LITERATURE REVIEW

Improving oral bioavailability of drugs those given as solid dosage forms remains a challenge for the formulation scientists due to solubility problems. Most of the newly invented chemical entities are poorly water soluble. As a result formulating them as oral solid dosage forms is a hurdle to the specialists. Many techniques have been exercised to improve oral bioavailability of drugs. Among several methods, solid dispersion has attracted attention of the researchers for previous 50 years. Different formulation strategies have been taken to prepare solid dispersions. It is evident that solid dispersions improve solubility of drug particles thus enhancing dissolution characteristics of drugs they increase the oral bioavailability.

Ford et al., 1978 "Evaluated the phase diagram of the binary system of indomethacin (I) and polyethylene glycol 6000 (II)" were determined from data obtained by differential scanning Calorimetry and hot stage microscopy. The solubility of I in II solutions and the dissolution rate profiles of I and II compressed and melt disks were determined. Results showed that II increased the solubility and dissolution rate of I, an optimum being obtained for the 15% I and 85% system. The melts exhibited higher dissolution rates than the compressed disks.

Sanghavi et al., 1981 “Studied the solid dispersions of methaqualone in Polyethylene glycol (PEG) 6000” were obtained by using melting and solvent methods. They were then evaluated for their physical properties, viz. Stability, solubility and Homogenity. Dissolution rate studies of this prepared dispersion were studied in detail and compared with the pure drug.

Ford et al., 1985 “Formulated the drug release from indomethacin (I) -polyethylene glycol 6000” solid dispersions with 5-40% I content in 3 different size fraction was examined. Release rates were highest from dispersions containing 5% I and showed greater increases at lower stirring rates. As the percentage of I in the dispersions increased, dissolution rates decreased, with incomplete dissolution when I was \GE/ 15%.
Animal studies demonstrating differences in gastrototoxicity among the various particle size fractions are also included.

Mohamed et al., 1985 “Studied the solid dispersions containing ibuprofen (I) in varying amounts of polyethylene glycol 6000” (II) were prepared by the melt method, and dissolution characteristics of the drug were studied. Optimal dissolution occurred when I and II were present in equimolar amounts. The complexing nature of the solid dispersions was confirmed by the continuous variation method and melting behavior.

Mummaneni. et al., 1990 “Studied the aqueous solubility and dissolution of famotidine from solid glass dispersions of xylitol”, prepared by the fusion method, were investigated. Both famotidine and xylitol exhibited minimal degradation during the fusion process.

Akbuga et al., 1991 “Studied the effect of additive type and concentration on drug dissolution from furosemide: povidone (polyvinylpyrrolidone: PVP) solid dispersion” systems was studied: cellulose microcrystalline (Avicel pH 101), croscarmellose sodium (Ac-Di-Sol), sodium starch olycolate (Primojel), crospovidone (Kollidon CL) and silicon dioxide colloidal (Aerosil) were used as additives and 2 different drug: PVP ratios were used with additives in low (2%) and high (20%) concentration. The solid dispersions were sensitive to the incorporation of additives. Kollidon CL was the best additive. A retardant effect was observed by the addition of Ac-Di-Sol. The effect of Avicel pH 101, Primojel, and Aerosil dependent on the drug: PVP ratio and also concentration of additives.

Rabasco et al., 1991 studied a method for the elaboration of solid dispersions, the weight ratios of diazepam to polyethylene glycol 6000 and the particle size of drug in the solid dispersion have been investigated.

Nakagami. et al., 1991 A method of increasing the dissolution rates of glass-forming, poorly water-soluble drugs was investigated. It is based on the concept of
preparing the powder form of a glassy drug dispersed in an inert carrier by melting. Indomethacin (IMC) and griseofulvin were used as model drugs, and fumed silicon dioxide was used as the carrier. The drug-silica (1:2) mixture was heated until the drug melted. The properties of the solid dispersion thus obtained were examined using powder X-ray diffractometry (XRD), differential scanning, Calorimetry (DSC), infrared (IR) spectroscopy, and scanning electron microscopy (SEM). XRD showed that the drugs were converted from a crystalline state to an amorphous state in the solid dispersions. On DSC thermograms, a pure IMC glass showed an endothermic peak corresponding to glass transition, then an exothermic peak corresponding to transformation to a metastable crystal and an endothermic peak corresponding to melting of the metastable form. The IMC-silica solid dispersion, however, shows no transition peak in its thermogram, indicating that solid dispersions showed IR spectra characteristics of pure amorphous drugs but somewhat different from those of crystalline drugs. SEM revealed that the drug-silica solid dispersions had none of the characteristics observed in crystalline drugs. The dissolution rates of drugs from the solid dispersions were much higher than those from physical mixtures and from pure crystalline drugs.

Chowdary et al., 1991 Evaluated the application of water soluble cellulose polymers, HPC-SL, HPMC and HEC in solid dispersions of a poorly soluble drug, naproxen. Solid dispersions in HPC-SL, HPMC and HEC were prepared by common solvent method and the dispersions were evaluated by TLC, IR, Moisture absorption, and Dissolution rate studies. TLC and IR studies indicated no interaction between drug and carrier. The dispersions were found to be non-hygroscopic. Marked increase in dissolution rate and efficiency of naproxen was observed in the case of solid dispersions. Dissolution of naproxen from the solid dispersions obeyed Hixson and Crowell's cube root dissolution rate equation.

Saers et al., 1992 investigated the solubility, melting and dissolution behavior of methyl, ethyl, propyl and butyl p-aminobenzoates (PABAs) have been studied, both alone and as, dispersions in polyethylene glycol (PEG) 6000 prepared by the fusion method. The aqueous solubility was found to decrease logarithmically with molecular weight of
the PABAs, while a linear increase was found between solubility and initial dissolution rate. The phase diagrams of physical mixtures of PABAs and PEG 6000 were monotectic in nature, while evidence was found for eutectic formation when the samples were prepared as dispersions. A linear relationship was found between the initial dissolution rate of the dispersions and the aqueous solubility of the PABAs, with the 10% w/w dispersions showing the fastest dissolution rates and the 20% w/w and 50% w/w dispersions and pure PABAs yielding similar results.

Sjokvist et al., 1992 studied the nonionic surfactants polysorbate 80 and polyethylene dodecyl ether (Brij 35), the anionic surfactant sodium dodecyl sulphate (SDS) and the cationic surfactant, dodecyltrimethyl ammonium bromide (DTAB) were incorporated in dispersions of 10% w/w griseofulvin with PEG 3000 as a carrier. An almost instant and complete dissolution was obtained for dispersions with 1 and 2% w/w SDS.

