2. LITERATURE REVIEW

2.1. PAST STUDIES ON SOLID DISPERSIONS

2.1.1. Solid dispersions of telmisartan were prepared by surface solid dispersion method using polymers like Poloxamer 407, PEG 6000 by solvent evaporation method. The drug was solubilized by surfactants and/or polymers then adsorbed onto the surface of extremely fine carriers to increase its surface area and to form the surface solid dispersion which give more surface area for absorption of the drug. A $2^2$ full factorial design was used to investigate carrier the joint influence of formulation variables: Amount of carrier and adsorbent. Saturation solubility studies showed improved solubility of SSD8 than other batch and pure drug. (Bhumika, 2012).

2.1.2. Rosuvastatin orodispersible tablets were prepared by exploiting the solubilizing effect of HP-β-CD. Drug–CD complex systems, prepared by different techniques, were characterized. The inclusion complex containing RST: HPβ-CD (1:1) was formulated into tablets using super disintegrants like sodium starch glycolate, crosspovidone and crosscarmellose by direct compression and evaluated. A significant improvement of the drug dissolution profile was achieved from tablets containing drug–CD systems (Kneaded products showed the best dissolution profiles, reaching more than 97.46% drug release in 20 min.). (Akbari, 2011).

2.1.3. Solid dispersion of prednisolone was prepared with PEG 6000 or different carbohydrates such as lactose and dextrin with various ratios of drug to carrier i.e., 1:10, 1:20 and 1:40 by co-evaporation method and were evaluated. The results indicated that lactose was suitable carrier to enhance the in vitro dissolution rate of prednisolone. The data from the x-ray diffraction showed that the drug was still detectable in its solid state in all solid dispersions except solid dispersions prepared by dextrin as carrier. The results from infrared
spectroscopy showed no well-defined drug–carrier interactions for coevaporates. (Milani, 2011).

2.1.4. Solid dispersions of gliclazide with polyethylene glycol were prepared by the fusion method. In vitro dissolution study of gliclazide, its physical mixture and solid dispersion were carried out to demonstrate the effect of PEG 6000. Analytical techniques such as FT-IR, DSC and XRD were used to characterize the drug in the physical mixtures and solid dispersions. The dissolution studies of solid dispersion and physical mixture showed greater improvement compared to that of the pure drug. The FT-IR spectra suggested that there was no interaction between gliclazide and PEG 6000 when prepared as a solid dispersion. DSC and XRD study indicated that the drug was converted in the amorphous form. (Patil, 2011).

2.1.5. A combination of melt and adsorption techniques was employed for the preparation of solid dispersions. PEG 4000, PEG 6000, and Gelucire 44/14 were used as hydrophilic carriers, and lactose monohydrate was used as an adsorbent. Phase solubility curves are of AL type, indicating a linear relationship between drug solubility and carrier concentration. Dissolution studies reveal an improvement of in vitro drug release. Physicochemical characterization of solid dispersions by FTIR, DSC and PXRD suggests a reduction in drug crystallinity following dissolution enhancement. (Komal, 2011).

2.1.6. Metformin hydrochloride (MET) sustained-release solid dispersions (SD) were prepared by the solvent evaporation and closed melt method using compritol 888 ATO as the polymer with five different drug-carrier ratios. Characterization of solid dispersion was carried out by FTIR spectroscopy, Ultraviolet spectroscopy (UV), DSC, XRPD. FTIR and UV studies suggested that no bond formation had occurred between the polymer and the drug. DSC and XPRD results ruled out any interaction or complex formation between the
drug and the polymer. The solvent evaporation method was found to be more helpful than the closed melt method, giving the sustained release action. (Jagdale, 2011).

2.1.7. Orally fast-disintegrating tablet (FDT) was prepared by direct compression, containing a poorly soluble drug (Perphenazine, PPZ) formulated as a stable solid dispersion. The stability studies of the fast dissolving 5/1, 1/5, 1/20 (w/w), PPZ/ PVP K30 or polyethylene glycol 8000 (PEG)) solid dispersions, and amorphous PPZ were conducted. It was found that 1/5 PPZ/PEG was the most stable dispersion under elevated temperature and/or humidity. FDTs containing 60% of mannitol, 15% of calcium silicate, 15% of crospovidone, and 10% of 1/5 PPZ/PEG solid dispersion exhibited fast disintegration times and fast onset of drug dissolution and these properties were found to be retained with storage. (Riikka, 2010).

