ejpmr, 2020,7(7), 393-404

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

SOLID DISPERSION A METHOD FOR SOLUBILITY ENHANCEMENT: A REVIEW

Suraj Mali*, Deeliprao Derle and Shaila Govind

Department of Pharmaceutics, NDMVP's College of Pharmacy Nashik, (MH) India.

***Corresponding Author: Suraj Mali**

Department of Pharmaceutics, NDMVP's College of Pharmacy Nashik, (MH) India.

Article Received on 04/05/2020 **Article Revised on 25/05/2020** **Article Accepted on 15/06/2020**

ABSTRACT

Strong scatterings have pulled in impressive enthusiasm as proficient methods for improving the disintegration rate and henceforth the bioavailability of a scope of hydrophobic medications. This article surveys the different arrangement procedures for strong scattering and gathers a portion of the ongoing innovation moves. The various kinds of strong scatterings dependent on the atomic plan have been featured. A portion of the functional angles to be considered for the readiness of strong scatterings, for example, determination of transporter and strategies for physicochemical portrayal, alongside knowledge into the sub-atomic plan of medications in strong scatterings are likewise examined. At last, an inside and out method of reasoning for restricted commercialization of strong scatterings and ongoing restoration has been thought of.

KEYWORDS: Strong scatterings, transporter, dissolvability, disintegration, bioavailability.

INTRODUCTION

The oral course of medication organization is the most well-known and favoured technique for conveyance because of comfort and simplicity of ingestion. From a patient's point of view, gulping a dose structure is an agreeable and a recognizable method for taking medicine. Therefore, understanding consistence and consequently tranquilize treatment is normally increasingly successful with orally directed meds as contrasted and different courses of organization, for instance, parenteral. In spite of the fact that the oral course of organization is liked, for some medications it very well may be a dangerous and wasteful method of conveyance for various reasons. Restricted medication assimilation bringing about poor bioavailability is central among the potential issues that can be experienced while conveying a functioning specialist by means of the oral course. Medication retention from the gastrointestinal (GI) tract can be restricted by an assortment of elements with the most critical benefactors being poor watery dissolvability as well as poor layer porousness of the medication atom. While conveying a functioning operator orally, it should initially break down in gastric or potentially intestinal liquids before it would then be able to saturate the films of the GI tract to arrive at foundational flow. In this way, a medication with poor fluid solvency will ordinarily show disintegration rate restricted assimilation, and a medication with poor film penetrability will regularly display penetration rate constrained ingestion. Consequently, two zones of pharmaceutical research that emphasis on improving the oral bioavailability of dynamic specialists include: (I) upgrading dissolvability and disintegration pace of ineffectively water-solvent medications and (ii) upgrading penetrability of inadequately porous medications. This article centers around the previous, specifically, the utilization of strong scattering innovations to improve the disintegration.

Qualities of inadequately water-dissolvable medications and thus their oral bioavailability. Various strong scattering frameworks have been shown in the pharmaceutical writing to improve the disintegration properties of inadequately water-dissolvable medications. Different strategies, for example, salt development, complexation with cyclodextrins, solubilization of medications in solvent(s), and molecule size decrease have additionally been used to improve the disintegration properties of inadequately water-dissolvable medications; notwithstanding, there are significant restrictions with every one of these procedures. Then again, definition of medications as strong scatterings offers an assortment of handling and excipient alternatives that consider adaptability while planning oral conveyance frameworks for ineffectively water dissolvable medications.

A significant part of the exploration that has been accounted for on strong scattering advances includes drugs that are ineffectively water-dissolvable and exceptionally penetrable to natural layers similarly as with these medications disintegration is the rate constraining advance to assimilation. Consequently, the theory has been that the pace of assimilation in vivo will be simultaneously quickened with an expansion in the pace of medication disintegration. In the

Biopharmaceutical Classification System (BCS) drugs with low fluid dissolvability and high film penetrability are arranged as Class II drugs Presentation.

The oral course of medication organization is the most well-known and favored technique for conveyance because of comfort and simplicity of ingestion. From a patient's point of view, gulping a dose structure is an agreeable and a recognizable methods for taking medicine. Therefore, understanding consistence and consequently tranquilize treatment is normally increasingly successful with orally directed meds as contrasted and different courses of organization, for instance, parenteral. In spite of the fact that the oral course of organization is liked, for some medications it very well may be a dangerous and wasteful method of conveyance for various reasons. Restricted medication assimilation bringing about poor bioavailability is central among the potential issues that can be experienced while conveying a functioning specialist by means of the oral course. Medication retention from the gastrointestinal (GI) tract can be restricted by an assortment of elements with the most critical benefactors being poor watery dissolvability as well as poor layer porousness of the medication atom. While conveying a functioning operator orally, it should initially break down in gastric or potentially intestinal liquids before it would then be able to saturate the films of the GI tract to arrive at foundational flow. In this way, a medication with poor fluid solvency will ordinarily show disintegration rate restricted assimilation, and a medication with poor film penetrability will regularly display penetration rate constrained ingestion. Consequently, two zones of pharmaceutical research that emphasis on improving the oral bioavailability of dynamic specialists include: (I) upgrading dissolvability and disintegration pace of ineffectively water-solvent medications and (ii) upgrading penetrability of inadequately porous medications. This article centers around the previous, specifically, the utilization of strong scattering innovations to improve the disintegration.

Qualities of inadequately water-dissolvable medications and thus their oral bioavailability. Various strong scattering frameworks have been shown in the pharmaceutical writing to improve the disintegration properties of inadequately water-dissolvable medications. Different strategies, for example, salt development, complexation with cyclodextrins, solubilization of medications in solvent(s), and molecule size decrease have additionally been used to improve the disintegration properties of inadequately water-dissolvable medications; notwithstanding, there are significant restrictions with every one of these procedures. Then again, definition of medications as strong scatterings offers an assortment of handling and excipient alternatives that consider adaptability while planning oral conveyance frameworks for ineffectively water dissolvable medications. In this way, strong scattering innovations are especially encouraging for improving the oral ingestion and bioavailability of BCS Class II drugs. With ongoing advances in sub-atomic screening strategies for recognizing potential medication competitors, an expanding number of ineffectively water-dissolvable medications are being distinguished as potential remedial operators. Actually, it has been evaluated that 40% of new substance elements as of now being found are inadequately water-solvent Unfortunately, a considerable lot of these potential medications are relinquished in the beginning periods of advancement because of dissolvability concerns. It is in this way turning out to be progressively increasingly significant that techniques for beating dissolvability restrictions be distinguished and applied industrially with the end goal that the potential helpful advantages of these dynamic particles can be figured it out Meaning of strong scatterings: The term strong scattering alludes to a gathering of strong items comprising of in any event two unique parts, by and large a hydrophilic lattice and a hydrophobic medication. The network can be either crystalline or indistinct. The medication can be scattered molecularly, in indistinct particles (bunches) or in crystalline particles.[2,9,36]

