid Compact Techniques: Principles, Applications and Characterizations

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ABSTRACT

For the majority of therapeutic agents, oral drug administration has proven to be one of the most practical and widely recognised methods of delivery. Because of its clear benefits of convenience, better patient compliance, and ease of administration, it is one of the most often utilised drug delivery methods. A unique idea in medication delivery, the Liquisolid Compact System can alter the pace at which pharmaceuticals that are insoluble in water dissolve. A more modern method known as "powdered solution technology," also known as "Liquisolid technology," has been used to turn medications that are insoluble in water into fast-acting solid dosage forms. One of the industry's most difficult challenges in creating the perfect solid dosage form unit is the restricted solubility of pharmaceuticals. The liquidsolid strategy is a fresh and effective way to deal with this outcome. The method is predicated on dissolving the insoluble drug in a non-volatile solvent and combining drug-loaded solutions with suitable carriers and coating materials to create powders that flow and compress into acceptable forms. The specific chemical moieties have no bearing on the choice of non-toxic hydrophilic solvent, carrier, coating materials, or their ratios. Either a larger surface area of the drug that is accessible for release, an increase in the drug's aqueous solubility, or better wettability of the drug particles are the causes of the higher bioavailability.

1. Introduction

Bioavailability is the critical determinant of a drug for its helpful viability, which thus relies on the solvency of that drug in gastrointestinal liquid. Solubility is one of the significant boundaries to accomplish the ideal convergence of drug in fundamental course for pharmacological reaction. [1,2] Inadequately water-solvent drugs will be intrinsically delivered at a sluggish rate inferable from their restricted solubility inside the GI items. The disintegration rate is much of the time the rate-deciding move toward the drug assimilation. The test for inadequately water-dissolvable drugs is to upgrade the pace of disintegration. This thus therefore further develops ingestion and bioavailability. Detailing strategies focused on at disintegration improvement of inadequately dissolvable substances are constantly presented. Bioavailability of ineffectively water-dissolvable drugs is restricted by their solubility and disintegration rate. A few examinations have been completed to expand the disintegration pace of drugs by diminishing the molecule size, by making nano and microparticles. [3,4]

Liquisolid development is a promising new procedure that can change the deterioration speed of

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prescriptions. The new evolved strategy by Tower as liquisolid framework further develops the disintegration properties of water insoluble or inadequately solvent drugs. The expression "liqui-strong systems" (LS) is a powdered type of fluid drug planned by changing over fluid lipophilic drug or drug suspension or arrangement of water-insoluble strong drug in reasonable non-volatile solvent frameworks, into dry looking, non-follower, free-streaming and promptly compressible powdered combinations by mixing with chosen transporter and covering material [2,4].

Liquisolid was used to additionally foster the crumbling speed of incapably water dissolvable meds. The pace of disintegration in the gastrointestinal plot much of the time controls the oral assimilation rate for class drugs (class IV) and ineffectively dissolvable drugs (class II). The new "Liquisolid" development structures liquid meds (for instance plans, suspensions, or emulsions of smooth liquid drugs and water major areas of strength for insoluble moved in a non-erratic liquid carrier) into powders sensible for tableting or exemplification can be applied Different grades of cellulose, starch, lactose, and so on are utilized as the transporters, though extremely fine silica powder is utilized as the covering (or covering) material. [2, 5, 6] The great stream and pressure properties of Liqui-strong might be ascribed because of enormous surface area of silica and fine molecule size of avicel. Subsequently, Liqui-strong compacts containing water-insoluble drugs expected to show upgraded disintegration qualities and thusly worked on oral bioavailability.