2.1.8. Solid dispersions of predinisolone were prepared and characterized the prepared solid dispersions by Fourier transform infrared (FTIR) spectroscopy, powder X-ray diffraction, and thermal analysis techniques. The optimized formulations of solid dispersions were prepared by employing different methods using different carriers with various drug: carrier ratios. Their dissolution behavior was also compared. The results indicated that in vitro dissolution rate of PRD was remarkably improved in the solid dispersion of the drug compared with physical mixture and drug alone. (Mohanraj, 2010).

2.1.9. Fenofibrate solid dispersions were prepared using hot melt extrusion and compared the difference of Eudragit E100 and polyvinylpyrrolidone-vinyl acetate copolymer S630 (PVP-VA) in dissolution. In vitro dissolution test and in vivo bioavailability of the drug was studied. Eudragit E100 (1:4) solid dispersion has lower dissolution in 0.1N HCl and higher dissolution in water. Hot-melt extrusion was an excellent method to improve the dissolution and therefore the bioavailability of Fenofibrate. (Haibeng, 2010).
2.1.10. Solid dispersions of nifedipine and carbamazepine were prepared by melting method from the water-insoluble model drugs carbamazepine and nifedipine and polyethylene glycol 1500 or 1:1 mixtures of PEG 1500 and polyvinylpyrrolidone (PVP 30, PVP 12), polyvinylpyrrolidone-co-vinylacetate (PVPVA) and Eudragit. Their dissolution behaviours were also compared. The results indicated that in vitro dissolution rate was remarkably improved in the solid dispersion of the drug compared with pure drug alone. (Heike, 2010).

2.1.11. Solid dispersions of gliclazide using PEG 4000, PEG 6000 was prepared by fusion method and dispersions using PVP K 30 were prepared by solvent evaporation method. It was observed that dissolution rate was enhanced compared to pure drug. The study clearly showed addition of PVP K 30 improved dissolution rate significantly due to solubilization and improved wetting of drug in PVP K 30. The study concluded that solid dispersion of Gliclazide using hydrophilic polymer would improve the solubility and dissolution rate. (Shavi, 2010).

2.1.12. Stability studies of Solid dispersions were successfully performed. Production of amorphous solid dispersions proved to be successful; the alterations seen in the physical state of itraconazole upon storage affect its dissolution behaviour. For the 50/50 dispersion, crystallization of itraconazole reduced the dissolution performance of the powder. For the 40/60 dispersion, some crystallization could be observed. 30/70 and 20/80 dispersions showed the absence of crystallization. For the 40/60, 30/70 and 20/80 dispersions, an increase in dissolution performance was seen after 10 months of storage. In vivo results in the rat proved the presented approach to be potentially useful for the formulation of solid dispersions of itraconazole. (Bernard, 2009).

2.1.13. Solid dispersions of Furosemide were prepared and the study showed that the dissolution rate of furosemide was enhanced considerably by formulating it as a solid
dispersion using sodium starch glycolate by kneading method. Incorporation of superdisintegrants in the solid dispersions played a critical role in dissolution enhancement. (Ganesh, 2009).

2.1.14. The effect of polyethylene glycol 4000 (PEG 4000) on in vitro dissolution of gliclazide from solid dispersions prepared by the melting or fusion method was studied. The dissolution behaviour was also compared. The results indicated that in vitro dissolution rate of gliclazide was remarkably improved in solid dispersion of drug compared with physical mixture and drug alone. In conclusion, dissolution of gliclazide can be enhanced by the use of hydrophilic carrier. (Moreshwar, 2009).

2.1.15. Solid dispersions of indomethacin by using polymers like Gelucire 50/13 and PEG 4000 were prepared by hot melt method at 1:1, 1:2, 1:4 drug to polymer ratio. The highest ratio of polymer (1:4) enhanced drug solubility about 4 folds and 3.5 folds in case of PEG and gelucire respectively. An increase in dissolution rate was observed at pH 1.2 and 7.4. They observed that formation of indomethacin – PEG solid dispersion destroyed almost completely the crystallinity of drug and represents a suitable modification for improving its bioavailability. (Badry, 2009).