Table 1: In light of their atomic course of action, six unique kinds of strong scatterings can be recognized as appeared in.[4,9,21,40,47,50,53,58,74]

Sr. No.	Type of strong dispersion	Polymer(nature)	Drug (nature)	Remark	Reference
1	Eutectics	Crystalline	Crystalline	The first sort of strong scattering prepared	(Chiou and Riegelman, 1971)
2	Amorphous precipitations in crystalline matrix	Crystalline	Amorphous	Rarely encountered	(Breitenbach AH, 2002); (Mullins and Macek, 1960)
3	Solid arrangements				
	Consistent strong solutions	Crystalline	Molecularly scattered	Miscible at all structure, never prepared	(Goldberg et al., 1965)
	Spasmodic strong solutions	Crystalline	Molecularly dispersed	Partially miscible, 2 stages despite the fact that medication is molecularly dispersed.	Sekiguchi K and Obi N (1961)

	Substitutional strong solutions	Crystalline	Molecularly dispersed	Molecular distance across of medication (solute) varies under 15% from the lattice (dissolvable) measurement. All things considered the medication and lattice are substitutional. Can be ceaseless or intermittent. At the point when intermittent: 2 stages despite the fact that medication is molecularly dispersed	(Rastogi and Verma, 1956); (Wilcox et al., 1964)
	Interstitial strong solutions	Crystalline	Molecularly dispersed	Drug (solute) atomic measurement under 59% of network (dissolvable) distance across. Normally constrained miscibility, broken. Model: Drug in helical interstitial spaces of PEG.	(Chiou and Riegelman, 1971)
4	Glass suspension	Amorphous	Crystalline	Particle size of scattered stage subject to cooling/dissipation rate. Acquired after crystallization of medication in formless matrix	(Chiou and Riegelman, 1971); (Sarkari M et al., 2002)
5	Glass suspension	Amorphous	Amorphous	Particle size of scattered stage subject to cooling/dissipation rate numerous strong scatterings are of this type	(Chiou and Riegelman, 1971); (Sarkari M et al., 2002)
6	Glass arrangement	Amorphous	Molecularly dispersed	Requires miscibility OR strong solvency, complex development or upon quick cooling OR dissipation during planning, many (later) models particularly with PVP	Simonelli AP et al., 1969

First generation

In the first generation, strong scatterings was created by crystalline transporters. When all is said in done, the crystalline bearers, for example, sugar and urea are utilized. The crystalline bearers are thermodynamically progressively steady. In any case, the impediment is some of medications are not reasonable with crystalline bearers its can't discharge the medication in disintegration media as a result of crystalline nature of API. In this crystalline bearers unfit to change over medication nature from crystalline to formless. By nearness of crystalline nature of medication it prompts low dissolvability and bio accessibility.[24,33]

Second generation

The second-generation strong scatterings are utilized as nebulous bearers rather than crystalline transporters like polymers. When contrasted with the original, second-generation transporters are progressively useful by changing over medication in formless nature, which was increasingly valuable for sedate solvency in disintegration media. Various polymers, for example, polyvinylpyrrolidone (PVP), hydroxypropylmethyl cellulose (HPMC), polyethylene glycol (PEG), and HPMC. Utilizing these polymers, the medication nature was changed over and improves in bioavailability **[39, 66].**

Third generation

These days, the third-generation strong scatterings are utilized ceaselessly for improving better dissolvability reason. In this third generation, both the mix of surfactant and polymers and mix of polymers were utilized. It will progressively supportive for changing over medication crystalline nature to undefined nature and improved dissolvability in disintegration media in view of surfactant. In this third generation strong scattering procedure is best to upgrade dissolvability and bio accessibility of ineffectively water solvent medications.[13,28]

Preferences OF Strong Scattering

1. Particles with decreased molecule size

Atomic scatterings, as strong scatterings, speak to the keep going state on molecule size decrease, and after transporter disintegration the medication is molecularly scattered in the disintegration medium. Strong scatterings apply this rule to tranquilize discharge by making a blend of an ineffectively water dissolvable medication and profoundly solvent transporters A high surface territory is shaped, bringing about an expanded disintegration rate and, thusly, improved bioavailability.[32]

a) Particles with improved wettability

A solid commitment to the upgrade of medication solvency is identified with the medication wettability improvement verified in strong dispersionsIt was seen that even transporters with no surface action, for example, ureaimproved sedate wettability. Bearers with surface action, for example, cholic corrosive and bile salts. At the point when utilized, can significantly expand the wettability property of medication. In addition, bearers can influence the medication disintegration

profile by direct disintegration or co-dissolvable impacts.[25,46,54]

b) Particles with higher porosity

Particles in strong scatterings have been found to have a higher level of porosity The increment in porosity likewise relies upon the bearer properties; for example, strong scatterings containing direct polymers produce bigger and more permeable particles than those containing reticular polymers and, in this way, bring about a higher disintegration rate.[20,68]

c) Drugs in shapeless state

Inadequately water dissolvable crystalline medications, when in the shapeless state will in general have higher dissolvability The improvement of medication discharge can for the most part be accomplished utilizing the medication in its nebulous state, in light of the fact that no vitality is required to separate the gem grid during the disintegration process In strong scatterings, drugs are introduced as supersaturated arrangements after framework disintegration, and it is conjectured that, if drugs hasten, it is as a metastable polymorphic structure with higher solvency than the most steady gem structure

For drugs with low gem vitality (low dissolving temperature or warmth of combination), the indistinct sythesis is principally directed by the distinction in softening temperature among medication and bearer. For drugs with high gem vitality, higher undefined creations can be gotten by picking transporters, which show specific cooperations with them.[25,32,37,45,63,72]

Planning Of Strong Scatterings

Different planning techniques for strong scatterings have been accounted for in writing. These strategies manage the test of blending a grid and a medication, ideally on an atomic level, while network and medication are commonly ineffectively miscible. During a large number of the arrangement methods, de-blending (mostly or complete), and development of various stages is watched. Stage detachments like crystallization or arrangement of undefined medication groups are hard to control and subsequently undesirable. It was at that point perceived in one of the principal concentrates on strong scatterings that the degree of stage detachment can be limited by a quick cooling technique Generally, stage division can be forestalled by keeping up a low atomic versatility of grid and medication during arrangement. Then again, stage partition is forestalled by keeping up the main impetus for stage division low for instance by keeping the blend at a raised temperature in this manner keeping up adequate miscibility for whatever length of time that conceivable **[9, 53].**