Considering the way that liquid tablets contain a response of prescription in a sensible dissolvable. The possibility of "liquid solid tablet" was brought into the world from "powder deterioration advancement" that suggests "liquid". A strong drug dispersed in a reasonable non-volatile fluid transporter is alluded to as a "fluid drug." Powdered excipients are made by just consolidating these "fluid drugs" with the favored transporter and covering material. These excipients have a dry appearance, are non-tacky, are exceptionally flowable, and are very much endured. [7, 8]

2. Liquisolid Compacts

By and large, liquisolid compacts are relatives of 'powdered arrangements', a more seasoned method which depended on the transformation of an answer of a drug in a nonvolatile solvent into a dry-looking, nonadherent powder by fundamentally adsorbing the fluid onto silicas of enormous explicit surfaces. Such arrangements, be that as it may, have been explored for their disintegration profiles while being in a powder scattering structure and not as packed elements, essentially on the grounds that they couldn't be compacted into tablets. [9, 10] In later examinations on powdered arrangements, pressure enhancers, for example, microcrystalline cellulose were included such scatterings to expand the compressibility of the frameworks. In these examinations, in any case, huge amounts of silicas were all the while being utilized, and the stream and pressure properties of the items were never approved and normalized to modern particulars and necessities. [11,12] Liquisolid compacts, then again, are acceptably streaming and compressible powdered types of fluid drugs, and have modern application. What's more, the term 'fluid medicine' doesn't just suggest drug arrangements, as in powdered arrangements, yet in addition drug suspensions, emulsions, or fluid sleek drugs. [13,14]

In this way, as opposed to 'powdered arrangements', the term 'liquisolid compacts' is more broad and it might envelop four unique definition frameworks specifically, [2, 8]

1. Powdered drug arrangements
2. Powdered drug suspensions
3. Powdered drug emulsions
4. Powdered fluid drug

Moreover, the prior term 'powdered arrangements' is by all accounts lacking even in depicting the first frameworks, since it has not been demonstrated that the drug stays in arrangement in the fluid vehicle after its statement on the very enormous powder surfaces of silica utilized. The new 'liquisolid' procedure might be applied to figure out fluid prescriptions [i.e., slick fluid drugs and arrangements, suspensions or emulsions of water-insoluble strong drugs conveyed in nonvolatile fluid vehicles] into powders appropriate for tableting or epitome. Straightforward mixing of such fluid prescriptions with determined amounts of a powder substrate comprising of certain excipients alluded to as the transporter and covering powder materials can yield dry-looking, nonadherent, free-streaming, and promptly compressible powders [2, 8].

3. Idea of Liquisolid Procedure

At the point when a drug that has been disintegrated in a fluid vehicle is integrated into a transporter material with a permeable surface and thickly caught strands inside, for example, cellulose, both retention and adsorption occur. Liquid at first held inside the particle is gotten by the inward development of the particle. Adsorption of fluids happens on the internal and external surfaces of the permeable transporter particles when this cycle arrives at immersion. Second, covering materials with high adsorption properties and enormous unequivocal surface locales award positive stream properties to liquid solid structures. [15,16] In the Liquisolid system, the medicine is presently separated in the liquid vehicle and is conveyed by the powder. The wettability of pellets in crumbling media is one of the parts proposed to figure out the extended breaking down rate from liquid pellets. The non-temperamental dissolvable present in the Liquisolid structure works with the wetting of the medicine particles by cutting down the interfacial strain between the crumbling medium and the tablet surface. Likewise, liquid solids can be expected to show additionally created release profiles for water-insoluble drugs, as the fruitful surface area for wettability and deterioration is uncommonly extended. the component of drug conveyance from liquisolid compacts and is predominantly answerable for the superior disintegration profiles displayed by these arrangements. The wettability of the compacts by the disintegration media is one of the proposed instruments for making sense of the upgraded disintegration rate from the liquisolid compacts. The nonvolatile solvent present in the liquisolid framework works with wetting of drug particles by diminishing interfacial pressure between disintegration medium and tablet surface. [17,18]