2.1.16. Solid dispersions of ibuprofen were prepared using polyethylene glycol 20000 by physical mixing and solvent evaporation method. Solid dispersions were characterized by scanning electron microscopy (SEM), differential scanning calorimetry (DSC) and fourier transform infrared spectroscopy (FTIR), and evaluated for solubility and in vitro drug release. A significant improvement of the drug dissolution profile was achieved from solid dispersions containing drug–polyethylene glycol20000 systems. (Madhuri, 2008).

2.1.17. Solid dispersions of ibuprofen were prepared and they were evaluated for solubility, in vitro release and oral bioavailability of ibuprofen in rats. Quicker release of ibuprofen from
SDs in rat intestine resulted in a significant increase in AUC and \( C_{\text{max}} \), and a significant decrease in \( t_{\text{max}} \) over pure 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. (Madhuri, 2008).

2.1.18. Piroxicam solid dispersions containing hydroxypropyl methylcellulose acetate succinate (HPMCAS-LF, -HF) as a carrier were prepared. Binary (Piroxicam–HPMCAS) and ternary (Piroxicam–HPMCAS–Carbopol 940) solid dispersions were prepared by spray-drying method. \textit{In vitro} release was studied using a flow-through cell technique. Studies of dissolution rate of piroxicam from solid dispersions were carried out in comparison with corresponding physical mixtures and drug alone. The dissolution profiles depend on the presence of carbopol 940 in solid dispersions. (Renata, 2008).

2.1.19. Solid dispersion of celecoxib containing drug and hydrophilic carriers were prepared in ratios of 9:1, 4:1, 2:1, 1:1, 1:4 and 1:9 of drug:carrier by physical mixing, co-evaporation and co-grinding. SSDs of celecoxib with superdisintegrants were characterized. IR spectroscopy and DSC showed no significant change in solid state of celecoxib in the surface solid dispersions and physical mixtures of celecoxib and carriers. The increase in the dissolution rate and consequent enhancement of anti inflammatory effect in rats of celecoxib were attributed to reduced particle size of celecoxib deposited on the surface of carrier and enhanced wettability of the drug particles brought about by the carrier. (Dixit, 2007).

2.1.20. Solid dispersions of carbamazepine were prepared by using PVPK-30, Polyethylene glycol 4000, Polyethylene glycol 6000 as water soluble carrier at various proportions by employing solvent evaporation method. It was found that dissolution rate and dissolution parameter of the drug from the physical mixture as well as solid dispersion was higher than those of the intact drug. (Prajapati, 2007).
2.1.21. A study on enhancement of intestinal absorption of few Cox-2 inhibitors through interaction with β-cyclodextrin. The water solubility of these drugs was enhanced by complexion with β-cyclodextrin. Studies also revealed that as the concentration of complexing agent increases the rate of absorption also increases proportionately. This indicates a strong positive correlation between the in-vitro drug dissolution and absorption of the drug through everted gut. (Swati, 2007).

2.1.22. Fast dissolving tablets of oxcarbazepine were prepared by wet granulation method using Avicel pH 102 as diluent, Ac-Di-Sol as superdisintegrant and starch as binder. An effective, stable and pleasant tasting formulation containing 12% Ac-Di-Sol, 25% Avicel and 8.5% starch was found to have a good hardness of 4-4.5 Kg/cm², disintegration time of 28±5 sec and drug release of not less than 90% within 30 min. (Sheetal, 2007).

2.1.23. Felodipine solid dispersions in the presence of various carriers were prepared using solvent wetting method. Dissolution profiles were found to depend on the carrier used; the dissolution rate of felodipine increased slowly for solid dispersions prepared using HPMC, where as rapid initial dissolution rates were observed for solid dispersions prepared using polyvinyl pyrrolidone or poloxamer. Increase in dissolution rate was partly dependent on the ratios of Felodipine to carrier. (Kim, 2006).