Fujii et al., 1993 Prepared the solid dispersion (SD) preparation method of indomethacin (IM, mp 161°C) with phosphatidylcholine (PC) was investigated. The melting point of PC is high, above 200°C, making a melting method inapplicable. However, PC shows a phase transition at about 100°C when its acyl chains are stearic acid and it is an anhydride. In the case of mole fraction or IM in SD being 0.50 X-ray diffraction patterns suggest that IM is in an amorphous state after heating at 90°C for 1 h, at 110°C for 10 min or at 180°C for 6 min. when the mole fraction of Im is as low as 0.25 or 0.33. IM is also present in an amorphous state after heating at 70°C for 2 and at 90°C for 10 min. the obtained SD showed endothermic peaks from about 40°C to 70°C upon thermal analysis. It is possible to prepare SD above 70°C, but this requires a long heating time, therefore, heating at above the phase transition temperature is most suitable. The dissolution patterns of IM from SD compressed into tablet form were fitted to Higuchi's square root equation and the dissolution rate was found to be 1.5-fold that from a physical mixture of the same composition.

Fernandez et al., 1993 Prepared the solid dispersions were used to increase the solubility of active ingredients, with the ultimate goal of optimizing their bioavailability.
when incorporated into pharmaceuticals. The studies described were designed to improve the dissolution kinetics of piroxicam by using solid dispersions in polyethylene glycol 4000 and investigating the pharmaceutical availability of the solid dispersions in powdered form and in rigid gelatin capsules. Solid dispersions (melting-solvent method) and physical mixtures were prepared at drug: carrier proportions ranging from 10:90 to 80:20, gelatin capsules were also prepared in our laboratory. The dissolution assay was performed in artificial gastric juice without pepsin at 37°C. The results showed that PEG 4000 increased the amount of piroxicam dissolved in both physical mixtures and solid dispersions.

Kale et al., 1993 Studied the solid dispersions of piroxicam were prepared by fusion and solvent methods using polyethylene glycol 6000 as carrier. Three different carrier proportions were used in each case. Uniform drug distribution was found in case of all solid dispersions. Thin layer chromatography indicated no inter-action between the drug and the carrier. All the solid dispersions showed increased dissolution rate as compared to the dissolution rate of pure piroxicam. Drug dissolution followed first order kinetics. Fusion method was found to be superior to solvent method. Storage of the solid dispersions at room temperature for 60 days showed no significant change in dissolution. Dissolution of aged samples also followed first order kinetics.

Craig et al., 1993 investigated the dissolution characteristics of nortriptyline hydrochloride dispersions in a range of different molecular weight polyethylene glycol carriers have been investigated. The release rate was found to be higher from dispersions in PEG 3400 than from the drug alone, while a logarithmic decrease was seen with increasing carrier molecular weight.

Ahmed et al., 1993 studied an inclusion complex of bropirimine (ABPP) with beta-cyclodextrin (beta-CD) and its solid dispersion with polyethylene glycol 6000 (PEG-6000) were prepared by the co precipitation method. Comparative dissolution studies revealed that the solid complex exhibited a markedly faster dissolution rate compared to
the PEG 6000 solid dispersions and physical mixtures in water and phosphate buffer (pH 7.4).

Kedzierewic et al., 1993 Prepared tolbutamide PEG 6000 solid dispersions as well as tolbutamide beta-cyclodextrin complexes were prepared with a view to increase the bioavailability of this poorly soluble drug. Absolute and relative bioavailability was determined by comparison with the administration of a commercial solution of the drug. The study was carried out in rabbits (n=5 per dosage form). The aqueous solution of tolbutamide (Dolipol) was administered either intravenously (10 mg/ kg) or orally (20 mg/ kg). Bulk powder, comelt, coprecipitative and solid complex of tolbutamide were administered orally at a dose of 20 mg/ kg. Plasma tolbutamide concentrations were measured by an HPLC method. Our results indicate that the absorption of tolbutamide is not increased in comparison with either bulk powder or a solution of the drug. However, there are obvious differences in the kinetics of absorption: indeed, tolbutamide is absorbed rapidly from the complex and the bulk powder.

Kerc et al., 1993 studied solid dispersions containing different proportions of felodipine to urea and relodipine to mannitol have been prepared and studied in water dissolution media. Enhanced dissolution rate as a result of both surface area increase and solubilization was noticed. As the most decisive factors for improving the felodipine dissolution, the preparation method, drug ratio, carriers and surfactant concentration were found.

Popli. et al., 1993 investigated solid dispersions systems developed as a drug delivery system for sulfamethoxaole and nitrofurantoin were evaluated. X-ray diffraction data revealed an increase in the dissolution profile for solid dispersions. The solubilities of the various solid dispersions showed higher solubility than the basic drug.

Veiga. et al., 1994 investigated to improve the dissolution of mequitazine using the fusion method, solid dispersions and physical mixtures of varying concentration ratios of mequitazine and polyethylene glycol 6000 (PEG 6000) were prepared and evaluated for dissolution and drug-carrier interaction using thermal analysis. The drug was dissolved
totally or partially into the polyethylene glycol. In addition, the formulations improved the dissolution profiles compared with drug alone. It was concluded that a solid dispersion prepared by the fusion method containing polyethylene glycol 6000 and mequitazine may be beneficial in improving the dissolution of the drug.

Tanabe. et al., 1994 investigated the rectal absorption of oxaprozin using solid dispersion with povidone (polyvinylpyrrolidone), oxaprozin suppositories were prepared and in vivo rectal absorption studies were carried out in rats; the amorphous state of oxaprozin with povidone was obtained and the effect of this solid dispersion on the dissolution of oxaprozin was also determined. Enhanced rectal absorption of oxaprozin in the amorphous state was observed in the oxaprozin-povidone solid dispersion systems.

Kearney et al., 1994 prepared solid dispersions of CI-987 {5-((3,5-is(1,1-dimethylethyl)-4-hydroxyphenyl)- methylene) -2,4- thiazolidinedione) having varying concentrations of polyvinylpyrrolidone (PVP K 28-32), were prepared in an attempt to improve the dissolution rate of CI-987. The physical characteristics of these solid dispersions were investigated by X-ray diffraction and dissolution rate studies. The dissolution rate of CI-987 significantly increased by increasing the weight fraction of PVP in the solid dispersions.

Jayaswal et al., 1994 studied the Furosemide- Eudragit RL 100 (Fur-RL), Furosemide-Eudragit RS 100 (Fur-RS) and Furosemide-Ethyl cellulose (Fur-EC) solid dispersions were prepared with different drug: carrier ratios by employing solvent evaporation technique. In-vitro drug release followed Higuchi’s diffusion kinetics. Drug release was found to increase as the granule size was decreased. Inclusion of Polyethylene glycol (PEG) in the coat material resulted in enhanced dissolution, an effect which was attributed to hydration, increased porosity and increased wettability associated with the presence of PEG’s.

Khidr. et al., 1994 studied the effect of poloxamer 407 (Pluronic F-127) on the dissolution rate of water-insoluble drugs in solid dispersions of poloxamer and povidone.
K-30 (polyvinylpyrrolidone K-30; PVP K-30) at different drug: polymer ratios is described, using nifedipine as a model drug. The solid dispersion technique using both polymers dramatically increased the dissolution rates of nifedipine.