4. Hypothesis of Liquisolid Frameworks [15-22]

A powder can hold just restricted measures of fluid while keeping up with satisfactory stream and pressure properties. To work out the necessary measures of powder excipients (transporter and covering materials) a numerical methodology for the detailing of liquisolid frameworks has been created by Spireas. This approach depends on the stream capable (Φ-esteem) and compressible (Ψ-number) fluid maintenance potential presenting constants for each powder/fluid mix. [15] The Φ-worth of a powder addresses the greatest measure of a given non-volatile fluid that can be held inside its mass [w/w] while keeping a stream capacity. The stream capacity not set in stone from the powder stream or by estimation of the point of rest. [17,18] The Ψ-number of a powder is characterized as the most extreme measure of fluid the powder can hold inside its mass [w/w] while keeping up with acceptable similarity bringing about compacts of adequate hardness with no fluid spilling out during pressure. [19,20]

The compactability not entirely settled by the purported "plasticity" which depicts the most extreme (level) pounding strength of a one-gram tablet compacted at adequately high pressure powers. The expressions "acceptable flow and compression properties" suggest the ideal and consequently when the ideal fluid burden not entirely settled, the suitable amounts of carrier (Qo) and coating (qo)material properties which should be met by the last liquisolid definition. Depending on the excipient ratio (R) of the powder substrate an acceptably flowing and compressible liquisolid system can be obtained only if a maximum liquid load on the carrier defined as the weight ratio of the liquid formulation (W) and the carrier material (Q) in the system: [21,22]

$$Lf = W/Q \text{------} (1)$$

R represents the ratio between the weights of the carrier.

(Q) and the coating(q) material present in the formulation:

$$R = Q/q \text{------} (2)$$

The liquid load factor that ensures acceptable flowability (Lf) can be determined by:

$$Lf = \Phi + \varphi.(1/R) \text{ ----- } (3)$$

where Φ and φ are the Φ-values of the carrier and coating material, respectively. Similarly, the liquid load factor for production of liquisolid systems with acceptable compact ability

(ΨLf) can be determined by:

$$\Psi Lf = \Psi + \psi * (1/R) \text{ ------- } (4)$$

where Ψ and ψ are the Ψ-numbers of the carrier and coating material, respectively.

Therefore, in liquisolid formulation parameters of various powder excipients with commonly used liquid vehicles are listed. Therefore, the optimum liquid load factor(Lo) required to obtain acceptably flowing and compressible liquisolid systems are equal to either ΦLf or ΨLf, which ever represents the lower value. required to convert a given amount of liquid formulation (W) into an acceptably flowing and

compressible liquisolid system may be calculated as follows:

$Q0 = W/Lo$ and $q0 = Q0/R$

The validity and applicability of the above mentioned principles have been tested and verified by producing liquisolid compacts possessing acceptable flow and compaction properties.

5. Concept of Liquisolid Technology

Retention and adsorption occur when the drug breaks down in the fluid medium and fuses into a transporter material with a permeable surface and tightly knotted filaments inside, similar to cellulose. The interior surface of the particle initially absorbs the fluid. [23,24] Adsorption of fluid onto the interior and external surfaces of the permeable transporter molecule happens after submersion. By then, the covering material's large surface zone and high adsorptive qualities offer the liquid-solid structure engaging stream characteristic.

The enhanced weakening rate from Liquisolid compacts is suggested to be partially explained by the wettability of compacts in disintegrating medium. [24] Wetting of arranging particles is made possible by the non-inconsistent dissolvable in the liquidsolid structure, which lowers the interfacial load between the tablet surface and the disintegrating medium. Liquisolid tablets' broad wettability expansion and attractive surface area for separation means that they may be trusted to disclose redesigned discharge profiles of water-insoluble medications. [25,26]

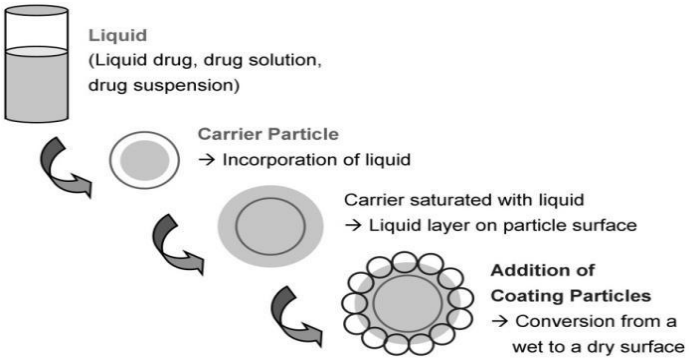

Fig. 1 Concept of Liquisolid Technology

6. Liquisolid Systems' Improved Medication Release Mechanisms

The three recommended devices have a larger pharmaceutical surface area that may be released, a larger medication fluid solubility, and better medication particle wettability. [27]

