# Chapter - 2. Literature Survey

<table>
<thead>
<tr>
<th>S. No</th>
<th>Name of the Sub Title</th>
<th>Page No</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>Method Related – Nanoemulsion</td>
<td>32-45</td>
</tr>
<tr>
<td>2.2</td>
<td>Drug Related</td>
<td>45-48</td>
</tr>
<tr>
<td>2.3</td>
<td>Method Related – Soliddispersion</td>
<td>48-54</td>
</tr>
<tr>
<td>2.4</td>
<td>Bioanalytical Method Related</td>
<td>54-55</td>
</tr>
</tbody>
</table>
CHAPTER - 2

LITERATURE SURVEY

2.1 METHOD RELATED - NANOEMULSION

Rajendra Chouksey, et al., (2011) developed and characterized nanoemulsion containing atorvastatin (AT) with an objective to increase its solubility and bioavailability. The various components were safe for the internal use and various excipients selected were oil phase- Safsol 218 and Oleic acid mixture, surfactants-Tween 20 and the cosurfactants- Carbitol. To detect the region of nanoemulsion pseudo ternary phase diagrams were constructed (using aqueous titration method). These phase diagrams were used to observe different concentrations of oil and surfactant used for the formulation, which formed nanoemulsions. Best formulations were detected based on the various thermodynamic stability test and dispersibility test. To perform the in vivo study optimized formulation was selected based on the various evaluation tests like optimum globule size, higher drug release, lower viscosity, minimum polydispersity value, and overall concentration of lower surfactant and co-surfactant. They have found significant difference in tmax of the formulated nanoemulsion when it is compared to drug suspension. At the same time it has also observed that there was no significant difference when it was compared to tablet. Whereas there is a significant difference in Cmax value of nanoemulsion when compared with the API drug suspension and tablet suspensions. From the above result they have confirmed the
efficacy of nanoemulsion to increase the bioavailability of lipophilic drugs.

**Gulshan Chhabra, et al., (2011)** formulated and evaluated nanoemulsion (NE) of amlodipine besilate which is a less water soluble drug by spontaneous emulsification method with an objective to increase the oral bioavailability of the drug and to release the drug at target site. To identify the nanoemulsion region pseudoternary phase diagrams were constructed. Selected formulations from the nanoemulsion region were evaluated for the various thermodynamic study to find the stable formulation. These formulations were also tested for the zeta potential, droplet size determination, refractive index, transparency, viscosity and polydispersibility. Formulated nanoemulsion was also subjected to in vitro dissolution study to understand the dissolution profile of the drug from the nanoemulsion. The dissolution study of the nanoemulsion indicated that there was a significant difference in the drug release from nanoemulsion when it has been compared with the tablet formulation. The selected optimal formulation was the formulation which contains 15% Labrafil M – as oil, 35% [Tween 80: ethanol (2:1)] – as smix, and 50% aqueous phase. This formulation was carefully evaluated by transmission electron microscopy (TEM) to observe the particle size and was also characterised for thermodynamic stability. The bioavailability studies performed on the formulation reviled that there was a significant difference in the bioavailability study when compared with the suspension of the drug. It has also observed that the residence time of
the formulation has also been increased when it was formulated in the nanoemulsion form.

**Vikas Bali, et al., (2010)** have developed and characterised nanoemulsion of ezetimibe which is a less water soluble drug and also evaluated its stability, pharmacokinetic and pharmacodynamic potential. Various oils were used to determine solubility of the ezetimibe. Two groups of different surfactants and cosurfactants were combined for the construction of pseudoternary phase diagrams. Various formulations were chosen from the o/w nanoemulsion region of pseudoternary phase diagrams and were subjected to various evaluation tests such as thermodynamic stability, refractive index, transparency, globule size determination, zeta potential, viscosity and dispersibility tests. Optimised formulation was also subjected to in vitro dissolution study to know its release rate.