Kuchekar et al., 1995 Prepared and evaluated f5-Cyclodextrin ([3-CD) and Dextrin as carriers for solid dispersions of Paracetamol a poorly soluble drug. Solid dispersions of paracetamol were prepared using Dextrin and [ -Cyclodextrin as carriers in different ratios following common solvent evaporation method using ammonia as a solvent. Three different carrier proportions were used in each case. Uniform drug distribution was found in case of all solid dispersions. The solid dispersions were evaluated by TLC, Moisture absorption and dissolution rate studies. TLC indicated no interaction between the drug and the carriers. The solid dispersions were found to be non-hygroscopic. Marked increase in the dissolution rate of paracetamol was observed in case of all the solid dispersions. Among the two carriers used, Dextrin was found to increase the dissolution rate faster than [ -cyclodextrin.

Betageri. et al., 1995 The preparation of solid dispersions and lyophilization of the dispersions designed to increase the solubility of glyburide using polyethylene glycol (PEG) 4000, PEG 6000, and a mixture of the two, are described. Dissolution studies indicated a significant increase in dissolution of glyburide when dispersed in PEGs.

Chowdary et al., 1995 To improve the dissolution rate and efficiency of nimodipine by solid dispersion in individual and combined carriers and to study the physicochemical nature of the dispersions. Solid dispersions of nimodipine in povidone (polyvinylpyrrolidone), hydroxypropyl methylcellulose, polyethylene glycol 6000, and cellulose microcrystalline (Avicel) were prepared and evaluated for content uniformity, drug-carrier interactions, dissolution rate, and efficiency. A marked increase in the dissolution rate and efficiency of nimodipine was observed with all solid dispersions. Solid dispersions in combined carriers gave much higher improvement in the dissolution rate and efficiency than was possible with individual carriers. Among the carriers studied, the cellulose microcrystalline-povidone combination gave the highest improvement in
dissolution rate and efficiency of nimodipine. Nimodipine was present in the amorphous form in the solid dispersions. IR spectra indicated no interaction between drug and carrier. Dissolution of nimodipine from the dispersions obeyed Hixon-Crowell cube root dissolution rate equation.

Lheritier. et al., 1995 Solid dispersions of SR 33557 in preparations containing from 30 to 80% w/w polyethylene glycol 6000 (PEG 6000) were prepared by the fusion method. The solubility of the drug substance either alone or in solid dispersions was determined in pH 1.2 and 4.5 media (extraction fluid NFXII, without enzyme). A large increase in the solubility was noted from the 80% w/w PEG preparation.

Guyot. et al., 1995 Developed to increase the water solubility and dissolution of norfloxacin, solid dispersions containing varying concentrations of polyethylene glycol 6000 were compared with inclusion complexes containing varying molecular ratios of either beta-cyclodextrin (Kleptose) or hydroxypropyl -beta- cyclodextrin: compounds were evaluated for physicochemical characteristics, solubility, and dissolution. The solubility and dissolution rate of norfloxacin were significantly increased with polyethylene glycol dispersions and cyclodextrin complexes as well as with norfloxacin and cyclodextrin physical mixtures.

Arias et al., 1995 To investigate the effects of spray drying in the preparation of solid dispersions, dispersions containing 10-40% w/w triamterene and mannitol (D-mannitol) were prepared by spray drying or the melting carrier method: dispersions were evaluated for dissolution and physico-chemical characterization. Strong drug-carrier interactions were present in the spray dried dispersions, but only weak interactions were present in those prepared by the melting carrier method. Spray dried dispersions demonstrated reduced dissolution times as compared to melting carrier dispersions.

Sheen et al., 1995 Developed a suitable water-soluble or miscible carrier systems for a solid dispersion formulation of RP-69698 with improved bioavailability were investigated in beagles by using polyethylene glycol 3350 (PEG 3350), polysorbate 80,
ethoxydiglycol (Transcutol), and Labrasol in various combinations with the drug in an oral dosage form. The formulation with PEG 3350, ethoxydiglycol, and Labrasol demonstrated an 11.8% bioavailability, a 2-fold increase compared with a baseline aqueous suspension. With only Labrasol in the formulation, the bioavailability was 12.9%. The addition of 10% polysorbate 80 to the initial formulation increased the bioavailability from 11.8 to 27.6%. An increase in the surfactant concentration did not further increase the bioavailability.

Lu. et al., 1995 Nimodipine-polyethylene glycol (PEG) solid dispersions was prepared by the melting method and evaluated. The formation of a eutectic mixture between drug and carrier was demonstrated by differential scanning Calorimetry and dissolution studies. The dissolution rate of the solid dispersions was greater than that of pure drug. Statistical analysis showed a significant difference between the drug and solid dispersion.

Pawar. et al., 1995 To improve the dissolution of trimethoprim by solid dispersion techniques, solid dispersions of trimethoprim were prepared by fusion method using polyethylene glycol 4000, polyethylene glycol 6000, and 2 different proportions of trimethoprim and mannitol as a carrier. All solid dispersions showed increased dissolution rates as compared to pure trimethoprim. Mannitol dispersion showed higher dissolution rates than polyethylene glycol 4000 and polyethylene glycol 6000 dispersions. TLC indicated no interaction between the drug and the carrier.

Sheen et al., 1995 Attempted to improve the bioavailability of a poorly water-soluble drug, RP 69698 (i), solid dispersion formulations were investigated in beagle dogs. The formulations were prepared by a melting method with water-soluble carriers in which I is highly soluble. When incorporated into a solid dispersion formulation composed of polyethylene glycol (PEG) 3350, Transcutol and Labrasol, the bioavailability of 1 was determined to be 11.8%. This represented about 2-fold improvement over 6% bioavailability observed previously with an aqueous suspension of the drug in 0.5% methylcellulose. When the formulation contained only Labrasol, in
which 1 was completely solubilized, the bioavailability of 1 was 12.9%. Addition of a surfactant, polysorbate 80, at a strength of 10% to the dispersion with PEG 3350 and Labrasol as carriers increased the bioavailability of 1 from 11.8 to 27.6%.

Anguiano. et al., 1995 To investigate the effect of clofibrate concentration and molecular weight of polyethylene glycols on the structure and dissolution rates of solid dispersions, dispersions containing polyethylene glycols of molecular weights of 10,000 - 35,000 and 2.5-20% clofibrate were prepared and evaluated for structure and dissolution. Dissolution rates increased with molecular weight of polyethylene glycol and drug concentration.

Betageri et al., 1995 Evaluated the preparation of a solid dispersion of tolazamide in polyethylene glycol 8000 by solvent and melt methods is reported, and the dissolution of tolazamide from these dispersions is reported. The rate of dissolution of tolazamide was faster in the solid dispersions than in physical mixtures and pure tolazamide. Dispersions prepared by the solvent method showed faster dissolution rates compared to the melt method.