6.1 Increased Drug Surface Area

When the drug within liquisolid framework has completely disintegrated in the fluid medium, it is found in the powder substrate in an atomically dispersed, solubilised condition. [28] Thus, the amount of drug surface area that is available for release is significantly more than the amount of medication particles contained in simply packed tablets. Consequently,

$$FM = Sd \; / \; Cd$$

where, FM =1 if Sd ≥ Cd

6.2 Increased Aqueous Solubility of the Drug

It is common that Cs, the medicine's solvency, may be increased using liquisolid frameworks, even in the absence of the main improvement factor for medication release. In actuality, the rather restricted amount of fluid vehicle in a liquisolid molecule is insufficient to increase the drug's overall solvency in the aqueous disintegration medium. [29] However, given that the fluid vehicle functions as a co-dissolvable agent, the amount of fluid vehicle that diffuses out of a single liquisolid molecule along with the medication atoms may be sufficient to increase the medication's watery solubility at the strong/fluid point of interaction between the liquisolid essential molecule and the delivery medium in this microenvironment. [30, 31]

6.3 Improved Wetting Properties

Wetting of the liquisolid vital particles is advanced because the fluid vehicle can function as a surface dynamic specialist or has a reduced surface strain.

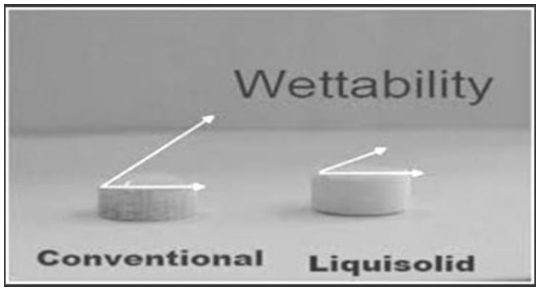

Fig. 2 Comparison of wettability between conventional tablet and Liquisolid compacts

7. Components of liquisolid compact [33-35]

7.1 Drug

The drug used in liquisolid systems must be water insoluble, low dose drug. It must be in BCS class II. It should have water insolubility or fairly dissolvable in water.

7.2 Non-Volatile Solvent

It must be inert water miscible, not highly viscous and should have high boiling point.
Eg: PEG 200 and 400, Glycerin, N, N dimethyl acetamide, Span 80 and19, Tween 80and19 Propylene glycol and Fixed oils etc.

7.3 Carrier Materials

These are highly porous materials and have a wide surface area and the recommended to absorb the drugs on to them.
Eg: Cellulose (microcrystalline and amorphous), starch, sorbitol, Lactose, MCC (Avicel PH102), DCP, Eudragit RS and RL.

7.4 Coating Materials

There are fine materials having a particle size range from 10 nm to 5000 mm in diameter. These must be highly adsorptive to cover the carrier particles and show dry look.
Eg: Silica of various grades like cab-o-sil M5, Aerosil200 and Syloid 244fp etc.

7.5 Disintegrants

These are used to break the compacts to smaller particles.
Eg: Crosscarmellose sodium, Crosspovidone, Explotab and Pre gelatinized starch etc.

7.6 Lubricants

These are intended to reduce the friction.
Eg: Stearic acid, Stearic acid salts and Talc etc.

7.7 Glidants

Intended to promote the flow between particles by reducing the friction. Eg: Silica derivatives, Talc and Corn starch etc.