**Emad B. Basalious, et al., (2010)** have develop and optimize SNEDDS formulations containing surfactants (which are reported as bioenhancers) for improvement of dissolution profile and oral absorption of a drug lacidipine (LCDP). Various oils and smix compositions were screened to choose the component combination of the nanoemulsion. To get a nanoemulsion which contains less amount of surfactant, more amount of lipids and have increased emulsification and dissolution characteristics D-optimal mixture experimental design was applied. In the design 3 formulation variables were included, they are a. the oil phase X1 (a combination of Labrafil and Capmul), b. the surfactant X2 (a combination of Cremophor and
Tween 80) and c. the co-surfactant X3. The formulation was then evaluated for size of droplet, absorbance of light, optical clarity, emulsification efficiency and drug release. Transmission electron microscopy (TEM) shows spherical droplet morphology of the formulations. The stability of the optimized formulation was unchanged after storage at temperature of 40°C and 75% RH for three months. The optimized formulation of the drug indicates improve in dissolution rate as compared to the drug suspension. Their results show that the optimized formulation, containing bioenhancing surfactants, can improve oral absorption of lacidipine.

Chakraborty S, et al., (2009) described the application of endogenous and exogenous lipids in the formulation of nanoemulsion and their role in increasing bioavailability of lipophilic drugs. They have also described the mechanism involved behind that, various approaches available for the design of oral drug delivery systems based on lipid, morphological characteristics of the lipids on digestion and in vitro- in vivo (IVIVC) correlation.

Shakeel F, et al., (2008) studied the stability and evaluation of celecoxib nanoemulsion containing Tween 80 as surfactant and prepared by a method called low energy emulsification. Stability of the formulation were checked for 3 months and it was observed that viscosity, droplet size and refractive index were slightly increased during storage under refrigerator and room temperature. At room temperature shelf life of the nanoemulsion formulation was found to
be 2.73 years. This research concluded that the stability of the drug can be enhanced in nanoemulsion formulation containing Tween 80.

**Porter CJH, et al., (2008)** explained the mechanism of intraluminal lipid processing and drug solubilization in stomach and small intestine. They also described the lipid formulation classification system (LFCS) and they concluded that lipid-based drug delivery systems provide an effective and practical solution to the problem of formulating drugs where low solubility in the fluids of the GIT limits drug exposure.

**RP Dixit and MS Nagarsenker, (2008)** have formulated self-nanoemulsifying granules (SNGs) to enhance the bioavailability of the ezetimibe. Different oils and smix (surfactant and cosurfactant mixtures) were screened and composition of SNS was optimized. Diluted SNS was evaluated for mean globule size to detect the particle size and stability. By using different proportions of water soluble colloidal silicon dioxide (as an adsorbing agent) the formulated selfnanoemulsifying systems were converted to free flowing selfnanoemulsifying granules. These self-nanoemulsifying granules were then characterized by various evaluation process like differential scanning calorimetry (DSC), X-ray diffraction pattern, in vitro dissolution profile and in vivo performance of the formulation in rats. The result of X-ray diffraction studies shows loss of crystallinity or solubilisation of the drug, ezetimibe in the prepared self-nanoemulsifying granules. It was also supported by SEM studies,
which didn’t show any proof of precipitation of the drug, ezetimibe on the carrier surface. There is an increase in the in vitro dissolution profile when it is compared with the plain drug.

**Ahmed Abdalla, et al., (2008)** developed novel pellet based self-emulsifying (SE) drug delivery system for hydrophobic drug (to deliver the formulation orally). Oil phase were selected based on the self-emulsifying properties of the oils, which is composed of Solutol HS fifteen and medium chain glycerides. The liquid SE lipid was then mixed with microcrystalline cellulose (MCC) and made into pellets by extrusion or spheronization process. The pellets were evaluated for shape, surface characteristics, size, and friability. In vitro dissolution study and digestion experiments were performed using physiological dissolution medium. When there was change in the oil to Solutol HS ratio it largely affected the diameter of the droplet in the dispersed SE mixtures. Another side it has also been observed that, digestion of SE mixtures have changed the solubilisation capacity of Progesterone. Pellets which are having good properties like shape, size, and friability, have been formulated through the addition of a selected SE mixture into microcrystalline cellulose (MCC). They have concluded that, extrusion or spheronization is a suitable process for the formulation of solid selfemulsifying pellets with up to 40% load of a liquid SE mixture.