Suzuki et al., 1996 Formulated to improve the poor organic solubility of benidipine hydrochloride, 2 kinds of solvent systems, an organic solution of Eudragit E-100 (OSE) and binary solvent mixtures, were used for preparing solid dispersions by the solvent removal process; the dissolution profile of the drug from these solid dispersions was investigated. In the OSE, the presence of Eudragit E-100 in methylene chloride (dichloromethane) resulted in an appreciable increase in drug solubility. However, in ethyl alcohol (ethanol), this solubilization effect of the polymer was completely inhibited. In the binary solvent mixture, enhanced solubility of the drug was obtained in ethyl alcohol-methylene chloride mixtures. Further, the addition of povidone (polyvinylpyrrolidone) or hydroxypropyl methylcellulose (HPMC) to this system did not deposit the dissolved drug. In these 2 solvent systems, solubilization of benidipine hydrochloride was presumed to be caused by intermolecular interactions.
Palmieri et al., 1996 Prepared solid dispersions of fenofibrate in polyethylene glycol 4000 (PEG 4000) with carrier/drug weight ratios ranging from 90/10 to 10/90 were prepared by the solvent and fusion methods, and the systems were characterized using differential scanning calorimetry, x-ray diffractometry, and Fourier transform IR spectroscopy. The solid dispersions were easily prepared by the fusion or co-evaporation methods. Both preparation methods gave very similar results in the formation of solid solutions and in the improvement of fenofibrate water solubility.

Kai et al., 1996 Studied a new triazol antifungal agent, (+)-2-(2, 4-difluorophenyl)-3-methyl-i-(iH-1,2,4-triazol-i-yl)-3-(6-(iH-1,2,4-triazol-I-ly) pyridazin-3-ythio) butan-2-ol (MFB-i04i), shows poor oral absorption and is practically insoluble in water (1-2 μg/ml). Solid dispersion systems with an enteric polymer such as hydroxypropylemethyl cellulose phthalate (HP-55) and carboxy- methylcellulose (CMEC), and a nonenteric, hydroxy-propyl-methylcellulose (Metolose) were evaluated to improve drug absorption and solubility. The oral bioavailability of these solid dispersions in beagle dogs were over 6 times higher than that of a suspension system with increasing drug solubility in an alkaline medium, X-Ray powder diffraction measurement of the solid dispersion showed a complete drug phase change from a crystal to an amorphous state.

Torrado et al., 1996 Prepare and evaluate solid dispersion systems of the sparingly water soluble drug, albendazole (ABZ), were mixed with varying concentrations of polyvinylpyrrolidone (PVP K 12) in an attempt to improve the solubility and dissolution rate of ABZ. Physical characteristics were investigated by Powder X-ray diffraction. As expected, the albendazole dissolution rate, expressed as the dissolution efficiency, and also the solubility coefficient were increased when albendazole was mixed with PVP. An increase in the concentration of the polymer in the solid dispersion produced an increase in both parameters.

Ho et al., 1996 To studied the solid dispersion of a poorly water-soluble drug, nifedipine, were prepared in hydroxy-propylmethylcellulose (HPMC) on sugar spheres.
using a fluidized-bed coating system and characterized by differential scanning Calorimetry (DSC) and dissolution measurements. A mixture of acetone and water (7:3) was found to be suitable as a spraying solution for simultaneous application of nifedipine and HPMC. DSC studies showed that the peak corresponding to the melting point of nifedipine became broadened when nifedipine was incorporated in a solid dispersion with HPMC at both ratios of 1:1 and 1:3. The result demonstrated that dissolution rates were fastest at the lowest nifedipine loading. Furthermore, the dissolution rate of nifedipine increased as more HPMC was added to the solid dispersions.

Habib et al., 1998 developed a solid dispersion formulation of flurbiprofen and phospholipid with improved characteristics. The FLP powders were blended with PL to produce FLP-PL physical mixtures and made into solid dispersions with PL by the solvent method. The FLP exhibited significantly improved dissolution rates in PL coprecipitates (coppt) compared to the physical mixtures or FLP alone. The dissolution studies suggested that less than a 20:1 ratio of FLP to PL was required to disperse FLP completely in the carrier. Thus, a small PL: FLP ratio improved the dissolution to a significant level. Thus, an FLP: PL dispersion may have the clinical advantages of quick release and excellent bioavailability.

Khan et al., 1998 developed solid dispersion of Ibuprofen by solvent evaporation method using polyethylene glycol 10000 (PEG), talc, and PEG-talc as dispersion carriers. The drug-carrier(s) interactions in the solid state were investigated using scanning electron microscopy (SEM), deferential scanning calorimetry (DSC), and x-ray diffraction analysis. Interactions in the solution were studied by performing dissolution experiments. No important and well-defined chemical interaction was found between the ingredients. The increase in the IBF dissolution rate from the solid dispersions with the carriers used in this study could be attributed to several factors such as improved wettability, local solubilization, and drug particle size reduction.

Chowdary et al., (1999), Studied nimesulide suspensions were formulated employing its solid dispersions in PVP, PEG and pre-gelatinised starch (PGS) and
studied, suspensions formulated with dispersions in PGS gave highest dissolution rate of nimesulide.

Sreenivasa et al., (1999), Studied the flurbiprofen is non-steroidal anti-inflammatory, analgesic and antipyretic drug. It is effective in the treatment of rheumatoid arthritis and degenerative joint diseases. Solid dispersion by common solvent method was used to enhance the solubility of poorly soluble flurbiprofen.

Ruckmani et al., (2000), Studied Carbamazepine, an anti-epileptic drug which is water insoluble was formulated as solid dispersion using PEG 6000 as carrier to improve its solubility and dissolution behavior. The resultant solid dispersions were subjected and Infra red spectroscopic studies. Solid dispersions were found to increase the solubility and dissolution of Carbamazepine.

Danarajuh et al., (2001), Studied Griseofulvin solid dispersions were prepared using polyethylene glycol 6000 (PEG) and polysorbate 80 (Tween 80) mixture using fusion technique. The solid dispersion was evaluated by DSC studies. The dissolution of griseofulvin from there dispersions were studied. The in vitro dissolution release studies indicated that drug release from PEG with Tween 80 provided dissolution rates faster than dispersion prepared with PEG alone. The incorporation of surface active agent such as Tween 80 has a considerable effect in the in vitro dissolution profile of griseofulvin.