8. Classification of Liquisolid Systems

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

The first two can be made by converting drug suspensions (like gemfibrozil suspension in Polysorbate) or drug solutions (like prednisolone solution in propylene glycol) into liquisolid systems. The latter can be made by formulating liquid drugs (like clofibrate, liquid vitamins, etc.). Because the drug solution or suspension is made with non-volatile solvents, the liquid vehicle does not evaporate, allowing the medication to be carried inside the liquid system and distributed throughout the finished product. [36]

B. Based on the formulation technique used, liquisolid systems maybe classified into two categories:

1. Liquisolid compacts
2. Liquisolid microsystems

Liquisolid microsystems are based on a novel concept that uses a similar methodology along with the addition of an additive, such as Polyvinylpyrrolidone [PVP], in the liquid medication that is incorporated into the carrier and coating materials to produce an acceptably flowing admixture for encapsulation. Liquisolid compacts are prepared using the previously described method to produce tablets or capsules. The benefit of this novel method is that liquisolid microsystems produced by it may have unit sizes up to five times smaller than liquisolid compacts. [37]

9. General Procedure for Liquisolid Tablets

The first step in the liquisolid tablet production process is weighing and dissolving a precisely measured quantity of pure medication in a solvent to a molecularly dispersed state. Trial and error techniques were employed to achieve desirable flow features, such as adjusting the carrier:coating material ratio from 50:1 to 5:1 ratios in accordance with Liao's newly presented mathematical model expressions. Pour the appropriate amount of this liquid medicine onto the carrier material. A appropriate disintegrant is added to the carrier material after the liquid drug has been absorbed both internally and outwardly. In order to obtain good compression characteristics, coating material was applied at the end to make it seem dry and cling to the carrier material. [38]

Liquid medicine is mixed with cellulose-based carrier material, which has a porous outside and tightly matted fibres inside. Both absorption and adsorption occur, meaning that once the process reaches saturation, the liquid is adsorbed onto the internal and exterior surfaces of the porous carrier particles. The liquid is absorbed into the interior of the particles and is retained by its internal structure.

The best excipients for this stage are those with tiny, extremely adsorptive particles, including different forms of amorphous silicon dioxide (silica). To create liquisolid compacts in the dosage form of tablets or capsules, several substances, such as lubricants, disintegrants, polymers, and binders, can be included with the completed liquisolid systems prior to compression or encapsulation. [20, 21]

Drug determination using several non-volatile solvents. These are accomplished by making saturated drug solutions in non-volatile solvents and performing spectrophotometric analysis on them. In order to create saturated solutions, an excess of the medication is added to the vehicles, and they are shaken steadily for the designated amount of time on a shaker. Subsequently, the solutions undergo filtration and spectrophotometric analysis. [22]

10. Advantages of liquisolid tablets [15, 35, 38]

1. Soft gelatin capsules are more expensive than liquidsolid solutions.
2. The process of production is comparable to that of regular tablets.
3. With the right chemicals in the formulation, drug release may be altered.
4. The formulation allows for molecular dispersion of the medication.
5. It is also feasible to produce goods industrially.
6. Better bioavailability than with traditional pills can be achieved.

11. Uses for Liquisolid Compacts [15, 35, 38]

1. Liquid-solid compositions yield rapid release rates.
2. These work well for both liquid lipophilic medicines and solid medications that are insoluble in water.
3. This approach has been used to achieve sustained release of water-soluble medications, such as propranolol hydrochloride.
4. Improvement of solubility and dissolution.
5. Creating tablets with controlled release.
6. Use in probiotic formulations.

12. Limitation [32, 35]

1. Not relevant to the insoluble drug formulation at large doses.
2. The pill becomes difficult to swallow when extra carrier is added to create free-flowing powder, increasing the weight to more than one gramme.
3. Because liquid medication may be forced out of the liquid-solid tablet during compression, leaving tablets with an inadequate hardness level, acceptable compression qualities might not be reached.
4. It might not be possible to introduce this technique on an industrial scale and find a solution to the issue of combining tiny volumes of viscous liquid solutions onto huge amounts of carrier material.