**Lijuan Wang, et al., (2008)** prepared self –nanoemulsifying drug delivery systems (SNEDDS) to improve the dissolution profile of the
drug, ibuprofen. Various oil and surfactants were used for the formulation of the nanoemulsion. The effects of surfactant and HLB value on the formulation of nanoemulsion were systemically screened. It has also observed that decrease in the size of the droplets of the nanoemulsion increases the dissolution rate of ibuprofen and it was faster than the conventional tablet.

Abhijit A. Date, et al., (2007) have developed self-nanoemulsifying drug delivery systems (SNEDDS) to overcome the problems associated with the delivery of cefpodoxime proxetil (CFP). It is having poor bioavailability, it is also a high dose antibiotic which is having pH dependant solubility. To identify various components of SNEDDS solubility of drug in oily phases & surfactants was checked. To check the activity to emulsify the selected oily phases various surfactants and co-surfactants were evaluated. To detect the total area of nanoemulsification ternary phase diagrams were constructed for the selected formulation. The effect of drug and the dilution medium pH on the phase behavior of selected formulation were assessed. To detect the role of pH on its behavior the globule size of optimized CFP SNEDDS in various dissolution media was determined. It has seen that the optimized drug SNEDDS needed surfactant content less than 40% and the SNEDDS is having mean globule size of 170 nm, which was unaffected by the dilution medium pH. The optimized SNEDDS released drug completely within 20 min irrespective of the dissolution medium pH.
Sanjula Baboota, et al., (2007) investigated the efficacy of nanoemulsion formulations for transdermal delivery of celecoxib. The data’s of in vitro skin permeation of selected formulations was compared with drug gel and nanoemulsion gel formulation. It has seen that there is a significant increase in the enhancement ratio (Er), steady state flux (Jss) and permeability coefficient (Kp) in nanoemulsion formulations. These results indicate that for improved transdermal delivery of the drug nanoemulsions can act as a potential vehicles.

Shafiq S, et al., (2007) studied the formulation development and optimization of ramipril using nanoemulsion technique. Spontaneous emulsification method was used to formulate the nanoemulsion of the drug, ramipril which was used as antihypertensive and posses less solubility in water. The attempt was taken to increase the solubility of the drug, followed by increasing the bioavailability. On the basis of the solubility study Sefsol 218 was chosen as the oil phase for the formulation of the nanoemulsion. Various formulation have been prepared using oil and combination of surfactant and cosurfactant. It has also seen that there is no significant difference in the droplet size of the formulation selected from the phase diagram. At the same time it has also been observed that there is less polydispersity in the formulation which contains oil 20%, Smix 27% and water 53%. The sizes of the droplets were determined using TEM and it was found to be 34.5 nm. It has also observed that this nanoemulsion is having solubilisation capacity then the simple miceller solution and it has
also observed that it is having more thermodynamic stability than the other dispersion. Therefore, this technique can be used successfully to increase the solubility of the drug which are having less or poor aqueous solubility. Nanoemulsion also offers more advantages when compared to emulsion and suspension as it requires less energy input to manufacture it and having more stability. Author has also explained the construction method of the pseudoternary phase diagram and selection of the formulation from the phase diagram to avoid metastable formulation.