Rama et al., (2001), formulated the Piroxicam (PPX) dispersions in pregelatinized starch (PGS) were prepared in different drug and carrier ratios and were characterized by X-ray diffractograms (XRD), differential scanning calorimetry (DSC), differential thermal analysis (DTA) and dissolution studies. Bioavailability studies were conducted on PRX-PGS dispersions and PRX pure drug in healthy human subjects as per cross over randomized block design (RBD). From Time Vs blood concentration data $C_{\text{max}}$, $T_{\text{max}}$, $K_{\alpha}$, AUC and $T_{{\text{y_2}}}$, were calculated. Higher dissolution rates were noted with dispersions when compared to piroxicam as such. PRX-PGS dispersions also gave fast absorption and higher blood levels of piroxicam when compared to pure drug.
parameters namely Cmax, percent absorbed in 1 and 2 h, Ka, AUC were higher indicating faster absorption of PRX from dispersions.

Rao et al., 2001, studied the enhancement of dissolution efficiency of Naproxen using solid dispersions. Solid dispersions were prepared by melting method as well as common solvent method using three hydrophilic carriers Viz., Polyethylene glycol-6000, polyethylene glycol-4000 and polyvinyl pyrrolidone, employing chloroform as a common solvent. All the dispersions obtained were fine, free flowing powders, those obtained from melting method were relatively harder than those obtained from common solvent method. Infra-red spectra and thin layer chromatographic studies results indicated that the possibility of drug-carriers incompatibility was ruled out. Naproxen showed only 56.51% dissolution at the end of 90 minutes in pH 7.4 phosphate buffer, where as solid dispersions showed enhanced drug release, the increase in carrier ratio in the formulation increased the drug release. Dispersions prepared by melting methods showed faster dissolution rate than common solvent method. The formulations containing 75:25, drug: carrier ratio prepared by melting method showed highest drug release i.e. 63.21% at initial 10 minutes and 95.51% at the end of 90 minutes.

Himasankar. et al., (2002), studied solid dispersions of glipizide were prepared using water-soluble carriers such as polyvinylpyrrolidone and polyethylene glycol by common solvent method in an attempt to increase the dissolution rate of glipizide, a practically insoluble drug in water. Differential scanning calorimetry, x-ray diffractometry and in vitro dissolution studies were used to characterize the solid dispersions. No chemical interaction was found between glipizide and polyvinylpyrrolidone/polyethylene glycol. The results from Different scanning calorimetry and x-ray diffractometry studies show that polyvinylpyrrolidone/polyethylene glycol inhibits the crystallization of glipizide. The solid dispersions prepared in this study were found to have higher dissolution rates compared to intact glipizide and physical mixtures of polyvinylpyrrolidone/ polyethylene glycol and glipizide. It was found that the optimum weight ratio for glipizide: carrier is 1:5 for polyvinylpyrrolidone and 1:7 for polyethylene glycol.
Pignatello et al., 2002[^2] studied the mechanisms of interaction between Eudragit RS100 (RS) and RL100 (RL) polymers with 3 nonsteroidal anti-inflammatory drugs: diflunisal (DIF), flurbiprofen (FLU), and piroxicam (PIR). Solid dispersions of polymers and drugs at different weight ratios were prepared by co evaporation of their ethanol solutions. The resulting coevaporates were characterized in the solid state (Fourier-transformed infrared spectroscopy (FT-IR), differential scanning Calorimetry, powder-x-ray diffractometry) as well as by studying the in vitro drug release in a gastro enteric environment. The interactions are related to the chemical structure of the drugs and to their dissociated or undissociated state. The dispersion of drugs in the polymer matrices strongly influenced their dissolution rate, which appeared slower and more gradual than those of the pure drugs, when polymer ratios were increased in case of Eudragit RL.

Sanjula et al., (2002), Evaluated the inclusion complexes of meloxicam with β-cyclodextrin (β-CD) were prepared by various methods like grinding, kneading, solid dispersion and freeze drying. The prepared complexes were evaluated by FTIR, X-ray diffraction, differential scanning calorimetry and scanning electron microscopy. The in vitro dissolution rate of drug-β-CD complex was faster compared to the drug alone.

Gowthamarajan et al., (2002), Studied the α-Cyclodextrin complexes of meloxicam were prepared by solvent evaporation technique in different ratios to enhance the solubility of the drug. The complex was characterized by infrared spectroscopy and differential scanning calorimetry studies. There was no interaction between drug and carrier. Based on physical characters and in vitro drug release pattern, 1:3 drug-carrier ratio was selected as ideal batch for suppositories. A water-soluble base, polyethylene glycol, was selected as ideal base for the preparation of suppositories. The suppositories were prepared by moulding technique. The ideal batch of solid dispersion was incorporated into suppository base. The prepared suppositories were characterized for hardness, melting point, disintegration time and drug content. All these properties were found to be ideal. The in vitro drug release pattern was determined by rotating dialysis.
bag method. The in vitro release of meloxicam from its solid dispersion incorporated suppositories was a significantly improved when compared to the intact bulk drug incorporated suppositories.

Saha et al., (2002), An attempted has been made to enhance solubility and dissolution of nimesulide and ibuprofen by solid dispersion techniques and complexation using various hydrophilic excipients. Drug-excipients solid dispersions and complexes of nimesulide were prepared by solvent evaporation and fusion-solvent method. Solid dispersions of ibuprofen were prepared by fusion, solvent evaporation and fusion-solvent method. Solubility profiles of the drug from the solid dispersions and complexes of nimesulide were studied in buffered pH 6.6, whereas the solubility of drug-excipients dispersions of ibuprofen were evaluated in 0.1 N sodium hydroxide media. Solid dispersions of nimesulide with PEG-6000 enhanced the solubility of nimesulide by more than 1000%. Dispersion of ibuprofen in sorbitol showed maximum enhancement of solubility (upto 75%). Dispersions in combined carriers: PVP k-30 MCC and PVP k-30-PEG-6000 also markedly increased the solubility of ibuprofen.

Kusum et al., (2003), The presented study has three primary objectives. Firstly, in view of the low aqueous solubility of celecoxib, solid dispersions of the drug were prepared and evaluated. Different carriers were chosen and a constant drug to carrier ratio was maintained. The solid dispersions obtained were subjected to solubility and dissolution studies including dissolution rate and efficiency. The best carrier was polyvinylpyrrolidone-vinyl acetate co-polymer, as it increased the solubility by a factor of ten. It also exhibited marked increase in the dissolution rate and efficiency.

Guangxi et al., (2003), Investigated and evaluated the bioavailability in rats after oral administration of puerarin or puerarin-phospholipid solid dispersion. A simple and sensitive HPLC method was developed for determination of puerarin in rat plasma. It was shown that its plasma concentration reached a peak of 0.35 |µg/ ml at 0.64 h after oral administration (50 mg/ kg). However, after intake of puerarin-phospholipid solid dispersion, a peak of 0.78 | µg/ml occurred at a later time, 1.06 h.
Tanno et al., 2004 \cite{81} compared and evaluated the utility of hypromellose acetate succinate (HPMCAS), a cellulosic enteric coating agent, as a carrier in a solid dispersion of nifedipine (NP) with other polymers, including hypromellose (HPMC), hypromellose phthalate (HPMCP), methacrylic acid ethyl acrylate copolymer (MAEA), and povidone (PVP). An X-ray diffraction study showed that the minimum amount of HPMCAS required to make the drug completely amorphous was the same as that of other cellulosic polymers, and less than that in dispersions using non-cellulosic polymers. Hypromellose acetate succinate showed the highest drug dissolution level from its solid dispersion in a dissolution study using a buffer of pH 6.8. Thus the results indicate that HPMCAS is an attractive candidate for use as a carrier in solid dispersions.

