If someone feels that they had never made a mistake in their life then it means they had never tried a new thing in their life.

- Einstein

Chapter 3

Review of literature
Hirofumi Takeuchi et al. [31] (2005) had described that the solid dispersion particles of indomethacin (IMC) were prepared with different types of silica, non-porous (Aerosil 200) or porous silica (Sylysia 350) by using spray-drying method. Powder X-ray diffraction analysis showed that IMC in solid dispersion particles was in amorphous state irrespective of the type of silica formulated. In DSC analysis, the melting peak of IMC in solid dispersion particles with Sylysia 350 shifted to lower temperature than that in solid dispersion particles with Aerosil 200 although the peak of each solid dispersion particles was much smaller than that of original IMC crystals. Dissolution property of IMC was remarkably improved by formulating the silica particles to the solid dispersion particles. In comparing the effect of the type of the silica particles, the dissolution rate of solid dispersion particles with Sylysia 350 was faster than that with Aerosil 200. The formulation amount of IMC did not affect on the amorphous state of IMC in the resultant solid dispersion particles in powder X-ray diffraction patterns. However, the area of the melting peak of IMC in the solid dispersion particles increased and an exothermic peak owing to recrystallization was observed with increasing the IMC content in the DSC patterns. The dissolution rate of IMC from the solid dispersion particles with Sylysia 350 was faster than that of Aerosil 200 irrespective of IMC content. In stability test, amorphous IMC in the solid dispersion particles with each silica particles did not crystallize under storing at severe storage conditions (40 °C, 75% RH) for 2 months, while amorphous IMC without silica easily crystallized under same conditions.

Satomi Onoue et al. [32] (2010) had described that the aim of the present investigation was to develop solid dispersion (SD) formulations of cyclosporine A (CsA) for improving the oral bioavailability of CsA. Amorphous SDs of CsA with eight hydrophilic polymers were prepared with wet-mill employing zirconia beads. The physicochemical properties were characterized with a focus on morphology, crystallinity, thermal behavior, dissolution, and interaction of CsA with co-existing polymer. Although CsA molecules were found to be amorphous in all wet-milled formulations, some SD formulations failed to improve the dissolution. Of all CsA formulations, SD using polymer with HPC (SSL) exhibited the largest improvement in dissolution behavior. Pharmacokinetic profiling of orally dosed CsA in rats was carried out using UPLC/ESI-MS. After the oral administration of HPC (SSL)-based SD, enhanced CsA exposure was observed.
with increases in Cmax and AUC of ca. 5-fold, and the variation in AUC was ca. 40% less than that of amorphous CsA. Infrared spectroscopic studies suggested an interaction between CsA and HPC (SSL), as evidenced by the conformational transition of CsA. From the improved dissolution and pharmacokinetic data, the amorphous SD approach using wet-milling technology should lead to consistent and enhanced bioavailability, leading to an improved therapeutic potential of CsA.

Siling Wang et.al [33] (2006) had described that this study investigated the solid dispersion containing pellets of itraconazole for enhanced drug dissolution rate. The influence of process parameters used during high shear pelletization on the pellet properties including pellet size and dissolution rate was also studied. Solid dispersions of itraconazole were prepared with Eudragit® E100, a hydrophilic polymer, by a simple fusion method followed by powdered and characterized by differential scanning calorimetry and X-ray powder diffraction. Solid dispersions containing pellets were consequently prepared using a lab-scale high shear mixer. In order to improve the product quality, a central composite design was applied to optimize the critical process variables, such as impeller speed and kneading time, and the results were modeled statistically. Itraconazole was presented as an amorphous state in the solid dispersion prepared at a drug to polymer ratio of 1:2. Both studied parameters had great effect on the responses. Powdered solid dispersion and pellets prepared using the optimal parameter settings showed approximately 30- and 70-fold increases in dissolution rate over the pure drug, respectively. Solid dispersion prepared by simple fusion method could be an option for itraconazole solubility enhancement. Pelletization process in high shear mixer can be optimized effectively by central composite design.