Pradip Kumar Ghosh, et al., (2006) have designed and evaluated microemulsion based drug delivery system for acyclovir to improve its oral bioavailability. The purpose of this work was to design and develop an oral microemulsion formulation for increasing the bioavailability and solubility of acyclovir to increase its efficacy. A microemulsion formulation based on Labrafac (Labrasol as surfactant & Plurol Oleique as cosurfactant) was designed for oral administration of acyclovir. Phase behaviour of the microemulsion was characterized. With that the capacity of solubilization of the microemulsion system were also characterized. An in vivo bioanalytical study of acyclovir from the formulation was investigated in rats. There is a presence of single isotropic region in the pseudoternary phase diagrams developed using various Labrasol: Plurol Oleique: Labrafac ratios, which was due to the formulation of the bicontinuous microemulsion developed. When there is an increase of Labrasol concentration in the formulation, there is an increase of the microemulsion region area in
the pseudoternary phase diagram and the volume of water and Labrafac solubilized; on the other hand, when there is an increase of Plurol Oleique percentage in the formulation produced revers effects. The microemulsion system was also characterised in terms of other characteristics, like transparency, pH, interfacial tension, viscosity diffusion, refractive index and bioavailability.

Acyclovir, which is a poorly soluble drug, displayed high solubility from the microemulsion formulation which was prepared using various excipients like Labrasol (32%), Plurol Oleique (8%), Labrafac (10%), and water (50%). The result of in vitro intraduodenal diffusion study and in vivo study indicates an increase of bioavailability (12.78 fold) of the acyclovir after administration of the formulated microemulsion orally when it is compared with the commercial tablets.

Ghosh PK, et al., (2006) developed an oral microemulsion formulation using Labrasol and plurol oleique for enhancing the bioavailability of acyclovir. The optimum microemulsion formulation contained Labrafac (10%), Labrasol (32%), Plurol Oleique (8%), and which was a transparent and less viscous system. In vivo bioavailability study performed in rats, showed an absolute bioavailability of 27.83% for the microemulsion, it is 12.78 times more than that of commercial tablet.

and its potential to give sustain release dosage form in continuous
and prolonged manner.

**Kang BK, et al., (2004)** developed the SMEDDS of Simvastatin for
improving its oral bioavailability. *In vitro* dissolution studies revealed
that release of Simvastatin from SMEDDS was faster than the
conventional marketed tablet (Zocor®). *In vivo* studies were carried out
in beagle dogs, and the relative bioavailability of the SMEDDS was 1.5
times higher compared to marketed tablet.

**K.Bouchemal, et al., (2004)** have prepared nanoemulsion using
spontaneous emulsification method. This nanoemulsion was prepared
using organic and aqueous phase. The organic phase used was
homogenous solution of oil, water miscible solvent and oil soluble
surfactant, where as the aqueous phase consists of water and water
soluble surfactant in it. Various emulsions were prepared using the
different combination of different oil and aqueous phase. The result
showed that the composition of the initial oil phase have great impact
in the formulation of the nanoemulsion. It has also observed that oil
which is having more viscosity gives smaller particle size.

**Gursoy RN, et al., (2004)** described application of SMEDDS for the
oral administration of the drug with less aqueous solubility. Oral
deliveries of such candidates create more problems in bioavailability.
SMEDDS which is a isotropic mixture of oil, water, surfactant and
cosurfactant can be used to increase the solubility and bioavailability
of the lipophilic drug. They have described various excipients used in
SMEDDS, mechanism of self-emulsification, characterization and improvement of oral absorption by SMEDDS. They concluded that SMEDDS were a promising approach for the formulation of drug compounds with poor aqueous solubility. The capability of oral absorption of the drug from the SEDDS influenced by various formulation–related parameters, such as oil to surfactant ratio, concentration of surfactant, polarity of the emulsion, charge and size of the droplets, all together it determine the self-emulsification ability. Although various researches are going on in the laboratories there are very less number of the formulation available in the market. Which shows the difficulties related to the formulation of the nanoemulsion.

Porras M, et al., (2004) studied formation of water-in-oil nano-emulsions in water/mixed nonionic surfactant/oil system. It has been proved that mixtures of surfactants can provide better performance than pure surfactants. For low water concentration, nano-emulsions breakdown could be attributed to Ostwald ripening; and for high water concentration, NE breakdown could be attributed to coalescence.