2.1.24. Solid dispersions of etoricoxib with polyethylene glycol 4000 (PEG) and PVP K30 were prepared by physical mixing, solvent evaporation method and the influence of polyethylene glycol 4000 (PEG) and PVP K30 onin vitro dissolution of etoricoxib from solid dispersions was studied. Solid dispersions were prepared using the solvent evaporation method containing PEG was found to be more effective in increasing the drug dissolution compared to PVP. (Bhanubhai, 2006).
2.1.25. Meloxicam solid dispersions were prepared at various drug concentrations (5-40%) with polyethylene glycol 6000 by different techniques (physical mixing, solvent evaporation) and were characterized. The solubility of drug increased linearly with increase in polymer concentration showing A (L) type solubility diagrams. The solid dispersions of the drug demonstrated higher drug dissolution rates than physical mixtures and pure meloxicam, as a result of increased wettability and dispersibility of drug in a solid dispersion system. (Vijaya Kumar, 2006).

2.1.26. Solid dispersions of valdecoxib with mannitol, polyethylene glycol 4000 and PVP K-12 were prepared by various methods and were evaluated for drug release. Valdecoxib solid dispersion with PVP K-12 showed maximum drug release. Hence, the tablet formulation containing valdecoxib-PVP K-12 solid dispersion was prepared with a view to improve its water solubility. (Patel, 2006).

2.1.27. A powder SD of indomethacin (IM) with CrosPVP was prepared using mechanical mixing followed by heating to temperatures below the melting point. IM and CrosPVP interacted to produce IM in an amorphous state when its concentration was <40%. Solubility of IM was improved about four fold compared to IM crystal. SD had good fluidity, and tablets were prepared by direct compression. The dissolution of IM from tablets was similar to that of SD powder because CrosPVP, a disintegration agent, caused the tablets to break up rapidly. (Makiko, 2005).

2.1.28. A study to improve the solubility and dissolution of drug by formulating the solid dispersions of rofecoxib with various hydrophilic carriers (Polyethylene glycol 6000, Polyvinyl pyrrolidone K-30, Eudragit E-100) and inclusion complex with β-cyclodextrin. The dissolution was obtained as high as 75% in rofecoxib: β-cyclodextrin in molar ratio of 1:5 prepared by kneading method. (Soniwala, 2005).
2.1.29. Solid dispersion of nimodipine in water using PEG-2000 were prepared by melt embedding method to investigate cooling rate during preparation and storage conditions like temperature and relative humidity. The formulation showed high dissolution rate due to absence of crystalline form of drug. Physico chemical properties were investigated by thermal analysis, X-ray diffraction and macroscopic method. Results concluded that determination of crystallinity and dispersivity of drug in solid dispersion can be successful by combining different methods like DSC, hot stage microscopy, X-ray diffraction. (Urbanetz, 2005).

2.1.30. Tablet formulations of piroxicam containing polyvinyl pyrrolidone K-30 (PVP K30) and sodium lauryl sulphate were prepared with a view to increase aqueous solubility of drug. Solid dispersions containing drug and PVP K-30 in various ratios were prepared by the solvent evaporation method. Two formulations were developed for preparation of tablet dosage form of piroxicam-PVP K-30 solid dispersions containing sodium lauryl sulphate using two different disintegrating agents. (Patel, 2004).

2.1.31. Solid dispersions of indomethacin with polyethylene glycol (PEG) 6000, Myrj 52, Eudragit E100, and different carbohydrates such as lactose, mannitol, sorbitol, and dextrin were prepared and subjected to characterization studies. The solid dispersions were prepared by three different methods depending on the type of carrier. The results indicate that lactose, mannitol, sorbitol, and especially Myrj 52 are suitable carriers to enhance the in vitro dissolution rate of indomethacin at pH 7.2. Eudragit E100, Myrj 52, and mannitol increase the dissolution properties at pH 1.2. (Hadi. V, 2004).

2.1.32. Solid dispersions of 10% w/w griseofulvin in different polyethylene glycols (PEGs) with or without incorporation of alkali dodecyl sulphates were prepared by the melting method. The investigations concerned the solid state (X-ray powder diffraction). The critical
concentrations of SDS for the formation of solid solutions in varying PEGs were evaluated. (Craig, 2002).