AppaRao et.al [34] (2010) had described that Aceclofenac was a novel non-steroidal anti-inflammatory drug (NSAID) having anti-inflammatory and analgesic properties, and was widely used in the treatment of rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis. One of the major problems with this drug was its low solubility in biological fluids, which results into poor bioavailability after oral administration. Therefore, solid dispersions (SDs) of Aceclofenac were prepared using lactose, mannitol and urea to increase its aqueous solubility. Aceclofenac SDs was prepared in 9:1, 7:3 and 4:1 ratios of the drug to polymer (by weight). In vitro release
profiles of all SDs (F-1 to F-9) were comparatively evaluated and also studied against pure Aceclofenac. Faster dissolution was exhibited by solid dispersion containing 9:1 ratio of drug: lactose. The increase in dissolution rate of the drug may be due to increase in wettability, hydrophilic nature of the carrier and due to reduction in drug crystallinity. The prepared solid dispersion was subjected for % practical yield, drug content and infrared (IR) spectroscopic studies. Absence of significant drug-carrier interaction was confirmed by infrared spectroscopic (IR) data.

K. ArunPrasad1 et.al [35] (2010) had described that the study was aimed to formulate solid dispersion tablet of Terbinafine Hydrochloride by using carriers polyethylene glycol 6000 (by melting method) and polyvinyl pyrrolidone K 30 (by solvent method) in the drug carrier ratio of 1:1, 1:2 and 1:3. The prepared solid dispersions were characterized for their drug content, thermal studies, infrared spectral studies, differential scanning calorimetric studies, aqueous solubility studies and in-vitro release studies. From the results, it was clear that solid dispersion formulation showed improved dissolution rate than pure drug and physical mixture. The solid dispersion showing better release profile was chosen to formulate into a tablet dosage form of weight 600 mg. The tablets compressed were evaluated for its physical parameters like thickness, hardness, weight variation, friability, drug content and disintegration tests. The dissolution profile of formulated tablet was compared with the marketed product and the formulated tablet showed better release profile than the marketed product.

Mahmoud El-Badry et.al [36] (2007) had described that the aim of this study was to prepare and characterize solid dispersions of water insoluble non-steroidal anti-inflammatory drug, indomethacin (IND), with polyethylene glycol 4000 (PEG4000) and Gelucire 50/13 (Gelu.) for enhancing the dissolution rate of the drug. The solid dispersions (SDs) were prepared by hot melting method at 1:1, 1:2 and 1:4 drug to polymer ratios. Scanning electron microscopy (SEM), X-ray powder diffractometry (XRD) and differential scanning calorimetry (DSC) were used to examine the physical state of the drug. Furthermore, the solubility and the dissolution rate of the drug in its different systems were explored. The data from the XRD showed that the drug was still detectable in its solid state in all SDs of IND–Gelu and disappeared in case of higher ratio of IND–PEG4000. DSC thermograms showed the significant change in melting peak of the
IND when prepared as SDs suggesting the change in crystallinity of IND. The highest ratio of the polymer (1:4) enhanced the drug solubility about 4-folds or 3.5-folds in case of SDs of IND–PEG or IND–Gelu., respectively. An increased dissolution rate of IND at pH 1.2 and 7.4 was observed when the drug was dispersed in these carriers in form of physical mixtures (PMs) or SDs. IND released faster from the SDs than from the pure crystalline drug or the PMs. The dissolution rate of IND from its PMs or SDs increased with an increasing amount of polymer.

Nilüfer Yüksel et.al [37] (2003) had described that Piroxicam was a nonsteroidal anti-inflammatory drug that was characterized by low solubility-high permeability. The present study was designed to improve the dissolution rate of piroxicam at the physiological pH’s through its increased solubility by preparing semi-solid dispersions of drug using Gelucires and Labrasol. These excipients were essentially characterized by their melting points and HLB (hydrophilic–lipophilic balance) values. The dissolution tests of the preparations were performed in the media with different pH. Differential scanning calorimetry (DSC), were used to examine the interaction between piroxicam and excipients. Gelucire 44/14 and Labrasol at the concentration of 15% w/v in water provided 20- and 50-fold increase in the solubility of piroxicam, respectively. The semi-solid dispersion containing 1/20 of drug/excipient mixture (20% Gelucire 44/14 and 80% Labrasol in w/w) produced the dissolution not less than 85% of piroxicam within 30 min in each dissolution media (simulated gastric fluid (SGF), pH 1.2; phosphate buffers, pH 4.5 and 6.8; and water). DSC analysis of this semi-solid dispersion indicated that there was no chemical reaction between the drug and excipients, and that a solid-state solution of piroxicam with excipient formed.