A. Fusion strategy

The combination strategy is some of the time alluded to as the liquefy technique, which is right just when the beginning materials are crystalline. Accordingly, the more broad term combination strategy is liked. The principal strong scatterings made for pharmaceutical applications were set up by the combination technique. The scattering comprised of sulfathiazole and urea as a framework which were softened utilizing a physical blend at the eutectic structure, trailed by a cooling step. The eutectic arrangement was picked to acquire concurrent crystallization of medication and framework during cooling. This strategy brought about strong scatterings of type I. Poly (ethylene glycol) (PEG) is a hydrophilic polymer regularly used to plan strong scatterings with the combination technique. This frequently brings about strong scatterings of type III since numerous medications are consolidated as discrete particles in the helical structure present in a crystalline PEG. The helices are adjusted in organized style, representing that PEG effectively solidifies. Another polymer oftentimes applied as a grid in the combination technique is poly (vinyl pyrollidone) PVP. PVP, provided in the indistinct state, is warmed to over its Tg (glass change temperature). The medication needs to meld with or disintegrate in the rubbery lattice, which is thusly cooled to vitrify the strong scattering. When PVP is utilized as framework, strong scatterings of type V or VI are acquired. The method of joining of the medication relies upon the PVP-tranquilize miscibility and the readiness technique. Crushing is required to get the strong scattering as powder that is anything but difficult to handle. Although much of the time applied, the combination technique has genuine confinements. Right off the bat, a significant weakness is that the technique must be applied when medication and lattice are perfect and when they blend well at the warming temperature. At the point when medication and grid are contrary two fluid stages or a suspension can be seen in the warmed mixture which brings about an inhomogeneous strong scattering. This can be forestalled by utilizing surfactants Secondly, an issue can emerge during cooling when the medication network miscibility changes. For this situation stage detachment can happen. In reality, it was seen that when the blend was gradually cooled, crystalline medication happened, though quick cooling yielded formless strong dispersions Thirdly, debasement of the medication and additionally framework can happen during warming to temperatures important to combine network and medication. For instance, to soften a sugar framework of galactose a temperature of 169°C was required and so as to get the shiny PVP in the rubbery express a temperature of about 170°C is required. Poly ethylene glycols dissolve at around 70°C and are in this way regularly utilized for the planning of strong scatterings with the combination technique.[1,22,38,51,53,65]

B. Hot liquefy expulsion

Soften expulsion is basically equivalent to the combination strategy aside from that extraordinary blending of the segments is prompted by the extruder. When contrasted with softening in a vessel, the item soundness and disintegration are comparative however dissolve expulsion offers the possibility to shape the warmed medication framework blend into inserts, ophthalmic additions, or oral measurements shapes just

like in the conventional combination process, miscibility of medication and grid can be an issue. Dissolvability parameters are researched to foresee the solid-state miscibility and to choose lattices appropriate for soften expulsion. High shear powers bringing about high nearby temperatures in the extruder be an issue for heat delicate materials However, contrasted with the conventional combination strategy, this method offers the chance of consistent creation, which makes it appropriate for huge scope creation. Moreover, the item is simpler to deal with on the grounds that at the outlet of the extruder the shape can be adjusted to the following preparing step without crushing.[4,18,19,31]

C. Solvent technique

The initial phase in the dissolvable technique is the planning of an answer containing both framework material and medication. The subsequent advance includes the expulsion of solvent(s) bringing about arrangement of a strong scattering. Blending at the sub-atomic level is liked, in light of the fact that this prompts ideal disintegration properties. Utilizing the dissolvable strategy, the pharmaceutical architect faces two difficulties The main test is to blend both medication and network in one arrangement, which is troublesome when they vary essentially in extremity. To limit the medication molecule size in the strong scattering, the medication and grid must be scattered in the dissolvable as fine as conceivable ideally medication and framework material are in the broken down state in one solution. Various systems have been applied to disintegrate the lipophilic medication and hydrophilic network material together in one arrangement.

Low medication fixations are utilized to break down both medication and grid material in water however this requires dissipation of huge measures of dissolvable, making the procedure costly and illogical. Solubilisers like cyclodextrins or surfactants like Tween80® increment the fluid solvency of the medication significantly. Nonetheless, the measure of solubilisers or surfactants in the last item are regularly famous. This outcomes in strong scatterings that, to a huge degree, comprise of solubilisers or surfactants, materials that essentially change the physical properties of the framework (e.g., diminishing of Tg). In addition, just measurement structures with low medication loads are conceivable. Furthermore, they are not generally endured well in the body or may even be poisonous. Chloroform or dichloromethane have been utilized to break down both medication and PVP as framework at the same time. These solvents are utilized likewise in other planning techniques. Nonetheless, as per the ICH-Guidelines, these solvents have a place with Class I, involving the most poisonous solvents. In this way, the utilization of these solvents is unsatisfactory and unrealistic on the grounds that the measure of remaining dissolvable present in the strong scattering subsequent to drying must be beneath as far as possible. The last system for the disintegration of both medication and network is the utilization of dissolvable blends. Water and ethanol, or dichloromethane and ethanol have been utilized for this reason. Be that as it may, disintegration of medication and network in these blends isn't generally conceivable in the necessary focus or ratio The second test in the dissolvable strategy is to forestall stage partition, for example crystallization of either medication or network, during expulsion of the solvent(s).

Evaporating at high temperatures speeds the procedure and diminishes the time accessible for stage partition. Then again, at high temperatures the atomic portability of medication and lattice stays high, preferring stage partition (e.g., crystallization) To dry the arrangements, vacuum drying is frequently utilized The arrangement is dried by the use of vacuum and moderate warming. Now and again, the dissolvable vanishing is quickened by utilizing a rotating evaporator. Subsequently the framed strong scattering is regularly put away in a vacuum desiccator to evacuate the remaining dissolvable. Vacuum drying at raised temperature bears the danger of stage division in light of the fact that the versatility of medication and grid diminishes gradually. Another drying method is shower drying. The arrangement is scattered as fine particles in sight-seeing. Because of the huge explicit surface territory offered by the beads, the dissolvable quickly vanishes and the strong scattering is shaped in practically no time, which might be sufficiently quick to forestall stage partition. Besides, the strong scatterings arranged by shower drying comprise of particles of which the size might be altered by changing the bead size to meet the necessities for additional handling or application (e.g., free streaming particles or particles for inward breath). Splash drying for the most part yields tranquilize in the shapeless state, anyway some of the time the medication may have (somewhat) solidified during handling.