13. Evaluation of Liquisolid Systems [31-38]

13.1 Flow behavior

When making therapeutic dosage forms, a powder's flowability is essential to avoid excessive dose variations. The liquisolid systems' flow properties were verified by the utilisation of Hausner's ratio, Carr's index, and angle of repose. [31]

13.2 Pre Compression Studies of the Prepared Liquisolid Powder Systems

It is necessary to conduct FTIR, DSC, XRD, and SEM tests to ensure that the selected excipients are compatible. In order to determine the optimal compression formulas, flowability studies will be carried out prior to compressing the powders into dosage forms such as tablets and capsules. [33]

13.3 Fourier Transform Infra Red Spectroscopy (FT-IR)

The FT-IR spectra of generated melt granules are recorded using the FTIR-8400 spectrophotometer. Under the same circumstances, the potassium bromide (KBr) pellet technique is used to acquire the background spectrum. A single average scan with a ratio versus a background interfereogram, obtained between 400 and 4000cm-1, is used to construct each spectrum. Programs are utilised to assess spectra. [36]

13.4 Differential Scanning Calorimetry (DSC)

The medicine and excipients employed in the liquisolid system formulation are evaluated for their thermotropic qualities and thermal behaviours using differential scanning calorimetry, or DSC. When the distinctive drug peaks completely vanish, a drug solution forms in the liquisolid powdered system,

meaning the drug is molecularly distributed throughout the liquisolid matrix. [35]

13.5 X-Ray Diffraction (XRD)

X-ray diffraction (XRD) patterns are created for the manufactured liquisolid compacts and the physical combination of the medicine and excipients used in formulation in order to characterise the crystalline state. The X-ray diffractogram's liquisolid compacts' absence of positive individual drug peaks suggests that the drug has primarily transitioned from crystalline to amorphous or solubilised form. The medication was supposed to dissolve in the liquid vehicle and produce a solid solution inside the carrier matrix, which is why the liquisolid system lacked crystallinity. The drug's apparent solubility and rate of dissolution may benefit from this amorphization or solubilisation in the liquisolid compacts. [32, 34]

13.6 Scanning Electron Microscopy (SEM)

Scanning electron microscopy (SEM) is utilized to assess the morphological characteristics of the raw materials and the drug-carrier systems.

13.7 Contact Angle Measurement

The imaging approach is used to calculate liquidsolid tablet contact angles, which determines wettability. The most widely used approach, called the imaging method, measures the contact angle of a liquid drop directly on the flat surface of a solid. When the medication is soaked in dissolving medium, a drop of this solution is put to the tablet's surface. To find the contact angles, measurements are taken of the sphere drop's height and diameter on the tablet. [31, 32]

13.8 In Vitro Dissolution Studies

Several investigations have demonstrated that the liquisolid compact method might provide a workable solution for the formulation of non-water soluble drugs. Liquisolid compacts have been effective in boosting the release of drugs such piroxicam, hydrocortisone, prednisolone, and carbamazepine in vitro. Compared to their brand-name equivalents, nifedipine, gemfibrozil, and ibuprofen, among other water-insoluble drugs, have shown improved absorption in rats. [33, 34]

13.9 In Vivo Evaluation of Liquisolid Systems

It may be possible to improve the release of poorly soluble drugs by using this liquisolid approach. The study compared the absorption characteristics of commercial pills with hydrochlorothiazide liquisolid compacts using Beagle dogs. The area under the plasma concentration-time curve, absolute bioavailability, and peak plasma concentration of the liquisolid and commercial tablets differed noticeably from one another. For the average residence duration, average absorption time, and average absorption rate, no appreciable differences were found. Compared to the commercial form, liquidsolid compacts exhibited an absolute bioavailability of the medicine that was 15% higher. [37, 38]

14. Conclusion

Liquisolid technology is one of the most promising techniques for enhancing medication release and water solubility among other recognised techniques. By simply physically mixing liquids—such as solutions or suspensions of poorly soluble pharmaceuticals in a non-volatile liquid vehicle—with certain excipients known as the carrier and the coating material, this method transforms liquids into powders that flow and compress well. By choosing the right liquid vehicle, carrier, and coating materials, liquisolid compacts may be optimised for maximum drug release rates, which are found in products having a liquid part containing a drug solution. Drug release from liquisolid compacts may be expedited even further by the inclusion of disintegrants.