Angela Szu et.al [38] (2011) had described that this study focused on an investigation of the applicability of sucrose laurate as surfactant in solid dispersions. Although this surfactant had a US Drug Master File, it had not been used so far in internal pharmaceutical products. High drug-loaded solid dispersion systems consisting of gemfibrozil as a model drug and PEG 6000 as a carrier, with or without sucrose laurate (D1216), were prepared by the melting method. Cytotoxicity studies on CaCO₂ monolayer cells were also performed, in order to gain information on the applicability of D1216 in oral formulations. The results showed that the presence of the surfaceactive agent did not affect the solid-state characteristics of the model
drug significantly. A markedly improved dissolution of gemfibrozil from the ternary solid dispersion systems was observed as compared with the binary solid dispersion systems. The optimum concentration range of the D1216 in the formulations was determined to be 5–10%. The effective final concentrations of D1216 in the dissolution experiments proved to be non-toxic towards CaCo-2 cells. The results suggest the potential use of D1216 in innovative internal pharmaceutical formulations.

E. Squillante et.al [39] (2004) had described that this study compared the physicochemical properties of carbamazepine (CBZ) solid dispersions prepared by either a conventional solvent evaporation versus a supercritical fluid process. Solid dispersions of carbamazepine in polyvinylpyrrolidone (PVP) K30 with either Gelucire 44/14 or Vitamin E TPGS, NF (d-tocopheryl polyethylene glycol 1000 succinate) were prepared and characterized by intrinsic dissolution, differential scanning calorimetry, powder X-ray diffraction and Fourier transform infrared spectroscopy. CBZ/PVP K30 and CBZ/PVP K30/TPGS solid dispersions showed increased dissolution rate. The best intrinsic dissolution rate (IDR) was obtained for supercritically processed CBZ/PVP K30 that was four-fold higher than pure CBZ. Thermograms of various solid dispersions did not show the melting peak of CBZ, indicating that CBZ was in amorphous form inside the carrier system. This was further confirmed by X-ray diffraction studies. Infrared spectroscopic studies showed interaction between CBZ and PVP K30 in solid dispersions. The amorphous state of CBZ coupled with presence of interaction between drug and PVP K30 suggests fewer, if any, stability problems. Because the supercritical-based process produced solid dispersions with IDR better than conventional solid dispersions augmented with amphiphilic carriers, stability issues associated with lipid carriers do not apply, which, in turn, implies easier scale up under current Good Manufacturing Practice for this technique.

Adamo Finia, et.al [40] (2005) had described that a number of systems were prepared at five compositions (5, 10, 20, 30 and 40% w/w) of diclofenac/N-(2-hydroxyethyl) pyrrolidine salt and acidic diclofenac in PEG6000 and Gelucire 50/13, as physical mixtures and as solid dispersions. Powder X-ray diffractograms for the systems showed shifted and normal peaks, suggesting that the drug is present inside the samples in different physical states. Differential scanning calorimetry did not offer important information, since drug solubility into the carriers’ increases
with temperature and thermograms showed only the melting point peak of the carriers. Hotstage microscopy examination explains that, in high concentration samples, the drug was present either dissolved into the carriers or precipitated as microcrystals, or undissolved crystals of larger size. Gelucire 50/13 allowed the formation of larger crystals than PEG, using both the chemical forms of the drug. The release percentage of the drug from PEG6000/acidic diclofenac reaches 50% after few minutes in the most favourable case and appears to be dependent on the composition of the samples: the more diclofenac was present as dissolved in the pre-treated samples, the higher was the release. The optimum composition was found in the range of 5–10% w/w.

Giuseppe Trapani et.al [41] (1999) had described that Solid dispersions and physical mixtures of Zolpidem in polyethylene glycol 4000 (PEG 4000) and 6000 (PEG 6000) were prepared with the aim to increase its aqueous solubility. These PEG based formulations of the drug were characterized in solid state by FT-IR spectroscopy, Xray powder diffraction, and differential scanning calorimetry. By these physical determinations no drug-polymer interactions were evidenced. Both solubility and dissolution rate of the drug in these formulations were increased. Each individual dissolution profile of PEG based formulation fitted Baker–Lonsdale and first order kinetic models. Finally, significant differences in ataxic induction time were observed between Zolpidem orally administered as suspension of drug alone and as solid dispersion or physical mixture. These formulations, indeed, showed almost two- to three-fold longer ataxic induction times suggesting that, in the presence of PEG, the intestinal membrane permeability was probably the rate-limiting factor of the absorption process.