Mura et al., 2005 investigated the effect of incorporation of an anionic [sodium dodecyl sulfate (SDS) or dioctylsulfosuccinate (DSS)] or nonionic [Tween 60 (TW60)] surfactant on the properties of ketoprofen solid dispersions in polyethylene glycol 15000 (PEG). Physicochemical and morphological properties of the various solid systems were determined by differential scanning calorimetry, hot stage microscopy, X-ray powder diffraction analysis, and scanning electron microscopy. Binary solid dispersion of ketoprofen in PEG was effective in improving the drug dissolution properties in both percent of drug dissolved and dissolution efficiency (p<0.001). Also ternary dispersions exhibited a dramatic increase in relative drug dissolution rate at 5 min, which passed from 24.7 for binary coevaporates to 62 or 70 for ternary coevaporates with DSS or SDS, respectively. Therefore, the ACELOFENAC-PEG-SDS coevaporates appears to be the most suitable product for developing fast-release formulations of the drug, which could be particularly useful in the treatment of clinical conditions requiring quick pain relief.

Mura et al., 2005 develop and characterize naproxen-chitosan solid system to improved drug dissolution properties. Solid binary system at different drug polymer ratio have been prepared according to different techniques (mixing, co grinding, kneading, co-evaporation) using chitosan at low and medium molecular weight and tested for dissolution properties. Drug–carrier interaction were investigated in both the liquid and solid state, by phase solubility analysis, differential scanning calorimetry, X-ray powder
diffractometry, FT-IR spectroscopy and scanning electron microscopy. Drug dissolution parameters improved with increasing the polymer amount in the mixture, reaching the highest values at the drug polymer ratio 1:9 w/w. Thus the Co grinding method found strongest amorphizing effect towards the drug by enabling more than ten times its relative dissolution rate as the effective techniques.

Pandit et al., 2005 developed flurbiprofen-nicotinamide solid dispersions by the fusion method. The solid dispersions were evaluated for dissolution rate. The drug-carrier interaction in the liquid and solid states were studied by using phase solubility analysis, phase diagram, X-ray diffraction (XRD), and differential scanning calorimetry (DSC). Solid dispersions gave fast and rapid dissolution of flurbiprofen compared with the pure drug and the physical mixture. Phase diagram and DSC indicated that Indomethacinbiprofen and nicotinamide form a eutectic mixture. The aqueous solubility of Indomethacinbiprofen was enhanced in the presence of nicotinamide.

Palakurthi et al., 2005 conducted comparative biodistribution study between free indomethacin and lipo-indomethacin (LM and S-LM) in the arthritic rats by administering the formulations at a dose equivalent to 12 mg of indomethacin/kg. It was observed that the free drug as well as the encapsulated drug followed biphasic clearance from the blood. The high accumulation of the drug in arthritic paw with S-LM system may be accounted for by the reduced uptake by RES cells, and thereby, availability for extravascularization in the inflammatory tissues.

Taylor et al., 2006 studied the ability of various polymers to inhibit the crystallization of amorphous felodipine in amorphous molecular dispersions. Spin-coated films of felodipine with poly (vinylpyrrolidone) (PVP), hydroxypropylmethylcellulose acetate succinate (HPMCAS), and hydroxypropylmethylcellulose (HPMC) were prepared and used for measurement of the nucleation rate and to probe drug–polymer intermolecular interactions. Bulk solid dispersions were prepared by a solvent evaporation method and characterized using thermal analysis. It was found that each polymer was able to significantly decrease the nucleation rate of amorphous felodipine even at low concentrations (3–25% w/w).
Vippagunta et al., 2006 obtain a fundamental understanding of the factors, specifically the properties of poorly water-soluble drugs and water-soluble carriers, which influence predominantly, the formation of eutectic or monotectic crystalline solid dispersion and their dissolution behavior. A theoretical model was applied on five poorly water-soluble drugs (fenofibrate, Indomethacinbiprofen, griseofulvin, naproxen, and ibuprofen) having diverse physicochemical properties and water-soluble carrier (polyethylene glycol (PEG) 8000) for the evaluation of these factors. The current work provides valuable insight into factors affecting formation and dissolution of eutectic systems, which can facilitate the rational selection of suitable water-soluble carriers.

Wang et al., 2007 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. Itraconazole was presented as an amorphous state in the solid dispersion at the drug-to-polymer composition ratio of 1:2 (w/w) according to the results of DSC and X-ray diffraction and was released almost 30 times faster than pure drug. Impeller speed and kneading time are important parameters which affect the pellet characteristics complicatedly during high pelletization process. The method used to prepared solid dispersion of itraconazole in this study is relatively simple and safe because of the absence of specialized equipment and organic solvent.

Mutalik et al., 2007 developed “once daily” sustained release tablets of aceclofenac by direct compression using hydroxypropyl methylcellulose-K4M (HPMC). The solubility studies of aceclofenac were conducted to select suitable dissolution media. The drug excipients mixtures were subjected to Preformulation studies. The tablets were subjected to physicochemical, in vitro drug release and stability studies. Preclinical (anti-inflammatory, analgesic, pharmacokinetic and toxicity studies) and clinical pharmacokinetic studies were conducted for optimized tablets. Based on the
preformulation results, he selected microcrystalline cellulose (MCC), dicalcium phosphate and spray dried lactose (SDL) as directly compressible vehicles. Because of the incompatibility with aceclofenac, SDL was excluded from the study. By comparing the dissolution profiles with the marketed product, the tablet containing HPMC (45%) and MCC (30%) along with talc and magnesium stearate (1% w/w, each) (Tablet B7) was considered as a better formulation.

Mashru et al., 2007 studied dissolution enhancement efficiency and solid dispersion formation ability of hydrophilic swellable polymers such as sodium carboxymethyl cellulose (Na-CMC), sodium starch glycolate (SSG), pregelatinized starch (PGS), and hydroxypropylmethyl cellulose (HPMC) with carbamazepine using $3^2$ full factorial design for each of the polymers. Solid dispersions of carbamazepine were prepared using solvent evaporation method with around 70% solvent recovery. The independent variables were the amount of polymer and organic solvent. The dependent variables assessed were percentage drug dissolved at various time points and dispersion efficiency (ie, in terms of particle size of solid dispersion). HPMC showed increase in drug dissolution up to an optimized level; however, further increase in its concentration decreased drug dissolution.