2.1.33. In vitro and in vivo evaluation of carbamazepine-PEG 6000 solid dispersions was conducted. Solubility study showed that a linear increase in carbamazepine solubility with increase in PEG 6000 concentration. The dissolution profile indicated that percentage drug dissolved was dependent on proportion of PEG 6000. Statistical analysis of pharmacokinetic parameter showed that the carbamazepine: PEG 6000 binary systems displayed higher bioavailability of drug than pure drug. (Zerrouk, 2001).

2.1.34. Solid dispersions of nifedipine with polyethylene glycols (PEG4000 and PEG6000), HPβCD, and poloxamer 407 (PXM 407) in four mixing ratios were prepared by melting, solvent, and kneading methods. Highest dissolution rate and the $T_{80\%}$ as short as 15 min were obtained from PXM 407 solid dispersion prepared by melting method at the mixing ratio of 1:10. The wettability and solubility were markedly improved in the PXM 407 system. (Ritthidej, 2000).

2.1.35. Solubilising and non-solubilising solid dispersions containing amorphous Halofanterine free base using a simple fusion method requiring temperatures as low as 70°C were prepared. These formulations were evaluated in vivo in fasted beagles and in comparison to the commercial tablet, these afforded a five- to seven-fold improvement in absolute oral bioavailability. This study also showed that when Halofanterine was delivered in the amorphous form, the solubilising formulations did not offer significant bioavailability advantages over the non-solubilising formulation. A stability study of the non-solubilising Halofanterine: PEG 6000 formulation showed that it was stable at temperatures below 40°C and that a drug loading of 10% or less improved the stability of the formulation over longer periods. (Khoo, 2000).
2.1.36. Atenolol tablets were prepared from solid dispersions employing povidone, crospovidone, polyvinyl pyrrolidone/vinyl acetate and Eudragit E as polymers. The solubility and the release rate of atenolol from solid dispersions were compared to the drug alone. The influence of various parameters (type of polymer, drug to polymer ratio, pH) on the solubility and dissolution rate of the drug was also evaluated. The dissolution rates were considerably improved from solid dispersions of atenolol with povidone and crospovidone. (Moneghini, 1998).

2.1.37. Solid dispersions of etoposide were prepared by coprecipitating the drug with polyethylene glycols (PEG) of different molecular weights in various ratios. It was found that the coprecipitate of etoposide with PEG 8000 (1:10, PEG weight fraction of 0.91) increased its solubility 2-fold and dissolution rate 42-fold. The co precipitates with other PEG’s (PEG 1500, PEG 3400, PEG 6000) and PVP 40000 also increased etoposide dissolution rate to a great extent. (Shah, 1995).

2.1.38. Solid dispersions of tolbutamide were prepared by solvent method and co-precipitate method. The effect of aging on tolbutamide solid dispersions with PEG 6000 and tolbutamide-13-cyclodextrin inclusion complex was stored at three temperatures for 3 years by comparing the physicochemical characteristics followed by XRD, FTIR and DTA. In all cases, during the 3 years of storage, no differences in IR spectra were found with respect to the fresh solid dispersions or complex. Storage at room temperature and 5°C did not have any marked effect on the dissolution profiles for the tolbutamide-PEG 6000 coprecipitate. In conclusion, this study has demonstrated that it is possible to prepare stable solid dispersions for a long period of time. (Kedzierewicz, 1995).
2.2. PAST STUDIES ON SIMVASTATIN SOLID DISPERSIONS

2.2.1. To formulate simvastatin as orodispersible tablets by incorporating it as a solid dispersion using Pluronic® F68 as carrier. CCS was used as superdisintegant, MCC as filler, PVP K-30 as binder and 1:1 magnesium stearate/talc mixture as lubricant. Box- Behnken design was adapted to explore the main and interaction effects of three independent formulation variables, namely superdisintegant concentration (X1), lubricant mixture concentration (X2), and binder concentration (X3). The selected dependant variables were the in vitro and in vivo disintegration times, dissolution rate at 4 min, and dissolution efficiency after 30 min. Tablet formula, composing of 12% superdisintegant, 2% lubricant mixture and 3% binder, showed the highest dissolution rate with an acceptable disintegration time (43 sec). (Ahmed, 2012).