Bhaskar Chauhan et.al [42] (2005) had described that Solid dispersions (SDs) of glibenclamide (GBM); a poorly water-soluble drug and polyglycolized glycerides (Gelucire®) with the aid of silicon dioxide (Aerosil® 200); as an adsorbent, were prepared by spray drying technique. SDs and spray dried GBM in comparison with pure GBM and corresponding physical mixtures (PMs) were initially characterized and then subjected to ageing study up to 3 months. Initial characterization of SDs and spray dried GBM by DSC and XRPD showed that GBM was present in its amorphous form (AGBM). Improvement in the solubility and dissolution rate was observed for all samples. DRIFT spectroscopy revealed presence of hydrogen bonding in SDs. During
ageing study, almost no decrease of in vitro drug dissolution was observed, over the period of 3 months as compare with freshly prepared SDs. Slight crystallinity in SDs was observed in the DSC and XRPD studies during ageing. Moreover in vivo study in Swiss Albino mice also justified the improvement in the therapeutic efficacy of amorphous GBM in SDs over pure GBM. Thus, present study demonstrated the high potential of spray drying technique for obtaining stable free flowing SDs of poorly water-soluble drugs using polyglycolized glyceridescarriers with the aid of silicon dioxide as an adsorbent.

*Naima Zerrouk et.al [43] (2001)* had described that the present work extended previous physico-chemical investigations on the effects of solid dispersion on the solubility, the dissolution rate and the pharmacokinetic profile of carbamazepine. Solubility studies showed a linear increase in carbamazepine solubility with the increase of PEG 6000 concentration. There was no marked difference between physical mixtures and solid dispersions for the enhancement of carbamazepine solubility by PEG 6000. Less than 60% of pure carbamazepine was dissolved in 90 min. Physical mixtures (carbamazepine phase III) and solid dispersions (carbamazepine phase II) dissolution rates were higher in comparison of the parent drug. The dissolution of carbamazepine phase III was more pronounced than that evoked by the phase II. The dissolution profiles indicated that the percentage of the drug dissolved was dependent on the proportion of PEG 6000. In solid dispersions there was a remarkable enhancement in the dissolution rates of the drug in the vicinity of the eutectic composition as compared with those of corresponding physical mixtures. Hence, the optimum value for the solid dispersion was 80.5_1.7% of carbamazepine having dissolved within the first 10 min compared to 40_1% for the corresponding physical mixtures of the same composition. Statistical analysis of pharmacokinetic parameters confirmed that the carbamazepine: PEG 6000 binary systems displayed higher bioavailability of the drug than the pure carbamazepine. The area under the curve (AUC) values highlighted the evidence that only slight differences in the bioavailability of the drug occur between physical mixtures and solid dispersions prepared at the 80:20 and 50:50 drug: carrier compositions. However, the mean normalized plasma concentrations showed that standard error deviations were rather wide intervals for pure drug and physical mixtures in comparison to solid dispersions. One additional interesting point to consider was
the disappearance of the multiple peaks on the individual kinetic curves of the 50:50 solid dispersion compositions. Furthermore, our investigations have highlighted the interest of solid dispersions prepared at «near»-eutectic composition as our preliminary data show that the plasma concentration (C5h) of the drug for the 15:85

F. Cilurzo et.al [44] (2002) had described that the sublingual administration of nifedipine (NIF) is currently used in clinical practice. The sublingual administration of NIF solid dispersions (SD), by using a suitable dispenser, appears an interesting approach in the treatment of moderate and severe hypertensive emergencies. With this aim nine SD made of NIF and a low viscosity HPMC in different ratio were prepared by means of spray-drying technique and their structure was studied. Moreover, the drug dissolution properties from SD were verified. The characteristic peaks of crystalline NIF were not detectable by using the X-ray analysis when the NIF/HPMC ratios were lower than 50/50 w/w. In thermograms obtained from SD, the NIF melting endothermic peak disappeared when NIF/HPMC ratios were lower than 30/70 w/w; the experimental Tg values of SD were lower than the Tg values predicted by Gordon Taylor equation suggesting some type of non-ideality of mixing. In the SD FTIR spectra the NH stretching vibrations and the C_O stretch in esteric groups of NIF shift to free NH and C_O regions indicating the rupture of intermolecular hydrogen bond in the crystalline structure of NIF. The prepared SD improved the NIF dissolution rate in comparison with that of commercial NIF or NIF/HPMC physical mixtures. Moreover, the concentration of NIF in the dissolution medium increased decreasing the NIF content