An option in contrast to these drying procedures is freeze drying. In spite of the fact that it is finished up in writing this is a promising and reasonable procedure to fuse medicate substances in balancing out networks the method is ineffectively misused for the planning of strong scatterings. sublimation during freeze drying is just conceivable when the dissolvable remains solidified. Furthermore when the arrangement of a glass is visualized, the example temperature ought to be kept underneath the Tg of the maximally freeze concentrated division. In this way, low example temperatures are required which hinders the procedure. Betageri and Makarla, 1995 utilized a condenser temperature of -75°C, to dry an answer with cyclohexanol as the dissolvable. In table 2 an outline is introduced of a few natural solvents. To get a lyophiliation procedure of adequate term, the dissolvable ought to have an adequately high fume pressure. As can be found in table 2, dimethylsulphoxide (DMSO) has a high softening temperature however it has an exceptionally low fume pressure. Along these lines, DMSO isn't appropriate as a dissolvable for freeze drying. An appropriate dissolvable

that meets the two prerequisites is 2methyl-2-propanol or tertiary butanol (TBA), in light of the fact that it has a high softening temperature just as a high fume pressure. The utilization of TBA in lyophilization is examined by Teagarden Also blends of solvents can be thought of. For instance, while water and DMSO have dissolving purposes of 0°C and 19°C, the blend has eutectic focuses beneath 60°C. The example temperature of such a blend ought to be kept beneath this worth, which causes a moderate sublimation. A significant bit of leeway of freeze drying is that the medication is exposed to insignificant warm worry during the arrangement of the strong scattering. Notwithstanding, the most significant bit of leeway of freeze drying is that the danger of stage partition is limited when the arrangement is vitrified. A much additionally encouraging drying method is splash freeze drying. The dissolvable is splashed into fluid nitrogen or cold dry air and the solidified beads are consequently lyophilized.

The enormous surface territory and direct contact with the cooling specialist result in much quicker vitrification, consequently diminishing the hazard for stage partition to a base Moreover, splash freeze drying offers the possibility to redo the size of the molecule to make them reasonable for additional handling or applications like pneumonic or nasal organization In an electrostatic turning process a medication network arrangement is siphoned through a hole and afterward exposed to an electrical field to shape strands with a distance across of smaller scale or nano-scale. This procedure is confined to a constrained measure of frameworks, on the grounds that solitary a couple of high sub-atomic weight materials are fiber shaping materials. The fiber measurement can be balanced by surface pressure, electrical field and dielectric consistent After fast vanishing of the dissolvable, the filaments can be straightforwardly utilized or processed and further handled Evaporative precipitation into watery arrangements (EPAS) was utilized to cover a colloidal suspension of carbamazepine with square copolymers as settling surfactants. An answer of medication in dichloromethane was showered in a fluid arrangement containing polymeric surfactants as stabilizers. The acquired colloidal suspension was shower dried; freeze dried or splash freeze dried, bringing about strong scatterings of type IV/V. It was presumed that the undefined condition of the medication was best safeguarded with the splash freeze drying process.[10,12,15,23,26,31,42,43,50,56,64,69,73]

D. Supercritical liquid techniques

Supercritical liquid techniques are generally applied with carbon dioxide (CO2), which is utilized as either a dissolvable for medication and framework or as an enemy of dissolvable When supercritical CO2 is utilized as dissolvable, network and medication are disintegrated and showered through a spout, into a development vessel with lower weight and particles are promptly shaped. The adiabatic extension of the blend brings about quick cooling. This method doesn't require the utilization of natural solvents and since CO2 is viewed as earth well disposed, this strategy is alluded to as 'dissolvable free'. The procedure is known as Rapid Expansion of Supercritical Solution (RESS). In any case, the use of this procedure is constrained, in light of the fact that the dissolvability in CO2 of most pharmaceutical mixes is low (<0.01wt-%) and diminishes with expanding extremity. Hence, scaling up this procedure to kilogram-scale will be unreasonable. All other supercritical procedures are precipitation strategies. Albeit for the most part named as dissolvable free, all these supercritical liquid techniques utilize natural solvents to break down medication and network and adventure the low dissolvability of pharmaceutical mixes in CO2. Truth be told, these strategies speak to elective techniques to expel solvents from an answer containing commonly a medication and a polymer. Moneghini and colleagues (2001) announced their strategy as dissolvable free, yet they disintegrated PEG and carbamazepine in CH3)2CO. They utilized a method that is known as the Gas-Anti-Solvent procedure (GAS) or Precipitation from Gas Saturated Solutions (PGSS). The arrangement is brought into contact with packed CO2. The conditions are picked so CO2 is totally miscible with the arrangement under supercritical conditions, though medication and lattice will endless supply of the arrangement. At the point when the volume of the arrangement extends the dissolvable quality (for example the capacity to break down the medication) diminishes. This outcomes in precipitation of lattice and medication. Since this procedure is frequently applied with PEG as lattice, this strategy brings about development of a strong scattering with a crystalline network The second sort of precipitation method includes the showering of an answer containing medication and grid through a spout into a vessel that contains a fluid or supercritical enemy of dissolvable. The supercritical enemy of dissolvable quickly enters into the beads, in which medication and network become supersaturated, take shape and structure particles. The general term for this procedure is Precipitation with Compressed Anti-Solvent (PCA) More explicit instances of PCA are Supercritical AntiSolvent (SAS) when supercritical CO2 is utilized, or Aerosol Solvent Extraction System (ASES), and Solution Enhanced Dispersion by Supercritical liquids (SEDS).

Be that as it may, similarly as with the other dissolvable procedures portrayed in the past segment, the basic advance in these precipitation methods may be the disintegration of medication and lattice in one arrangement. The utilization of water is restricted, on the grounds that the water dissolvability in packed CO2 is constrained Usually natural solvents like dichloromethane or methanol must be applied to disintegrate both medication and network the medication is broken up in a supercritical liquid and presented to strong grid material that swells and ingests the supercritical arrangement. By fluctuating the weight and the hour of presentation, the dissemination procedure can

be controlled. The ingestion stops when the weight is diminished. This procedure is researched for poly (methyl methacrylate) however can be applied for different polymers also.[30,56,61,71]

Transporters Used In Solid Dispersion[49]

PVP

PVP is utilized in an alternate pharmaceutical plan for the most part strong oral dose structures. It is a fine, scentless, white to rich white-shaded hygroscopic material. It is accessible in various evaluations partitioned in its K-esteem. In light of atomic weight, K esteem accessible. K-esteem is from 12 to 120 having sub-atomic load of 2500–3,000,000. Liquefying purpose of PVP is 150°C.The dissolvability is unreservedly solvent in water, acids, chloroform, methanol, and ethanol. The consistency of fluid dissolvability relies upon its sub-atomic weight and fixation utilized **[16, 60].**

Copovidone

Copovidine is usually utilized as a transporter of splash dry innovation because of its low thickness and better restricting property. The depiction of copovidone is a white to yellowish white shading, and it is somewhat have smell part. The liquefying purpose of copovidone is 140°C and it is a steady part. The Tg of copovidone is 106°C. Because of low-temperature glass progress nature, it is utilized as hot liquefy expulsion innovation moreover. The solvency of copovidone is openly solvent in water, glycerol, PEG 400, and ethanol. The thickness is <10 mPas at a focus <10%.[29]