It is also possible to produce sustained release formulations with a zero order release pattern using the liquisolid technology. This will result in the achievement of a steady plasma level that is sustained over the course of the dosage interval. The choice and concentration of excipients, such as liquid vehicle, retarding agent (matrix forming material), carrier, and coating material, are crucial for sustained release liquisolid compacts. The cheap production costs, easy to use manufacturing technique, and potential for industrial manufacturing due to the compaction and superior flow characteristics of liquisolid formulations make the liquisolid approach a viable technology.

References

1. Sharma, A., Jain, C.P. Techniques to enhance solubility of poorly soluble drugs: a review. J.Global Pharm. Tech., 2010, 2: 18-28.
2. Saharan, V.A.,Kukkar, V., Kataria, M., Gera, M., Choudhury, P.K. Dissolution enhancement of drugs. Part I: technologies and effect of carriers. Int. J. Health Res.,2009, 2: 107-124.
3. Saharan, V.A., Kukkar, V., Kataria, M., Gera, M., Choudhury, P.K. Dissolution enhancement of drugs. Part II: effect of carriers. Int. J. Health Res, 2009, 2: 207-223.
4. S. Spireas, US Patent, US 6,423,339 B1.
5. SpirasS.Liqui-solid systems and methods for preparing same, United States patent6, 423,339 B1, (2002).
6. Spiras S, Bolton SM. Liqui-solid systems and methods for preparing same, United States patent 6,096,337, 2000.
7. Spiras S, Wang T, Grover R. Effect of powder substrate on dissolution properties of methylclothiazideLiqui-solid compacts, Drug. Dev. Ind. Pharm., 1999; 25: 63-168.
8. Charman SA, Charman WN. Oral modified release delivery systems, In: Rathbone MJ. Hadgraftb J, Roberts MS. Modified Release Drug Delivery Technology, New York, 2003; 1-9.
9. Papadimitriou SA, Bikiaris D, Avgoustakis K. Microwave-induced enhancement of the dissolution rate of poorly water-soluble tibolone from poly (ethylene glycol) solid dispersions. J Appl Polymer Sci, 2008; 108: 1249-1258.
10. Smirnova I, Suttiruengwong S, Seiler M, Arlt M. Dissolution rate enhancement by adsorption of poorly soluble drugs on hydrophilic silica aerogels. Pharm Dev Tech, 2004; 9: 443-452.
11. Fahmy RH, Kassem MA. Enhancement of Famotidine dissolution rate through liquisolid tablet formulation: In vitro and In vivo evaluation. Eur.J.Pharm. Biopharm, 2008; 69:993- 1003.
12. Charman SA, Charman WN. Oral modified release delivery systems, In: Rathbone MJ. Hadgraftb J, Roberts MS. Modified Release Drug Delivery Technology, New York, 2003; 1-9.
13. Papadimitriou SA, Bikiaris D, Avgoustakis K. Microwave-induced enhancement of the dissolution rate of poorly water-soluble tibolone from poly (ethylene glycol) solid dispersions.J Appl Polymer Sci, 2008; 108: 1249-1258.
14. Smirnova I, Suttiruengwong S, Seiler M, and Arlt M. Dissolution rate enhancement by adsorption of poorly soluble drugs on hydrophilic silica aerogels. Pharm Dev Tech, 2004; 9: 443-452.
15. Jarowski CI, Rohera BD, Spireas S. Powdered solution technology: principles and mechanism. Pharm Res, 9, 1992, 1351- 1358.
16. Barzegar JM, Javadzadeh Y, Nokhodchi A, Siahi-Shadbad MR. Enhancement of dissolution rate of piroxicam using liquisolid compacts. II Farmaco, 60, 2005, 361-365.