Natalija Zajca et.al [45] (2005) had described that Solid dispersions of nifedipine (NIF) with mannitol in preparations containing 10 and 50% (w/w) of drug were manufactured by the hot melt method. Physical properties and the dissolution behaviour of binary systems as physical mixtures and solid dispersions were investigated. In all samples, the crystal structure of NIF was confirmed using differential scanning calorimetry (DSC) and scanning electron microscopy (SEM). Fourier transform infrared spectroscopy (FTIR) revealed, there was no interaction between drug and carrier, however, FTIR spectra indicated formation of thermodynamically less stable polymorph of mannitol. The dissolution rate of NIF from solid dispersions was markedly enhanced, the effect being stronger at higher drug loading (50%, w/w, NIF). The
dissolution rate enhancement was attributed to improved wetting of NIF crystals due to mannitol particles, attached on the surface, as inspected by means of SEM. Thermal stability of NIF, mannitol and two other potential carbohydrate carriers (lactose and saccharose) during the hot melt procedure was investigated using 1H NMR. NIF was found to be thermically stable under conditions applied. As expected, among carriers only mannitol demonstrated suitable resistance to high temperature used in experiments.

Toshio Ohara et.al [46] (2005) had described that the purpose of this study was to investigate the release mechanism of poorly water-soluble drug from the extended release solid dispersion systems with water-insoluble ethylcellulose (EC) and watersoluble hydroxypropylmethylcellulose (HPMC) (1:1). Indomethacin (IND) was used as a model of poorly water-soluble drug. Two kinds of solid dispersions were prepared by the solvent evaporation methods, which consist of the same formulation but exhibit different physical performance. It appeared that the dissolution behavior of IND depended on the structures of EC–HPMC matrices, which were governed by the preparation method. In addition, the dissolution behavior showed pH dependency that the dissolution rate of IND was slower in acidic medium than that in neutral medium. The experimental results revealed that the hydrophobic interaction between IND and EC occurred under lower pH and strongly delayed the dissolution rate of IND. The relationship between this hydrophobic interaction and the dissolution rate of IND was also proposed.

Madhuri Newa et.al [47] (2007) had described that Ibuprofen–Poloxamer 188 (P 188) binary solid dispersions (SD) with different drug loadings were prepared, characterized by scanning electron microscopy (SEM), differential scanning calorimetry (DSC) and Fourier transform infrared spectroscopy (FTIR), and evaluated for solubility, in vitro release, and oral bioavailability of ibuprofen in rats. Loss of their individual surface properties during melting and solidification as revealed by SEM micrographs indicated the formation of effective SDs. Absence or shifting towards the lower melting temperature of the drug peak in SDs and physical mixtures in DSC study indicated the possibilities of its interactions with P 188. However, no such interactions in the solid state were confirmed by FTIR spectra which showed the presence of drug crystalline in SDs. Immediate and complete release of ibuprofen from SDs might be
because of the reduction in the drug crystalline due to eutectic formation, and their dosing to fasted rats resulted in a significant increase in the area under curve (AUC) of the plasma concentration versus time curve and the maximum plasma concentration (Cmax), and a significant decrease in the time to reach Cmax (Tmax) over ibuprofen and physical mixtures.

M.M.Gupta et.al [48] (2011) had described that Ibuprofen was (NSAID) non-steroidal anti-inflammatory drug and used as analgesic & anti-inflammatory drug. It can be also used in the treatment of rheumatoid arthritis, osteoarthritis, and primary dysmenorrhea. Ibuprofen was absorbed rapidly, bound avidly to protein, but it has low aqueous solubility so, it also lowers the dissolution profile of drug. To overcome this problem, various techniques were used, like solid dispersion, complexation, co-solvency, hydrotrophy, nano technology approach. In this study, the dissolution rate of poorly soluble drug Ibuprofen was increased by preparing solid dispersion with urea in ratio of (1:1), (1:3) & (1:5) by using melt dispersion method & solvent evaporation method. The rate of dissolution of Ibuprofen was increased with the proportion of (1:5) when compared to the other formulations.