HPMC

It is additionally called as hypromellose. It is broadly utilized in numerous pharmaceutical measurement frames in various ways because of its thickness ranges. The depiction of hypromellose is white to smooth white sinewy material of scentless, and it is hygroscopic in nature. It is accessible in different consistency scopes of extremely low thickness 3 mPas to high gooey scope of 200,000 mPas. The softening point is around 190–200°C and Tg is 170–180°C. the solvency of hypromellose is dissolvable in cool water and n boiling water, ethanol, ether, and dichloromethane. Hypromellose is over and again utilized as a transporter in hot dissolve innovation for change of crystalline polymorphic structure to indistinct polymorphous structure which was valuable for improving solvency.[11,75]

Hydroxypropyl Cellulose (HPC)

HPC is a cellulose where a portion of the hydroxyl gatherings of the cellulose have hydroxyl propylated shaping gatherings. It is a white to marginally yellow-shaded unscented powder. HPC is usually accessible in various evaluations relying upon its thickness. The consistency ranges from 50,000 to 1,250,000 mPas. It is a stable sub-atomic having liquefying point 130°C. The dissolvability of HPC is uninhibitedly solvent in water, dissolvable 1 of every 10 sections dichloromethane, and 1 in 2.5 parts in ethanol. The pH of HPC is 5.0–8.0.[48]

PEG

PEG is a hydrophilic substance. It is accessible in various evaluations dependent on various atomic loads of PEG 200–8000 having sub-atomic loads 190–9000. It is accessible in both fluid structure and strong structures up to review PEG 400 which are fluid materials. The portrayal of PEG fluid evaluations is clear somewhat yellow shading and strong PEG is grayish in shading. It is having extremely low dissolving purpose of 37–48°C. Because of its extremely low softening, nature may have steadiness issues. The solvency of PEG is uninhibitedly solvent in water, glycerine, CH3)2CO, and liquor.[9,70]

Soluplus

Soluplus is a unite copolymer it contains blend of polyvinyl caprolactam, polyvinyl acetic acid derivation, and PEG. The portrayal of Soluplus is white to somewhat yellowish granules. It is a hydrophilic transporter polymer significantly intended for ineffectively dissolvable medications. The benefit of Soluplus improves solubilization property and upgrades bioavailability. Because of its great extrudability, it is primarily utilized as a hot soften expulsion procedure to improve dissolvability. The dissolvability of Soluplus is unreservedly solvent in water, CH3)2CO (up to half), and methanol (up to 45%). The Tg is 70°C. Carboxymethyl cellulose The carboxymethyl cellulose is a steady, hygroscopic substance and portrayal is white to practically white scentless granular powder. It is accessible in various viscosities of low to high (10–12,000). It is basically insoluble in water and dissolving point likewise high 220°C. It has both cover and break down properties.[57,59]

Hypromellose acetic acid derivation succinate

Hypromellose acetic acid derivation succinate is a white to grayish powder and accessible in a few evaluations as per the pH at which polymer breaks up (low - L, medium - M, and high - H). the atomic weight is roughly 55,000–93,000 Da. It is a solvency upgrading operator through strong scattering and is insoluble in gastric liquid yet will grow and disintegrate quickly in the upper digestive system. The Tg is 113°C. The solvency is a blend of ethanol and dichloromethane in 1:1 proportion.[41]

Hypromellose acidic corrosive determination succinate

Hypromellose acidic corrosive determination succinate is a white to grayish powder and open in a couple of assessments according to the pH at which polymer separates (low - L, medium - M, and high - H). the nuclear weight is approximately 55,000–93,000 Da. It is a dissolvability overhauling administrator through solid dispersing and is insoluble in gastric fluid yet will develop and break down rapidly in the upper stomach related framework. The Tg is 113°C. The dissolvability is a mix of ethanol and dichloromethane in 1:1 extent.[55]

Acids

When all is said in done, acids are high solvent parts and are utilized as pH modifiers in pharmaceutical measurement structure which was helpful for pHsensitive atoms. Primarily citrus extract monohydrate and tartaric corrosive are regularly utilized in the plan. These are straightforward crystalline, hygroscopic nature. The low liquefying point acids are changes over into mollify in nature. Various evaluations are accessible dependent on molecule size distinction.[3]

Sugars

Basic sugars are named as monosaccharides which incorporate sucrose, dextrose, glucose, and fructose. A section from this sugar liquor is accessible which is called as polyols including sorbitol, mannitol, and xylitol. Sugars are high solvent hygroscopic substances. The liquefying point run is 160–186°C. Sugar alcohols are uninhibitedly solvent non-hygroscopic substances. These are generally utilized as strong oral dose frames as a plasticizer and diluent. Contrasted with sugars, sugar alcohols are steady substances. The regular liquefying range is 166–168°C. it is appropriate as dampness touchy dynamic fixings because of its non-hygroscopic nature.[35]

Surfactants

Surfactants assume a significant job in pharmaceutical items. Surfactants are surface dynamic operators which lessen surface strain. It improves the wettability of strong surface of medication particles it prompts improved dissolvability. In strong scattering innovation surfactants utilized for mix of polymers since it upgrades dissolvability, disintegration rate and improve the bioavailability. It is arranged into four kinds: Anionic, nonionic, cationic, and amphoteric surfactants. Anionic surfactants It breaks down in water adversely charged particles made. Sodium lauryl sulfate is anionic surfactant usually utilized in definitions.

Cationic surfactants It breaks down in water positive-charged particles made. Quaternary ammonium salts and amines with amide linkages are a portion of the instances of cationic surfactants.

Non-ionic surfactants It contains hydrophilic gatherings. Tweens and ranges are regular instances of non-ionic surfactants.

Amphoteric surfactants These are likewise called as zwitterionic surfactants and it contains both anionic and cationic focuses append to the equivalent sub-atomic. Models are sodium dodecyl sulfates phospholipids **[76].**

Portrayal of Strong Scattering

A. Detection of crystallinity in strong scatterings

A few distinctive sub-atomic structures of the medication in the network can be experienced in strong scatterings Many endeavors have been made to explore the sub-atomic course of action in strong scatterings. Be that as it may, most exertion has been placed into separate among shapeless and crystalline material. For that reason numerous methods are accessible which recognize the measure of crystalline material in the scattering. The measure of nebulous material is never estimated straightforwardly yet is generally gotten from the measure of crystalline material in the example. It ought to be noticed that through the appraisal of crystallinity as strategy to decide the measure of nebulous medication it won't be uncovered whether the medication is available as shapeless medication particles or as molecularly scattered atoms.[26]

At present, the accompanying procedures are accessible to identify (the level of) crystallinity