17. Spireas SS. Theoretical and Practical Aspects of liquisolid compacts. Ph.D. Thesis, St. John's University, New York, 1993.
18. Javadzadeh Y, Navimipour B, Nokhodchi A. Liquisolid technique for dissolution rate enhancement of a high dose water-insoluble drug [carbamazepine]. Int J Pharm 2007;341: 26-34.
19. Spiras S, Wang T, Grover R. Effect of powder substrate on dissolution properties of methyclothiazide Liquisolid Compacts. Drug Dev Ind Pharm 1999;25:63-168.
20. Banker GS, Anderson NL. Tablets. In: The theory and practice of industrial pharmacy. Lachman L, Liberman HA, Kanig JL. edn. 3rd. Varghese Publishing House, Bombay, India; 1987. p. 293- 345.
21. Javadzadeh Y, Siahi MR, Asnaashri S. An investigation of physicochemical properties of piroxicam liquisolid compacts. Pharm Dev Tech 2007;12:337-4.
22. Spiras S. Liquisolid systems and methods for preparing same, United States patent 2002;6:423, 339.
23. Spiras S, Bolton SM. Liquisolid systems and methods for preparing same, United States Patent 2000;6:96, 337.
24. Bolton S, Spireas S. Sustained-release liquisolid compacts. In:25th International Symposium on Controlled Release of Bioactive Materials., Nevada, USA; 1998. p. 138-9.
25. Staniforth J. Powder flow. In: M Aulton. Pharmaceutics: the Science of Dosage Form Design, Edinburgh; 2002. p. 197–210.
26. International Symposium on Controlled Release of Bioactive Materials., Nevada, USA; 1998. p. 138-9.
27. Wells J. Pharmaceutical Preformulation: The physicochemical properties of drug substances. In: Aulton M. Pharmaceutics: the Science of Dosage Form Design, Edinburgh; 2002. p. 114-38.
28. Nokhodchi A. The effect of type and concentration of vehicles on the dissolution rate of a poorly soluble drug (indomethacin) from liquisolid compacts. J Pharm Sci 2005;8:18-25.
29. Amrit B Karmarkar, Indrajeet D Gonjari, Avinash H Hosmani, Pandurang N Dhabale, Satish B Bhise. Liquisolid tablets: a novel approach for drug delivery. Int J Health Res 2009;2:45-50.
30. PM Sabale. Liquisolid technique for enchancement of dissolution properties of Fenofibrate. Int J Pharma Sci Res2012;3:1481-6.
31. Sambasiva RA, Naga AT. Liquisolid technology: an overview. Int J Res Pharm Biomed Sci 2011;2:401-9.
32. Subhramanyam CVS. Textbook of physical pharmaceutics. 2nd edition. Vallabh Prakashan. New Delhi; 2001.
33. Vajir S. Enhancement of dissolution rate of poorly watersoluble diclofenac sodium by liquisolid technique. Int J Pharm Chem Sci 2012;1:989-1000.edition. Vallabh Prakashan. New Delhi; 2001.
34. Patric JS. Martin's physical pharmacy and pharmaceutical sciences. 5th ed. Lippincott Williams and Wilkins; 2003.
35. Chuahan PV, Patel HK, Patel BA, Patel KN, Patel PA. Liquisolid technique for enhancement of dissolution rate of ibuprofen. Int J Pharm Res Scholars 2012;1:268-80.
36. Patric JS. Martin's physical pharmacy and pharmaceutical sciences. 5th ed. Lippincott Williams and Wilkins; 2003
37. Nighute AB, Bhise S B, Enhancement of dissolution rate of rifabutin by preparation of microcrystals using solvent change method, Int. J. PharmTech. Res. 1: 142-148 (2009).
38. Patel VP, Patel NM, Dissolution enhancement of glipizide using liquisolid tablet technology, Indian Drugs. 45(4): 318- 323 (2008).