Yong et al., 2008 prepared and evaluate fast dissolving ibuprofen polyethylene glycol 6000 solid dispersion in a relatively easy, simple, quick, inexpensive, and reproducible manner and characterized by scanning electron microscopy (SEM), differential scanning calorimetry (DSC), and Fourier transform infrared spectroscopy (FTIR). Preliminary results from this study suggested that the preparation of fast-dissolving ibuprofen SDs by low temperature melting method using PEG 6000 as a meltable hydrophilic polymer carrier could be a promising approach to improve solubility, dissolution, and absorption rate of ibuprofen.

Friesen et al., 2008 prepared spray dried dispersions of low solubility drugs by using the polymer Hydroxypropyl methylcellulose acetate succinate (HPMCAS). For a variety of drug structures, these SDDs provide supersaturation in vitro dissolution
determinations and large bioavailability increases in vivo. In bile-salt/lecithin in vitro solutions, these SDDs provide amorphous drug/polymer colloids and an increased concentration of free drug and drug in micelles relative to crystalline or amorphous drug.

Mutalik et al. 2008 studied significant effect of chitosan on improving the dissolution rate and bioavailability of aceclofenac demonstrated by simple solvent change method. Chitosan was precipitated on aceclofenac crystals using sodium citrate as the salting out agent. The considerable improvement in the dissolution rate of aceclofenac from optimized crystal formulation was attributed to the wetting effect of chitosan, decreased drug crystallinity, altered surface morphology and micronization. The optimized co-crystals exhibited excellent stability on storage at accelerated conditions. The in vivo studies revealed that the optimized crystal formulation provided a rapid pharmacological response in mice and rats besides exhibiting improved pharmacokinetic parameters in rats.

Trivedi et al., 2008 microencapsulated the anti-inflammatory drug (aceclofenac) to provide controlled release and minimize or eliminate local side effect by avoiding the drug release in the upper gastrointestinal tract. The drug was targeted to the colon and their aligned area for their local effect. Aceclofenac was microencapsulated with Eudragit (S 100, RL 100, and RS 100), using an O/W emulsion-solvent evaporation technique. Aceclofenac microspheres were subjected to micromeritic properties including angle of repose, bulk density, tapped density, Carr’s index, Hauser’s ratio, and particle size determination. Microspheres were subjected to drug loading, in vitro drug release as well as for scanning electron microscopy.

Radhika et al., 2008 formulated delayed release microspheres of aceclofenac using CAP by solvent evaporation technique and evaluated the effects of various other modern enteric polymers such as HPMCP, Eudragit L100 and Eudragit S 100 on the release of aceclofenac from CAP microspheres. Hence it was revealed that HPMCP exhibits positive influence whereas Eudragit L100, Eudragit S 100 exhibits negative effect on the drug release rate of CAP microspheres.
Tamizharasi et al., 2008 prepared Pentoxifylline loaded poly (ε-caprolactone) microspheres by solvent evaporation technique with different drug to carrier ratio F1 (1:3), F2 (1:4), F3 (1:5) and F4 (1:6). The microspheres were characterized for particle size, scanning electron microscopy, FT-IR study, percentage yield, drug entrapment, stability studies and for in vitro release kinetics. It was found that there was no interaction between drug and polymer by FT-IR study. No appreciable difference was observed in the extent of degradation of product during 60 d in the microspheres, which were stored at various temperatures.

Ghosh et al., 2009 aimed to develop matrix tablets for oral controlled release of aceclofenac. He prepared Matrix tablets of aceclofenac, using various viscosity of hydrophilic polymer HPMC in two different proportions, hydrophobic polymer ethyl cellulose and Guar gum by wet granulation method and subjected to in vitro drug release studies. Based on the results of the in vitro studies, it was concluded that the HPMC matrix tablets provided oral controlled release of aceclofenac.

Patel et. al., 2009 reported Novel Drug Delivery Technologies for the Treatment of Rheumatoid Arthritis. Rheumatoid Arthritis is a chronic autoimmune disease and a major cause of disability. Current treatment of arthritis involves administration of drugs mainly by oral and parenteral route. Frequent dosing often leads to patient non compliance. Accounting this problem, drug delivery technologies should be developed which reduces frequency of dosing along with sustained release of medicament. Various drug delivery systems are documented like albumin-based drug delivery systems, bio-reductive drug delivery systems, microspheres, nanoparticles, liposome’s etc. Conventional drugs like indomethacin, magesotrol acetate, methotrexate and cannabidiol have been modified into extended release formulations, nano crystal oral suspensions, topical gel and transdermal patch respectively. Targeting αγβ3 integrin has been shown to enhance drug delivery. Drugs delivered by intra-nasal route significantly reduce disease severity in experimental collagen induced arthritis model. This review reports a comprehensive overview of newly developed drug delivery technologies as therapeutic
targets of rheumatoid arthritis which may potentially reduce adverse extra-articular side effects.

Gattani et al., 2009 designed controlled release system for aceclofenac to increase its residence time in the stomach without contact with the mucosa. He achieved it through the preparation of floating microparticles by the emulsification solvent-evaporation technique consisting of eudragit RS 100 as a polymer. The shape and surface morphology of prepared microsphere were characterized by optical and scanning electron microscopy. The micromeritic properties of microspheres were found to be much improved. In-vitro drug release studies were performed and drug release kinetics was evaluated using the linear regression method. Effects of polymer concentration, stirring rate during preparation and effect of temperature on size and drug release was evaluated.

Baria et al., 2009 prepared SR suppositories containing aceclofenac microspheres. Microspheres were prepared by solvent evaporation method employing ethyl cellulose as a microsphere forming polymer. He investigated aceclofenac release and then formulated SR suppositories by incorporating aceclofenac microspheres having the highest drug loaded. He used PEG4000, PEG6000 and stearic acid as base. He employed in vitro dissolution test to estimate drug release. And he concluded that SR suppositories containing aceclofenac microspheres had sustained effect upto 8 h in vitro.

Shaikh et al., 2009 developed and evaluated the suitability of lecithin organogels containing aceclofenac for topical application and compared it’s In vitro and In vivo effects with conventionally used hydrogels. He demonstrated that organogels are more effective in faster drug release as compared to hydrogels.

Prabhu et al., 2009 microencapsulated aceclofenac using rosin by o/w emulsion solvent evaporation technique. He examined the effect of three formulation variables including the drug: polymer ratio, emulsifier (polyvinyl alcohol) concentration and organic solvent (dichloromethane) volume. It was revealed that drug: polymer ratio had a considerable effect on the entrapment efficiency, however particle size distribution of
microspheres was more dependent on the volume of dichloromethane and polyvinyl alcohol concentration rather than on the drug: polymer ratio.