Kim CK, et al., (2001) showed the improvement of solubility and bioavailability of poorly water-soluble biphenyl dimethyl dicarboxylate (BDD), a drug used in treating liver diseases, using Tween 80, Neobee M-5 and triacetin. Ratio of 2:1, and 35% of triacetin, considerably improves the bioavailability of a poorly water-soluble BDD after oral administration, possibly due to the increase in solubility and
immediate dispersion of drug in the GI tract. Therefore, premicroemulsion concentrate may provide a useful dosage form for oral intake of water-insoluble drugs such as BDD.

**Lawrence MJ, et al., (2000)** have explained the formation of microemulsion phase behaviour, the role of surfactant and characterisation of the microemulsion. They also explained the importance of the cosurfactant in the formulation of the microemulsion and how they increase the thermodynamic stability of the formulation. Various oil phase and surfactant and cosurfactant used for the formulation were listed in the article.

**Khoo SM, et al., (1998)** formulated lipidic self-emulsifying formulations of Halofantrine, a highly lipophilic antimalarial drug. They prepared medium chain triglyceride (MCT) SEDDS, MCT SMEDDS and long chain triglyceride (LCT) SMEDD. Oral bioavailability studies of these three formulations were compared with that of Halofantrine free base (Hf). It was found that mean absolute bioavailability of Hf free base for all three formulations ranged between 52-67% which was 6-8 fold higher than the commercially available tablet formulation.

**Attwood D, et al., (1992)** studied the factors influencing the droplet size in non-ionic oil-in-water microemulsions. The droplet size in o/w microemulsions formed from isopropyl myristate (IPM), sorbital (S), water and either polysorbate (P) 80, 60 or 40 was determined by total intensity light scattering measurements. The droplet size of all
microemulsions increased with increasing volume fraction of IPM. An increase of total P + S content from 40 to 45% w/w at a P/S ratio of 1:2.5 caused a decrease of the droplet size in microemulsions prepared with P80.

*Attwood D, et al., (1992)* observed the phase studies on oil-in-water phospholipids microemulsions and also they investigated the influence of the ratio of surfactant to cosurfactant on the area of existence of the oil-in-water microemulsion region. They prepared oil in water nanoemulsions using isopropyl myristate as oil phase, egg lecithin and soya lecithin as surfactants. They found microemulsions prepared with soya lecithin had lower oil content and were formed at lesser concentration of surfactant and cosurfactant mixture.

*Kale NJ, et al., (1989)* prepared microemulsions using Brij 96 as surfactants and glycerine, ethylene glycol and propylene glycol as co-surfactants. They found that microemulsions at low water content were of a gel-like consistency while those at high water content were fluid in nature. They also studied the effect of the surfactant and co-surfactant ratio on the internal diameter at a fixed oil ratio. It was found that the diameter of the internal phase (oil) was found to decrease as the surfactant and co-surfactant ratio increased.

### 2.2 DRUG RELATED

*PD Goswami, (2013)* developed UV-spectrophotometer method for the determination of terbinafine HCl in bulk and in tablet dosage form. For the determination Terbinafine HCl, 0.1N HCl was used as solvent
system and wavelength for the detection was 223 nm. It has seen that it was a simple, sensitive, costeffective, accurate, precise, reproducible and rapid UV –spectrometric method for the determination of Terbinafine HCl in bulk and the tablet dosage form.

Lalit Chauhan, et al., (2013) have formulated the topical microemulsion for antifungal activity of terbinafine HCl. Various oil and surfactants have been used for the formulation of microemulsion. Pseudo ternary phase diagram was developed for the selection of the optimized formulation. Microemulsions were evaluated and TEM image shown that the shape of the micro droplets were spherical in shape. Optimized formulation showed better antifungal activity for the effective treatment of topical fungal infection.