2.2.2. Solid dispersions of simvastatin with mannitol, pluronic F-68, PEG 4000 and PVP K-30 were prepared and evaluated. The formula of choice was compressed into fast disintegrating tablets and coated with Eudragit® S100. The effects of several variables related to both solid dispersion preparation and tablet coating on drug dissolution was studied. 1:5 simvastatin/ Pluronic® solid dispersions showed the greatest improvement in dissolution efficiency at the lowest carrier ratio. Best results were given by the 10% coat (20:2:1 w/w Eudragit S100/ triethylcitrate/ talc). (Ahmed, 2011)

2.2.3. Simvastatin solid dispersions were prepared in 1:1, 1:2, 1:3, 1:4 and 1:5 ratios of drug to carrier by solvent evaporation and kneading methods. The prepared solid dispersions were evaluated. Faster dissolution was exhibited by solid dispersion prepared by solvent evaporation containing 1:4 ratio of simvastatin: urea. It was observed that kneading method was more effective than solvent evaporation. In vitro drug release studies revealed that there was progressive improvement in the drug release rate from solid dispersions systems compared to pure drug alone. (Balaji, 2011).
2.2.4. Surface solid dispersions (SSDs) of simvastatin were prepared with two different super disintegrants in three different drug–carrier ratios by co evaporation method. Prepared SSD’s were characterized by DSC, PXRD, SEM, and IR and evaluated for drug content, saturation solubility, pH-dependent solubility, solubility in biorelevant media (i.e., fasted-state simulated intestinal fluid [FaSSIF] and fed-state simulated intestinal fluid [FeSSIF]), in vitro dissolution, and in vivo studies by a triton-induced hypercholesteremia model in rats. (Monica, 2010).

2.2.5. Solid dispersions of simvastatin with PEG 4000 and PEG 6000 were prepared by fusion method in various ratios of 1:1, 1:3, and 1:5 and inclusion complexes with HP-β-CD obtained by kneading method in a ratio of 1:1. The formulations were characterized by phase solubility studies, DCS, XRD, and FTIR spectroscopy. Inclusion complex prepared with HP-β-CD by kneading method showed highest dissolution rate than pure simvastatin and showed highest improvement in wettability and dissolution rate due to the amorphous nature and approximately 100% of drug dissolved within 60 min. (Dipika, 2010).

2.2.6. Solid dispersions of simvastatin were prepared using different ratios of β-CD by physical mixture, solvent evaporation, kneading and fusion method and evaluated. The solubility profile indicated that there is increase in solubility of Simvastatin when β-CD concentration is increased. The solid dispersion complex of drug (1:5 ratios) gave better dissolution profile as compared to pure drug and other solid dispersions (1:1 and 1:3). (Punitha, 2010).

2.2.7. Simvastatin solid dispersions with PEG 6000 or PVP K15 in 1:1, 1:2, 1:3, 1:4, and 1:5 ratios were prepared by melting method, solvent evaporation method and melting solvent method. Drug release from all solid dispersions was significantly improved when compared to their corresponding physical mixture or drug alone. The preparation of simvastatin SD
with PEG or PVP is a promising strategy to improve the bioavailability of the drug. (Taizia, 2010).

2.2.8. Solid dispersions of simvastatin (SIM) with inert carriers PEG 6000 or PVP K15 in 1:1, 1:2, 1:3, 1:4, and 1:5 ratios were prepared and their stability and dissolution properties were investigated. Solid dispersions were characterized. Tablets containing SD SIM : PEG 6000 were developed and their dissolution profile was evaluated. Drug release from all SD was significantly improved when compared to their corresponding physical mixture or SIM alone. SIM SD with PEG is more advantageous over the dispersions prepared with PVP because they do not show drug degradation during preparation. (Nivaldo, 2010).

2.2.9. Solid dispersions of simvastatin (SIM) with super disintegrants like crospovidone (CP), croscarmellose sodium (CCS) and sodium statrch glycolate (SSG) were prepared by solvent evaporation method. The solubility of SD with CP of SIM was improved about eightfold compared to SIM plain crystals. The SD had good fluidity, and tablets were prepared by direct compression and evaluated. The dissolution of SIM from tablets was almost similar to that of SD. (Bindu Madhavi, 2010).