Bikiaris et al., 2009 developed Solid dispersions of Fluvastatin with polyvinylpyrrolidone (PVP), eudragit RS100 (Eud), and chitosan (CS) as drug carrier matrices, were prepared using different techniques in order to evaluate their effect on Fluvastatin stability during storage. The characterization of the three different systems was performed with the use of differential scanning calorimetry (DSC) and wide angle X-ray diffractometry (WAXD). It was revealed that amorphization of the drug occurred in all of the solid dispersions of Fluvastatin as a result of drug dissolution into polymer matrices and due to physical interactions (hydrogen bonding) between the polymer matrix and Fluvastatin. This was established through the use of FTIR spectroscopy. SEM and micro-Raman spectroscopy showed that Fluvastatin was interspersed to the polymer matrices in the form of molecular dispersion and nanodispersion, too. Solid dispersions due to the evolved interactions of their reactive groups with Fluvastatin provide a sufficient physical and chemical stability. The extent of interactions seems to play the most important role in the drug stabilization.

Buckton et al., 2009 studied solid dispersion stability and dissolution properties of griseofulvin binary and ternary solid dispersions were evaluated. Solid dispersions of griseofulvin and hydroxypropyl methylcellulose acetate succinate (HPMCAS) were prepared using the spray drying method. A third polymer, poly [N-(2-hydroxypropyl) methacrylate] (PHPMA), was incorporated to investigate its effect on the interaction of griseofulvin with HPMCAS. These results reveal significant stability of the amorphous form due to the hydrogen bond formation with the polymer. The addition of the third polymer improved the stability but had a minor impact on dissolution.

Rao et al., 2010 developed aceclofenac loaded chitosan microparticles by ionotropic gelation method. He concluded that chitosan microparticles developed by ionotropic gelation method might become potential delivery system for prolonging the release of aceclofenac.
Choi et al., 2010 investigated the effect of cycloamylose on the aqueous solubility of Indomethacinbiprofen. To improve the solubility and bioavailability of flurbiprofen (poor water solubility), a solid dispersion was spray dried with a solution of Indomethacinbiprofen and cycloamylose at a weight ratio of 1:1. The physicochemical properties of solid dispersions were investigated using SEM, DSC, and X-ray diffraction. Cycloamylose increased solubility of flurbiprofen approximately 12-fold and dissolution of it by 2-fold. flurbiprofen was present in an unchanged crystalline state, and cycloamylose was a solubilizing agent for flurbiprofen in this solid dispersion. Thus, the solid dispersion may be useful to deliver flurbiprofen with enhanced bioavailability without changes in crystalline structure.

Khan et al., 2010 developed solid dispersion (SD) formulation of cyclosporine (CyA) using polyethylene glycol (PEG-6000) to enhance its dissolution rate followed by nondestructive method for the prediction of both drug and carrier. SD formulations were prepared by varying the ratio of CyA and PEG-6000 by solvent evaporation technique and characterized by dissolution, scanning electron microscopy (SEM), differential scanning calorimetry (DSC), Fourier transform infrared (FTIR), powder X-ray diffraction (PXRD), near infrared (NIR) and near infrared chemical imaging (NIR-CI). Thus chemometric applications of nondestructive method sensors provided a valuable means of characterization and estimation of drug and carrier in the novel formulations.

Srikanth et al., 2010 studied the dissolution rate enhancement of poorly water soluble drug antiandrogen agent bicalutamide using different solubilizing enhancers (Povidone K-30 and Poloxamer 407). Poloxamer 407 based dispersion exhibited higher dissolution rate than povidone K 30. Powder X-ray diffraction showed that degree of crystallinity decreased by increasing concentration of povidone K 30 carrier. FTIR studies showed that drug used was compatible with carriers. Solid dispersion prepared with povidone K30 changed crystalline form of drug to amorphous form.
Uddin et al., 2010 prepared solid dispersion to enhance the solubility and dissolution characteristics of atorvastatin calcium using solvent evaporation method. HPMC was used as the polymer in different drug to different polymer ratios. From the study it was found that HPMC at a drug polymer ratio of 2:1 improves the water solubility of the drug by 2 folds when prepared as solid dispersions by solvent evaporation methods.

Choi et al., 2011 developed a novel flurbiprofen-loaded solid dispersion without crystalline change. Various flurbiprofen loaded solid dispersions were prepared with water, sodium carboxymethyl cellulose (Na-CMC), and Tween 80. The effect of Na-CMC and Tween 80 on aqueous solubility of flurbiprofen was investigated. The physicochemical properties of solid dispersions were investigated using SEM, DSC, and X-ray diffraction. The dissolution and bioavailability in rats were evaluated compared to commercial product. Unlike conventional solid dispersion systems, the flurbiprofen-loaded solid dispersion gave a relatively rough surface and changed no crystalline form of drug. These solid dispersions were formed by attaching hydrophilic carriers to the surface of drug without crystal change, resulting in changing the hydrophobic drug to hydrophilic form. Thus, the flurbiprofen-loaded solid dispersion would be useful to deliver poorly water-soluble flurbiprofen with enhanced bioavailability without crystalline change.

Choi et al., 2011 investigate the effects of solid carriers on the crystalline properties, dissolution and bioavailability of flurbiprofen in a solid self-nanoemulsifying drug delivery system (solid SNEDDS), different solid SNEDDS formulations were prepared by spray-drying the solutions containing liquid SNEDDS and various carriers. Silicon dioxide, a hydrophobic solid carrier, produced an excellent conventional solid SNEDDS with a nanoemulsion droplet size of less than 100 nm, similar to the liquid SNEDDS and smaller than the other solid SNEDDS formulations. The drug was in an amorphous state in this solid SNEDDS.
Vippagunta et al., 2011 developed a physically and chemically stable amorphous solid dispersion of a poorly water soluble compounds NVS981 which is highly thermal sensitive and degrades upon melting at 165 °C. Hydroxy propyl methyl cellulose (HPMC) based polymers; HPMC3 cps, HPMC phthalate (HPMCP), and HPMC acetyl succinate (HPMC AS) were selected as carrier to prepare solid dispersion using hot melt extraction because of their low glass transition temperatures. The solid dispersion was compared for their ease of manufacturing, physical stability such as recrystallisation potential, phase separation, molecular mobility and enhancement of drug dissolution. In conclusion of the 3 polymer studied for preparing solid dispersions water soluble polymer HPMC3cps of thermally sensitive compound using hot melt extraction, HPMCAS was found to be the most promising as it was easily processible and provided stable solid dispersions with enhanced dissolution.

Yao et al., 2011 prepared solid dispersion by a conventional solvent evaporation method from the water-insoluble model drug 10-hydroxycamptothecin (HCPT) and mono methoxy poly (ethylene glycol) 2000 (mPEG 2000). And then one type of novel biodegradable nanoparticles, the solid dispersion (HCPT/mPEG-CHO) grafted with carboxymethyl chitosan (HCPT/mPEG-g-CMCTS) was synthesized. The increase in HCPT solubility of solid dispersion was up to 21-fold compared with the original drug. Thus this drug model found to be attractive candidates as delivery biosystems in tumor therapy.