Kaushal R Sabu, et al., (2013) have developed an emulgel formulation of an antifungal drug, terbinafine HCl. Carbopol 934 was used as a gelling agent. It was formulated so that it can bypass hepatic first-pass metabolism and improve the stability of the dosage form. Various formulation were prepared and evaluated for their physicochemical properties like homogeneity, pH, spreadability, colour etc. The selected formulation showed higher drug release then the marketed cream.

K Arun Prasad, et al., (2010) have prepared soliddispersion of terbinafine HCl by using PEG 6000 and polyvinyl pyrrolidone K30. Various ratio of the drug and carrier were used for the formulation of the soliddispersion. From the result it was clear that soliddispersion of
the drug shows better dissolution and drug release profile. Selected formulation was chosen for the preparation of 600 mg tablet dosage form which was again evaluated and its dissolution profile was compared with the dissolution of the drug from the marketed formulation. It has been seen that tablet prepared with solid dispersion shows better release profile than the marketed one.

**Ping Zhang, et al., (2008)** have developed a self-microemulsifying drug delivery system (SMEDDS) to increase the oral bioavailability of the lipophilic drug, oridonin. The various oil, surfactant and cosurfactant combination were screened and the various ratio of these components on the stability of the SMEDDS were checked. The formulation have been characterised by various evaluation procedures like determination of the size of the droplets, thermodynamic stability, Tem analysis, Refractive index, in vitro dissolution studies etc. The best formulation is the one which is composed of 30% Maisine 35-1 & Labrafac CC (1:1), 23.3% Transcutol P and 46.7% Cremophor EL. The result of *in vitro* release test indicates a 100% release of the drug, oridonin from SMEDDS with in a time period of 12 h. It has also been observed that there is a 2.2 fold increase in the bioavailability of the drug, oridonin from SMEDDS when compared with that of the suspension. Their studies demonstrated the potential use of SMEDDS for the delivery of oridonin by the oral route.
Narendra Kumar, et al., (2008) have prepared solid dispersion of the drug, Terbinafine hydrochloride as it is slightly soluble in the water. Prepared solid dispersion increased solubility and dissolution of the drug, terbinafine HCl. The main purpose of this research was to increase the dissolution rate of terbinafine hydrochloride by the solid dispersion technique with polyethylene glycol 6000 (PEG 6000) as carrier using fusion methods. The results show an increase in solubility of terbinafine HCl in the presence of PEG 6000 that is upto 10 % of carrier (36.89μg/mL). It has also observed that the dissolution rate improves with increase the amount of PEG 6000 in solid dispersion formulation. Fourier Transform Infrared - FTIR spectra shows no chemical interaction between drug and PEG 6000. Powder X-Ray Diffraction indicated the reduction in crystalinity of terbinafine HCl. The study clearly indicates the role of PEG-6000 to improves its dissolution rate.

2.3 METHOD RELATED – SOLIDDISPERSION

Charu Mendiratta, et al., (2011) had prepared solid dispersion of Lansoprazole to improve its saturation solubility and dissolution. This solid dispersion was prepared by using a novel amphiphilic polymer Soluplus and with a hydrophilic polymer PEG 4000. But the solid dispersion prepared with former polymer had shown highest saturation solubility. The prepared solid dispersion was further characterized by Fourier Transform Infrared spectroscopy, powder X-Ray diffraction, differential scanning colorimetry (DSC) Scanning
electron microscopy (SEM). By conclusion it was indicated a remarkable improvement in dissolution from the solid dispersion with 100% release in 20 minutes when compared with the pure LSP (40% release in 120 minutes).

MR Shivalingam, et al., (2011) worked on an anti-diabetic drug called Glipizide which is purely insoluble in water. Hence the solubility and dissolution of this lipophilic drug is enhanced by formulating solid dispersion. Solid dispersion was prepared using solvent evaporation method. Drug and carrier (HPMC, Cross carmellose sodium) in different ratios like 1:1, 1:2 and 1:3 by keeping drug weight constant was considered for formulating solid dispersions. Then the prepared solid dispersions were evaluated for phase solubility, in vitro dissolution study for drug release. From the evaluation study it was confirmed that 1:3 ratio of drug:carrier shows increased phase solubility & in vitro dissolution rate .Also it was confirmed from the FTIR spectra that extra peaks were not appeared during mixing of the drug and excipients. This indicates no interaction between drug and polymers in the formulated solid dispersions.