Li-Ping Ruan et al [49] (2005) had described that the aim of this study was to increase the solubility of ampelopsin (AMP) in water by two systems: solid dispersions with polyethylene glycol 6000 (PEG 6000) or polyvinylpyrrolidone K-30 (PVP K30) and inclusion complexes with ı-cyclodextrin (BCD) and hydroxypropylcyclodextrin (HPBCD). The interaction of AMP with the hydrophilic polymers was evaluated by differential scanning calorimetry (DSC), Fourier transformation-infrared spectroscopy (FTIR), scanning electron microscopy (SEM). The results from DSC, FTIR and SEC analyses of solid dispersions and inclusion complexes showed that AMP might exist as an amorphous state or as a solid solution. On the other hand, the SEM images of the physical mixtures revealed that to some extent the drug was present in a crystalline form. The influence of various factors (pH, temperature, type of polymer, ration of the drug to polymer) on the solubility and dissolution rate of the drug were also evaluated. The solubility and dissolution rates of AMP were significantly increased by solid dispersions and cyclodextrin complexes as well as their physical mixtures. The improvement of solubility using polymers was in the following order: HPBCD≈BCD> PVP K30 > PEG 6000.
Shaimaa M. Badr-Eldin et al [50] (2008) had described that the aim of this work was to investigate the inclusion complexation between tadalafil, a practically insoluble selective phosphodiesterase-5 inhibitor (PDE5), and two chemically modified β-cyclodextrins: hydroxypropyl-β-cyclodextrin (HP-β-CD) and heptakis-[2,6-di-O-methyl]-β-cyclodextrin (DM-β-CD), in comparison with the natural β-cyclodextrin (β-CD) in order to improve the solubility and the dissolution rate of the drug in an attempt to enhance its bioavailability. Inclusion complexation was investigated in both the solution and the solid state. The UV spectral shift method indicated guest–host complex formation between tadalafil and the three cyclodextrins (CDs). The phase solubility profiles with all the used CDs were classified as Ap-type, indicating the formation of higher order complexes. The complexation efficiency values (CE), which reflect the solubilizing power of the CDs towards the drug, could be arranged in the following order: DM-β-CD > HP-β-CD > β-CD. Solid binary systems of tadalafil with CDs were prepared by kneading and freeze-drying techniques at molar ratios of 1:1, 1:3 and 1:5 (drug to CD). Physical mixtures were prepared in the same molar ratios for comparison. Physicochemical characterization of the prepared systems at molar ratio of 1:5 was studied using differential scanning calorimetry (DSC), X-ray diffractometry (XRD), and Fourier-transform infrared spectroscopy (FTIR). The results showed the formation of true inclusion complexes between the drug and both HP-β-CD and DM-β-CD using the freeze-drying method at molar ratio of 1:5. In contrast, crystalline drug was detectable in all other products. The dissolution of tadalafil from all the prepared binary systems was carried out to determine the most appropriate CD type, molar ratio, and preparation technique to prepare inclusion complexes to be used in the development of tablet formulation for oral delivery of tadalafil. The dissolution enhancement was increased on increasing the CD proportion in all the prepared systems. Both the CD type and the preparation technique played an important role in the performance of the system. Irrespective of the preparation technique, the systems prepared using HP-β-CD and DM-β-CD yielded better performance than the corresponding ones prepared using β-CD. In addition, the freeze-drying technique showed superior dissolution enhancement than other methods especially when combined with the β-CD derivatives.
M. Narender Reddy et al [51] (2004) had described that Celecoxib, a specific inhibitor of cyclooxygenase-2 (COX-2) was a poorly water-soluble nonsteroidal anti-inflammatory drug with relatively low bioavailability. The effect of β-cyclodextrin on the aqueous solubility and dissolution rate of celecoxib was investigated. The possibility of molecular arrangement of inclusion complexes of celecoxib and β- cyclodextrin were studied using molecular modeling and structural designing. The results offer a better correlation in terms of orientation of celecoxib inside the cyclodextrin cavity. Phase-solubility profile indicated that the solubility of celecoxib was significantly increased in the presence of β-cyclodextrin and was classified as A_L-type, indicating the 1:1 stoichiometric inclusion complexes. Solid complexes prepared by freeze drying, evaporation, and kneading methods were characterized using differential scanning calorimetry, powder x-ray diffractometry, and scanning electron microscopy. In vitro studies showed that the solubility and dissolution rate of celecoxib were significantly improved by complexation with β-cyclodextrin with respect to the drug alone. In contrast, freeze-dried complexes showed higher dissolution rate than the other complexes.