1. Powder X-beam diffraction can be utilized to subjectively recognize material with long range request. More honed diffraction tops show increasingly crystalline material. As of late created X-beam gear is semi quantitative.
2. Infrared spectroscopy (IR) can be utilized to identify the variety in the vitality conveyance of communications among medication and lattice Sharp vibrational groups demonstrate crystallinity Fourier Transformed Infrared Spectroscopy (FTIR) was utilized to precisely distinguish crystallinities going from 1 to 99% in unadulterated material However in strong scatterings just subjective discovery was conceivable.
3. Water fume sorption can be utilized to separate among shapeless and crystalline material when the hygroscopicity is distinctive This technique requires precise information on the hygroscopicity of both totally crystalline and totally undefined examples.
4. Isothermal Microcalorimetry measures the crystallization vitality of nebulous material that is warmed over its glass progress temperature (Tg) However, this procedure has a few restrictions. Right off the bat, this method must be applied if the physical security is with the end goal that just during the estimation crystallization happens. Also, it must be expected that all shapeless material solidifies. Thirdly, in a twofold blend of two nebulous exacerbates a differentiation between crystallization energies of medication and lattice is troublesome.
5. Dissolution Calorimetry gauges the vitality of disintegration, which is reliant on the crystallinity of the example Usually, disintegration of crystalline material is endothermic, while disintegration of nebulous material is exothermic.
6. Perceptible strategies that measure mechanical properties that are diverse for nebulous and crystalline material can be characteristic for the level of crystallinity. Thickness estimations and Dynamic Mechanical Analysis (DMA) decide the modulus of flexibility and consistency and in this way influenced by the level of crystallinity. Be that as it may, likewise these methods require information about the additivity of these properties in personally blended paired solids.

7. A much of the time utilized procedure to distinguish the measure of crystalline material is Differential Scanning Calorimetry (DSC) In DSC, tests are warmed with a consistent warming rate and the measure of vitality fundamental for that is identified. With DSC the temperatures at which warm occasions happen can be distinguished. Warm occasions can be a glass to elastic change, (re)crystallization, liquefying or debasement. Besides, the dissolving and (re)crystallization vitality can be evaluated. The dissolving vitality can be utilized to recognize the measure of crystalline material. Perhaps, the recrystallization vitality can be utilized to figure the measure of shapeless material gave, that all formless material is changed to the crystalline state. In the case of during DSC-estimations, shapeless material solidifies, data is gotten on the crystallization energy and on the physical security of the indistinct example. To evaluate the measure of crystalline material, estimations ought to be finished before crystallization of shapeless material has begun. Now and again, this can be set up applying high checking rates.[6,7,8,17,27,44,52,63]

B. Detection of atomic structure in shapeless strong scatterings

The properties of a strong scattering are profoundly influenced by the consistency of the circulation of the medication in the lattice. The security and disintegration conduct could be distinctive for strong scatterings that don't contain any crystalline medication particles, for example strong scatterings of type V and VI or for type II and III. Be that as it may, not just the Knowledge on the physical state (crystalline or nebulous) is significant; the conveyance of the medication as indistinct or crystalline particles or as discrete medication atoms is pertinent to the properties of the strong scattering as well. By the by, truth be told, not many investigations focuson the segregation between formless fused particles versus sub-atomic conveyance or homogeneous blends.

1. Confocal Raman Spectroscopy was utilized to quantify the homogeneity of the strong blend of ibuprofen in PVP It was depicted that a standard deviation in medicate content littler than 10% was demonstrative of homogeneous circulation. On account of the pixel size of 2 µm3, vulnerability stays about the nearness of nano-sized shapeless medication particles.
2. Using IR or FTIR, the degree of associations among medication and network can be estimated. The connections are demonstrative for the method of fuse of the medication, in light of the fact that independently scattered medication atoms will have more medication framework communications than when the medication is available in indistinct bunches or other multi-particle plans.
3. Temperature Modulated Differential Scanning Calorimetry (TMDSC) can be utilized to survey the level of blending of a joined medication. Because of the adjustment, reversible and irreversible occasions can be isolated. For instance, glass changes (reversible) are isolated from crystallization or unwinding (irreversible) in indistinct materials. Moreover, the estimation of the Tg is a component of the arrangement of the homogeneously blended strong scattering. It has been indicated that the affectability of TMDSC is higher than regular DSC Therefore this procedure can be utilized to survey the measure of molecularly scattered medication and from that the part of medication that is scattered as isolated particles is determined.[5,10,14,34,67]

CONCLUSION

Strong scattering frameworks have been acknowledged as very valuable device in improving the disintegration properties of ineffectively water-solvent medications. As of late, a lot of information has been amassed about strong scattering innovation, yet their business application is constrained. Different techniques have been attempted as of late to beat the impediment and make the readiness essentially possible. The issues engaged with joining into detailing of measurements structures have been bit by bit settled with the approach of elective techniques. These incorporate strategies like showering on sugar globules and direct container filling.

In spite of the fact that there are a few obstacles like scale up and fabricating cost to survive, there lies an extraordinary guarantee that strong scattering innovation will rush the medication discharge profile of ineffectively water solvent medications.

REFERENCES

1. Allen LVJ, Yanchick VA and Maness DD. Dissolution rates of corticosteriods utilizing sugar glass dispersions. J. Pharm. Sci., 1977; 66(4): 494-496.
2. Amidon GL, Lennernas H, Shah VP and Crison JR. Theoretical basis for a biopharmaceutical drug classification: the correlation of in vitro drug product dissolution and in vivo bioavailability. Pharm Res., 1995; 12(3): 413-420.
3. Black SN, Collier EA, Davey RJ, Roberts RJ. Structure, solubility, screening, and synthesis of molecular salts. J Pharm Sci., 2007; 96:1053-68.
4. Breitenbach J. Melt extrusion: from process to drug delivery technology. Eur. J. Pharm. Biopharm., 2002; 54(2): 107-117.
5. Breitenbach J, Schrof W and Neumann J. Confocal Raman-spectroscopy: analytical approach to solid dispersions and mapping of drugs. Pharm. Res., 1999 16(7): 1109-1113.
6. Broman E, Khoo C and Taylor LS. A comparison of alternative polymer excipients and processing methods for making solid dispersions of a poorly water soluble drug. Int. J. Pharm., 2001; 222(1): 139-151.
7. Buckton G and Darcy P. The use of gravimetric studies to assess the degree of crystallinity of