NL Prasanthi, et al., (2010) worked on poorly water soluble drug Lacidipine which is an anti-hypertensivedrug. In their study they used some water soluble carriers such as PEG 4000, PEG 6000 , Hydroxy ethylcellulose and dextrins with an intension to improve its dissolution properties .Solvent evaporation method was used to prepare solid dispersions of the drug. Evaluation of the dispersions
was performed using dissolution studies, differential scanning colorimetry (DSC), Fourier Transform Infra Red Spectroscopy (FTIR) and X-Ray powder diffraction. The results obtained showed that the rate of dissolution of Lacidipine was considerably improved when formulated in solid dispersins as compared to pure drug.

**MM Patel, et al., (2010)** did their research work on Valdecoxib, a non-steroidal anti-inflammatory drug. It is mainly used for rheumatoid arthritis, osteoarthritis, and dysmenorrhea. The main problem associated with the drug was its solubility. This drug is very less soluble in the biological fluid and due to that it shows less therapeutic efficacy. Hence solid dispersions of the drug was prepared using different carriers like PEG 4000, mannitol, poly vinyl pyrrolidone K-12. The object behind this research work is to increase the solubility of the drug using the various carrier systems. Formulated solid dispersions were evaluated for different parameters like drug content, invitro dissolution study etc. The result shows Valdecoxib solid dispersion formulated with poly vinyl pyrrolidone K-12 showed maximum in vitro drug release. Based on the above observation tablets were formulation using Valdecoxib PVP K-12 solid dispersion with a view to increase its water solubility. The formulated solid dispersion was found to be stable for four weeks with no significant change in disintegration time, hardness, and in vitro drug release pattern.
Meka Lingam, et al., (2009) investigated the enhancement of solubility and dissolution rate of poorly water soluble drug using cosolvency and solid dispersion techniques. The low aqueous solubility of celecoxib (CB) and thus its low bioavailability is a problem. Thus, it is suggested to improve the solubility using cosolvency and solid dispersion techniques. Pure CB has solubility of 6.26 ± 0.23µg/ml in water but increases solubility of CB was observed with increasing concentration of cosolvents like PEG 400, ethanol and propylene glycol. Solid dispersions with different polymers like PVP, PEG were prepared and subjected to physico-chemical characterization using Fourier-transform infrared (FTIR) spectroscopy, X-ray diffractometry (XRD), differential scanning calorimetry(DSC), solubility and dissolution studies. Solid dispersion of PV5 and PV9 have shown highest saturation solubility and dissolution rate.

Vanshiv SD, et al., (2009) have performed physico-chemical characterization and invitro dissolution of domperidone by solid dispersion technique. The object of the study was to increase the solubility of a lipophilic drug, Domperidone by solid dispersion technique using spray dryer. In this method the solid dispersion were prepared with a lipid carrier. The absence of domperidone peaks in the X-ray diffraction pattern of solid dispersion suggests transformation of crystalline domperidone into an amorphous form. The IR spectra revealed the presence of hydrogen bonding in the solid
dispersion. The invitro dissolution study showed a significant increase in the release rate of domperidone in the solid dispersion as compared with pure domperidone.

**Nagasamy Venkatesh D, et al., (2009)** investigated dissolution enhancement of domperidone using water soluble carrier by solid dispersion technology. Domperidone is a highly water insoluble drug exhibiting poor dissolution pattern. This is the cause for its poor absorption. Solid dispersion of domperidone was prepared using different ratios of polyvinyl pyrrolidone as carrier by kneading method. IR spectral and DSC studies were used to characterize the solid dispersion and to study the possibility of complexation of drug with carrier. Dissolution profile of the drug from the solid dispersion shows better dissolution efficacy when compared with that of the pure drug.