Jagdale S. C et al [52] (2010) had described that the rate-limiting step to absorption of drugs from the gastrointestinal tract was often dissolution from the dosage form. Allopurinol was a commonly used drug in the treatment of chronic gout or hyperuricaemia associated with leukaemia, radiotherapy, anti-neoplastic agents. One of the major problems with allopurinol was that, it was practically insoluble in water, which results in poor bioavailability after oral administration. In the present study, solid dispersions of allopurinol were prepared by solvent evaporation method, kneading method, co-precipitation method, co-grinding method and closed melting method to increase its water solubility. In the present study amphiphilic carrier like gelucire 50/13 was used in the ratio of 1:1, 1:2 and 1:4. Prepared solid dispersions were characterized in the liquid state by phase solubility studies and in the solid state by Differential Scanning calorimetric analysis, Powder X-ray diffractometry and Fourier Transform Infrared spectroscopy. The aqueous solubility of allopurinol was preferential by the presence polymer with increasing concentration. Solid state characterizations indicated that allopurinol was present as an amorphous material and entrapped in polymer matrix. Mathematical modeling of in vitro dissolution data indicated the best fitting with Korsemeyer-Peppas model and the drug
release kinetics primarily as Non-Fickian diffusion. Therefore, the current study showed that gelucire 50/13 has a significant solubilizing effect on allopurinol.

Tejas Patel et al [53] (2010) had described that Fenofibrate was a lipid lowering drug used in the treatment of hyperlipidemia, which was not soluble in water and lower absorption in gastric fluid. In order to improve the solubility and oral absorption of the drug in gastric fluid and to enhance its dissolution rate solid dispersions and Lyophilization of dispersion was designed and evaluated. Solid dispersions of Fenofibrate were prepared using PEG 6000, Poloxamer 407 and a mixture of PEG 6000 and Poloxamer 407(1:1 mixture). The effect of melt and solvent methods of preparation of solid dispersion on dissolution behavior was also investigated. Dissolution studies indicated a significant increase in dissolution of Fenofibrate when dispersed in PEG6000 and Poloxamer 407. Physical mixtures containing PEG and Poloxamer 407 also showed improved dissolution of Fenofibrate as compared with that of pure drug, indicating the solubilizing effect of PEG6000 and Poloxamer 407. Solid dispersions containing Fenofibrate /Poloxamer 407, 1: 8, showed a 14-fold increase in dissolution after 60 min (D60) and another dispersion containing Fenofibrate /PEG 6000, 1:10, showed an 8-fold increase in the 0.1 N HCl systems. The dispersion containing six parts of the PEG 6000: Poloxamer 407 mixture (PEG 4000/PEG 6000, 1:1 mixture) showed a 12-fold increase in D60 as compared with pure drug. When multi-carrier solid dispersion containing six parts of mixture was prepared by the solvent method, the D60 value was about 2-fold that of the same dispersion prepared by the melt method. The dissolution of lyophilized solid dispersions further increased the dissolution of Fenofibrate significantly.

Eun-Jung Kim et al [54] (2006) had described that A straightforward solvent wetting method was used to prepare felodipine solid dispersions in the presence of various carriers. Dichloromethane was not needed when HPMC solid dispersions were produced using the solvent wetting method. The amount of ethanol used to prepare solid dispersions did not have a significant effect on the dissolution rate of felodipine. The results of X-ray diffraction and thermal analysis indicated that the drug was in the amorphous state when PVP, HPMC, and poloxamer were used as carriers. The dissolution rates of felodipine in PVP, HPMC, or poloxamer solid dispersions were much faster than those for the corresponding physical
mixtures. However, dissolution profiles were found to depend on the carrier used; the dissolution rate of felodipine increased slowly for solid dispersions prepared using HPMC, whereas rapid initial dissolution rates were observed for solid dispersions prepared using PVP or poloxamer. Increases in dissolution rates were partly dependent on the ratios of felodipine to carrier. No significant changes in crystal form were observed by X-ray diffraction or thermal analysis, and no significant changes in dissolution rate were observed when Sorbitol and mannitol were used as carriers.