predominantly crystalline powders. Int. J. Pharm., 1995; 123: 265-327
8. Bugay DE. Characterization of the solid-state: spectroscopic techniques. Adv. Drug Deliv. Rev., 2001; 48(1): 43-65.
9. Chiou WL and Riegelman S. Pharmaceutical applications of solid dispersion systems. J. Pharm. Sci., 1971 60(9): 1281-1302.
10. Cilurzo F, Minghetti P, Casiraghi A and Montanari L. Characterization of nifedipine solid dispersions. Int. J. Pharm., 2002; 242(1-2): 313-317.
11. Coppens KA. Hypromellose, ethylcellulose, and polyethylene oxide use in hot melt extrusion. Pharm Technol., 2005; 30:62-70.
12. Costantino HR, Firouzabadian L, Wu C, Carrasquillo KG, Griebenow K, Zale SE and Tracy MA. Protein spray freeze drying. 2. Effect of formulation variables on particle size and stability. J. Pharm. Sci., 2002; 91(2): 388-395.
13. Dannenfelser RM, He H, Joshi Y, Bateman S, Serajuddin AT. Development of clinical dosage forms for a poorly water soluble drug I: Application of polyethylene glycol-polysorbate 80 solid dispersion carrier system. J Pharm Sci., 2004; 93:1165-75.
14. De Meuter P, Rahier H and Van Mele B. The use of modulated temperature differential scanning calorimetry for the characterisation of food systems. Int. J. Pharm., 1999; 192(1): 77-84.
15. Eriksson HJC, Hinrichs WLJ, van Veen B, Somsen GW, de Jong GJ and Frijlink HW. Investigations into the stabilisation of drugs by sugar glasses: I. Tablets prepared from stabilised alkaline phosphatase. Int. J. Pharm., 2002; 249(1-2): 59-70.
16. Fikentscher H, Herrle K. Polyvinylpyrrolidone. Mod Plast., 1945; 23:157-218.
17. Forster A, Hempenstall J and Rades T. Characterization of glass solutions of poorly water soluble drugs produced by melt extrusion with hydrophilic amorphous polymers. J. Pharm. Pharmacol., 2001; 53(3): 303-315.
18. Forster A, Hempenstall J, Tucker I and Rades T. The potential of small-scale fusion experiments and the Gordon-Taylor equation to predict the suitability of drug/polymer blends for melt extrusion. Drug Dev. Ind. Pharm., 2001; 27(6): 549-560.
19. Forster A, Hempenstall, J, Tucker I and Rades T. Selection of excipients for melt extrusion with two poorly water-soluble drugs by solubility parameter calculation and thermal analysis. Int. J. Pharm., 2001; 226(12): 147-161.
20. Ghaderi R, Artursson P and Carifors J. Preparation of biodegradable microparticles using solution enhanced dispersion by supercritical fluids (SEDS). Pharm. Res., 1999; 16: 676-681.
21. Goldberg AH, Gibaldi M and Kanig JL. Increasing dissolution rates and gastrointestinal absorption of drugs via solid solutions and eutectic mixtures. I. Theoretical considerations and discussion of the literature. J. Pharm. Sci., 1965; 54(8): 1145-1148
22. Greenhalgh DJ, Williams AC, Timmins P and York P. Solubility parameters as predictors of miscibility in solid dispersions. J. Pharm. Sci., 1999; 88(11): 1182-1190.
23. Hernandez-Trejo N, Hinrichs WLJ, Visser, MR, Müller RH, Kayser O, Frijlink E. Enhancement of the in vitro dissolution rate of the lipophilic drug buparvaquone by incorporation into solid dispersions. In: PharmSci. Fair. Nice, France., 2005.
24. Kanig JL. Properties of fused mannitol in compressed tablets. J Pharm Sci., 1964; 53:188-92.
25. Karavas E, Ktistis G, Xenakis A and Georgarakis E. Effect of hydrogen bonding interactions on the release mechanism of felodipine from nanodispersions with polyvinylpyrrolidone. Eur. J. Pharm. Biopharm., 2006; 63: 103-114.
26. Kaushal AM, Gupta P and Bansal AK. Amorphous drug delivery systems: molecular aspects, design, and performance. Crit. Rev. Ther. Drug Carrier Syst., 2004; 21(3): 133-193
27. Kerc J and Srcic S. Thermal analysis of glassy pharmaceuticals. Thermo chem. Acta., 1995; 248: 81-95.
28. Khazaal MN, Tarik AA, Abd AV. Efficacy of combination solid dispersion technology on dissolution performance of nalidixic acid and cefdinir. Asian J Pharm Clin Res., 2017; 1:394-401.
29. Kolter K, Flick D. Structure and dry binding activity of different polymers, including kollidon VA 64, Drug Dev, Ind Pharm., 2000; 26:1159-65.
30. Kompella UB and Koushik K. Preparation of drug delivery systems using supercritical fluid technology. Crit. Rev. Ther. Drug Carrier Syst., 2001; 18(2): 173-199.
31. Langer M, Höltje M, Urbanetz NA, Brandt B, Höltje HD and Lippold BC. Investigations on the predictability of the formation of glassy solid solutions of drugs in sugar alcohols. Int. J. Pharm., 2003; 252(1-2): 167-179.
32. Leuner C and Dressman J. Improving drug solubility for oral delivery using solid dispersions. Eur. J. Pharm. Biopharm., 2000; 50: 47-60
33. Levy G. Effect of particle size on dissolution and gastrointestinal absorption rates of pharmaceuticals. Am J Pharm Sci Support Public Health., 1963; 135:78-92.
34. Li J, Guo Y and Zografi G. The solid-state stability of amorphous quinapril in the presence of beta-cyclodextrins. J. Pharm. Sci., 2002; 91(1): 229-243.
35. Liao X, Krishnamurthy R, Suryanarayanan R. Influence of processing conditions on the physical state of mannitol – implications in freezedrying. Pharm Res., 2007; 24:370-376.
36. Lipinski CA. Avoiding investment in doomed drugs, is poor solubility an industry wide problem Curr Drug Dis., 2001; 4: 17-19.
37. Lloyd GR, Craig DQ and Smith A. A calorimetric investigation into the interaction between paracetamol and polyethylene glycol 4000 in