2.2.10. Solid dispersions of simvastatin were prepared with polyethylene glycol 4000 by fusion cooling and solvent evaporation techniques where as with PVP K30 by solvent evaporation method in different drug to carrier ratios. Solid dispersion prepared with PVP showed highest improvement in wettability and dissolution rate of simvastatin. Tablets containing solid dispersion prepared with PEG and PVP showed significant improvement in the release profile of simvastatin as compared to tablet containing simvastatin without PEG or PVP. (Rakesh, 2008).

2.2.11. Amorphous solid dispersions of simvastatin with relatively lower glass transition temperature were prepared by spray drying technique and characterized. Dichloromethane
suspensions of simvastatin either alone or in combination with PVP (1:1 or 1:2 parts by weight) were spray dried with proposed quantity of Aerosil 200 (1:1, 1:1:1, 1:2:2 parts by weight of SIM, Aerosil 200 and PVP, respectively). There was dramatical improvement in rate and extent of in vitro drug release of SD 1:2:2. In vivo study in rats also justified the improvement in therapeutic efficacy. (Anshuman, 2005).

2.3. PAST STUDIES ON LOVASTATIN SOLID DISPERSIONS

2.3.1. Solid dispersions of lovastatin were prepared by using β cyclodextrin and polyvinylpyrrolidone K90 (PVP K90) as carriers in different drug-to-carrier ratios by solvent evaporation technique and characterized. Solid-state characterization indicated lovastatin was present as amorphous material in formulation with PVP K90, due to efficient entrapment in polymer matrix. Lovastatin in pure form has very slow dissolution rate, than compared to dispersions. Solid dispersions have efficient wetability and dispersability along with decreased crystallinity of the drug. (Ashis Kumar, 2012).

2.2.2. Lovastatin solid dispersions were prepared with PEG 6000 by physical mixing, fusion and co-grinding methods. The prepared solid dispersions were directly compressed into tablets along with solubility enhancing excipients like croscarmellose sodium, crospovidone, pregelatinized starch, etc. Solid dispersions of lovastatin with PEG-6000 (fusion method) were found to release drug faster than the pure drug. The dispersions prepared by fusion method were further compressed as tablets with various super disintegrants. Order of disintegration of various tablet preparations with super disintegrants was found to be crospovidone > pregelatinised starch > croscarmellose. (Vidyadhara, 2011).

2.3.3. The solubility and dissolution of lovastatin was improved by solid dispersion technique using hot melt, solvent evaporation and kneading method with Poloxamer F-68. Effects of various parameters such as type of carrier system used, drug: carrier ratio were studied. The
dissolution rate of lovastatin was directly proportional to increment in proportion of the carrier. Pure lovastatin showed only 61% drug release in 1 hour whereas the solid dispersion prepared by solvent evaporation method using poloxamer F-68 showed faster in vitro drug release in comparison to pure drug (plain tablet) and marketed formulation. (Kumar Katare, 2011).

2.34. Solubility of lovastatin was enhanced by using modified locust bean gum (LBG) as carrier using solid dispersion techniques. LBG was modified by heating which increased viscosity irreversibly. Increase in solubility of lovastatin with increase in concentration of MLBG (modified LBG) was observed. In vivo studies were carried out to measure HMG co-A reductase activity. They observed significant reduction in HMG co-A reductase activity in case of solid dispersion (LS) than pure drug. (Patel, 2008).

2.3.5. Solid Dispersions of lovastatin with PEG 4000 were prepared by fusion-cooling and solvent evaporation, whereas dispersions containing PVP K30 were prepared by solvent evaporation technique and characterized. Solid dispersion prepared with PVP showed the highest improvement in wettability and dissolution rate compared to pure lovastatin. Tablets containing solid dispersion prepared with PEG and PVP showed significant improvement in the release profile of lovastatin compared with tablets without PEG or PVP. (Patel, 2007).

2.3.6. Solid dispersions of lovastatin have been formulated to improve its solubility and dissolution characteristics, reduce dosing frequency and to improve its stability by solvent evaporation method and characterized. Dissolution data of all solid dispersions indicated increase in dissolution as compared to pure drug and increase was due to wetting phenomenon of superdisintegrants used for preparation of solid dispersions. The bioavailability also increased due to increased wettability of the solid. (Khayyam, 2011).