**Baliar Singh OP, et al., (2009)** investigated physico-chemical properties of Glimpiride in solid dispersion with PEG 20000 as carrier. The solubility of the drug in presence of different concentrations of Poly ethylene glycol 20000 in pH 7.4 buffer was checked at 37°C. The solid dispersions of Glimpiride with PEG 20000 were prepared at 1:1, 1:3 and 1:5 ratio of drug: carrier, by melting method. Mean dissolution time (MDT) of Glimpiride decreased significantly after preparation of solid dispersions and physical mixture of the drug with Poly ethylene glycol 20000. The study of FTIR spectroscopy explains the stability of Glimpiride and absence of well-defined Glimpiride Poly ethylene glycol 20000 interaction. Amorphous state of Glimpiride in
solid dispersions prepared using PEG 20000 were confirmed by XRD studies.

**Jani Rupal, et al., (2009)** had worked on Aceclofenac (potent anti-inflammatory analgesic agent) used in the treatment of rheumatoid arthritis (both acute and chronic), osteoarthritis. Aceclofenac is poorly water soluble. Solid dispersions of Aceclofenac in PEG-6000, PVP were prepared by solvent evaporation method. The solid dispersion was characterized for physical appearance, solubility, and IR. It is concluded that dissolution of Aceclofenac was increased by solid dispersion. It has also observed that Poly ethylene glycol 6000 based solid dispersions were effective to increase the dissolution profile of the drug.

**Batra V, et al., (2008)** studied on solubility and dissolution enhancement of Glipizide by solid dispersion technique. Glipizide is poorly water soluble anti-diabetic drug. Due to poor solubility of drug its bioavailability rate is limited by drug dissolution. An attempt has been made to increase solubility of Glipizide by solid dispersion using solvent evaporation techniques of Glipizide with poloxamer 188 and poloxamer 407 and to improve dissolution of drug. The evaluation of physical mixture and solid dispersion was done by IR spectroscopy, Solubility study and dissolution study. The dissolution rate of Glipizide was directly proportional to increment in proportion of surface active carrier. The 100% drug release was obtained from the solid dispersion of Glipizide: poloxamer 188 and Glipizide: poloxamer
407 (1:9) in 10 and 20 minutes respectively. The physical mixtures prepared from Glipizide:poloxamer 188 (1:9) and Glipizide:poloxamer 407(1:9) showed complete release in 20 and 30 minutes respectively. The enhanced dissolution rate with poloxamer may be attributed to their surfactant activity, which facilitate wetting and subsequent solubilization of drug. Solid dispersion prepared using poloxamer 188 showed fastest in vitro drug release.

2.4 BIOANALYTICAL METHOD RELATED

D Ozer Unal, (2010) have developed a rapid and reliable analytical method for the determination of terbinafine HCL from the human plasma by using HPLC and transferred to UPLC system as a model for method transfer. The developed was found to be less time consuming when compared to the HPLC method. This method can be utilised for the bioequivalence and pharmacokinetic studies.

Yin Li, et al., (2010) have developed a method using LC/MS/MS for the quantitative determination of the terbinafine HCl in nail hydrolysis. Results obtained from the study indicate that it is a reliable method established for the measurement of the drug in human nail hydrolysate.

Shafiq S, et al., (2007) have formulated ramipril nanoemulsion and evaluated its capacity in vitro and in vivo. Ramipril solubility was checked in various oils, and Sefsol 218 was selected as the oil phase. Tween 80 and Labrasol were used as surfactants and Carbitol and Plurol oleique used as cosurfactants. For the purpose of
characterization studies, the formulations were subjected to thermodynamic stability studies, dispersibility test, globule size analysis, viscosity determination and TEM studies. The in vivo studies revealed significantly greater extent of absorption than the conventional capsule formulation.