physical mixes and solid dispersions. Eur. J. Pharm. Biopharm., 1999; 48: 59-65.
38. McGinity JW, Maincent P and Steinfink H. Crystallinity and dissolution rate of tolbutamide solid dispersions prepared by the melt method. J. Pharm. Sci., 1984; 73(10): 1441-1444.
39. More SD, Sontakke SB. Solubility enhancement of gliclazide by solid dispersion method. Asian J Pharm Clin Res., 2013; 6:91-8.
40. Mullins JD and Macek TJ. Some pharmaceutical properties of novobiocin. J. Am. Pharm. Assoc. Sci. Ed., 1960; 49: 245-24.
41. Nakamichi K. Method of Manufacturing Solid Dispersion. United States Patent No; 1994.
42. Orienti I, Bigucci F, Luppi B, Cerchiara T, Zuccari G, Giunchedi P and Zecchi V. Polyvinyl alcohol substituted with triethylene glycol mono ethyl ether as a new material for preparation of solid dispersions of hydrophobic drugs. Eur. J. Pharm. Biopharm., 2002; 54(2): 229-233.
43. Paradkar A, Ambike AA, Jadhav BK, Mahadik KR. Characterization of curcumin-PVP solid dispersion obtained by spray drying. Int. J. Pharm., 2004; 271(1-2): 281-286.
44. Pikal MJ, Lukes AL, Lang JE and Gaines K. Quantitative crystallinity determinations for betalactam antibiotics by solution calorimetry: correlations with stability. J. Pharm. Sci., 2004; 67(6): 767-73.
45. Pokharkar VB, Leenata P Mandpe, Mahesh N Padamwar, Anshuman A. Ambike, Kakasaheb R. Mahadik and Anant Paradkar. Development, characterization and stabilization of amorphous form of a low Tg drug. Powder Technol., 2006; 167: 20-25.
46. Pouton CW. Formulation of poorly water-soluble drugs for oral administration: physicochemical and physiological issues and the lipid formulation classification system. Eur. J. Pharm. Sci., 2006; 29: 278-287.
47. Rastogi RP and Rama Varma KT. Solid-liquid equilibria in solutions of non-electrolytes. J. Chem. Soc., 1956; 2: 2097-2101.
48. Repka MA, McGinity JW. Influence of chlorpheniramine maleate on topical hydroxypropyl-cellulose films produced by hot-melt extrusion. Pharm Dev Technol., 2001; 6:297-304.
49. Rowe RC, Sheskey PJ, Quinn ME. Handbook of Pharmaceutical Excipients. 6th ed. London: Pharmaceutical Press., 2009.
50. Sarkari M, Brown J, Chen X, Swinnea S, Williams RO. Enhanced drug dissolution using evaporative precipitation into aqueous solution. Int. J. Pharm., 2002; 243(1-2): 17-31.
51. Save T and Venkitachalam P. Studies on solid dispersions of nifedipine. Drug Dev. Ind. Pharm., 1992; 18(15): 1663-1679.
52. Sebhatu T, Angberg M and Ahlneck C. Assessment of the degree of disorder in crystalline solids by isothermal microcalorimetry. Int. J. Pharm., 1994; 104: 135-14.
53. Sekiguchi K and Obi N. Studies on Absorption of Eutectic Mixture. I. A comparison of the behaviour of eutectic mixture of sulfathiazole and that of ordinary sulfathiazole in man. Chem. Pharm. Bull., 1961; 9: 866-872
54. Sekiguchi K and Obi N. Studies on Absorption of Eutectic Mixture II. Absorption of Fused Conglomerates of Chloramphenicol and Urea in Rabbits. Chem. Pharm. Bull. (Tokyo), 1964; 12: 134-144.
55. Sertsou G, Butler J, Hempenstall J, Rades T.Solvent change coprecipitation with hydroxypropyl methylcellulose phthalate to improve dissolution characteristics of a poorly water-soluble drug. J Pharm Pharmacol., 2002; 54:1041-1047.
56. Sethia S and Squillante E. Physicochemical characterization of solid dispersions of carbamazepine formulated by supercritical carbon dioxide and conventional solvent evaporation method. J. Pharm. Sci., 2002; 91(9): 1948-1957.
57. Shah NH, Lazarus JH, Sheth PR, Jarowski CI. Carboxymethylcellulose: Effect of degree of polymerization and substitution on tablet disintegration and dissolution. J Pharm Sci., 1981; 70:611-613.
58. Simonelli AP, Mehta SC and Higuchi WI. Dissolution rates of high energy polyvinylpyrrolidone (PVP)-sulfathiazole coprecipitates. J. Pharm. Sci., 1969; 58(5): 538-549.
59. Singh J. Effect of sodium carboxymethylcelluloses on the disintegration, dissolution and bioavailability of lorazepam from tablets. Drug Dev Ind Pharm., 1992; 18:375-83.
60. Stubberud L, Arwidsson HG, Hjortsberg V, Graffner C. Watersolid interactions. III. Effect of glass transition temperature, tg, and processing on tensile strength of compacts of lactose and lactose/ polyvinyl pyrrolidone. Pharm Dev Technol., 1996; 1:195-204.
61. Subramaniam B, Rajewski RA and Snavely K. Pharmaceutical processing with supercritical carbon dioxide. J. Pharm. Sci., 1997; 86(8): 885-890.
62. Taylor LS and Zografi G. Spectroscopic characterization of interactions between PVP and indomethacin in amorphous molecular dispersions. Pharm. Res., 1997; 14: 1691-1698.
63. Taylor LS and Zografi G. The quantitative analysis of crystallinity using FT-Raman spectroscopy. Pharm. Res., 1998; 15(5): 755-761
64. Teagarden DL and Baker DS. Practical aspects of lyophilization using non-aqueous co-solvent systems. Eur. J. Pharm. Sci., 2002; 15(2): 115-133.
65. Timko RJ and Lordi NG. Thermal analysis studies of glass dispersion systems. Drug Dev. Ind. Pharm., 1984; 10(3): 425-451
66. Urbanetz NA. Stabilization of solid dispersions of nimodipine and polyethylene glycol 2000. Eur J Pharm Sci., 2006; 28:67-76.

67. Vasanthavada M, WQ Tong, Y Joshi and MS Kislalioglu. Phase behavior of amorphous molecular dispersions I: Determination of the degree and mechanism of solid solubility. Pharm. Res., 21(9): 1598-1606.
68. Vasconcelos T and Costa P. Development of a rapid dissolving ibuprofen solid dispersion. In: PSWC – Pharmaceutical Sciences World Conference, DD-W103., 2007.
69. Verreck G, Chun I, Peeters J, Rosenblatt J and Brewster ME. Preparation and characterization of nanofibers containing amorphous drug dispersions generated by electrostatic spinning. Pharm. Res., 2003; 20: 810-817
70. Vila-Jato JL, Blanco J, Alonso MJ. The effect of the molecular weight of polyethylene glycol on the bioavailability of paracetamol-polyethylene glycol solid dispersions. J Pharm Pharm., 1986; 38:126-8.
71. Vincent MF, Kazarian SG and Eckert CA. Tunable diffusion of D2O in CO2-swollen poly (methyl methacrylate) films. AIChE., 1997; 43(7): 1838-1848.
72. Vippagunta SR, Karin A Maul, Siva Tallavajhala and David JW Grant. Solid-state characterization of nifedipine solid dispersions. Int. J. Pharm., 2002; 236(1-2): 111-123.
73. Weuts I, Kempen D, Verreck G, Decorte A, Heymans K. Study of the physicochemical properties and stability of solid dispersions of loperamide and PEG6000 prepared by spray drying. Eur. J. Pharm. Biopharm., 2005; 59(1): 119-126.
74. Wilcox WR, Friedenberg R and Back N (1964). Zone melting of organic compounds. Chem. Rev., 1964; 64: 187220.
75. Yamashita K, Nakate T, Okimoto K, Ohike A, Tokunaga Y, Ibuki R, et al. Establishment of new preparation method for solid dispersion formulation of tacrolimus. Int J Pharm., 2003; 267: 79-91.
76. Zhang H, Yao M, Morrison RA, Chong S. Commonly used surfactant, tween 80, improves absorption of P-glycoprotein substrate, digoxin, in rats. Arch Pharm Res., 2003; 26: 768-72.