CHAPTER-2
LITERATURE SURVEY

1. **E. Ramadan et al., (2016),** conducted a study on the development of novel drug delivery system for Lamivudine (LAM) in order to overcome the draw backs associated with Lamivudine short half life. In this study, the authors investigated the transdermal deliveries via passive and micro needles (MNs) - mediated transport for the prepared polymeric LAM- loaded nanoparticles. Double emulsion solvent evaporation method was used for the preparation of nanoparticles by using polylactic-co-glycolic acid (PLGA) as a polymer and bovine serum albumin as a stabilizer. The prepared nanoparticles were characterized with particle size, zeta potential, poly dispersity index, morphology, percent yield. When compared to the passive transport across the untreated skin, the steady state flux of the LAM- loaded NP 20 across the MNs –treated skin was significantly high [66].

2. **Dustin L Cooper et al., (2014),** conducted a study on the design and optimization of PLGA- based Diclofenac loaded nanoparticles. Emulsion-diffusion-evaporation technique was used for the formulation of nanoparticles with different concentrations of poly vinyl alcohol (PVA) or didodecyldimethylammonium bromide (DMAB). Evaluation of the resultant nanoparticles was done based on particle size, entrapment efficacy. The lowest particle size and the highest zeta potential were showed by DMAB formulated nanoparticles. The smallest particle size and the highest zeta potential were showed by PVA based nanoparticles formulation. This study indicates use of DMAB for enhanced nanoparticle stability during formulation and also supported the effective use of PLGA based nanoparticles formulation for Diclofenac [67].

3. **Melike Uner et al., (2014),** conducted a study on the preparation of solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) of Loratadine for the treatment of allergic skin reaction. In this study, the authors used the high pressure homogenization method for the preparation of SLN & NLC and loading capacity and entrapment efficiency were determined. During the 6 months of storage, the physical stability of nanoparticles was investigated at room temperature. *In vitro* release and *ex vivo* penetration of the drug was also studied in this study. Preparation of nanoemulsions was also done and characterized for comparison.
The highest penetration rate was showed by nanoemulsion. Finally, the authors concluded that with prolonged drug delivery via reservoir action solid lipid nanoparticles and nanolipid carriers of Loratadine are alternative formulation for immediate treatment of allergic skin reactions [68].

4. Vutpala Sreelola et al., (2014), conducted a study on the Ibuprofen loaded nanoparticles prepared by solvent evaporation technique. Comparison was done among the formulation in order to know the best polymer and stabilizer for Ibuprofen loaded nanoparticles. In this study, four formulations (F1, F2, F3, and F4) were prepared by changing the polymers and stabilizers. Ethyl cellulose and Eudragit S-100 were the polymers used and tween 80 and 0.4% PVA were the stabilizers used. For finding out the best formulation comparison was done between the Ethyl cellulose (F2) and Eudragit S-100(F3). In this study the authors finally concluded that, due to the smaller particle size, greater loading capacity, greater stability and encapsulation efficiency, F2 was considered to be the best formulation for Ibuprofen loaded nanoparticles preparation and drug release was sustained for 8 hrs [69].

5. Aenugu Saritha Reddy et al., (2014), studied the Aspirin loaded ethyl cellulose nanoparticles prepared by solvent evaporation method using Tween 20 as emulsifying agent and ethyl acetate as organic solvent. By variations in the concentration of polymer three formulations (F1, F2, and F3) were prepared. Parameters like composition, solvents mixture, emulsifying agent concentration and speed of stirring were examined. Evaluation was done for all the three formulation in the aspects of drug content, particle size, product yield, loading capacity and entrapment efficiency. To determine the best method for the preparation of Aspirin loaded ethyl cellulose nanoparticles, comparison was done and F2 formulation gave promising results. To determine the sustain release nature of the formulation in vitro drug release studies were performed. For the nanoparticles prepared by F2 formulation, the drug release was sustained up to 12hrs [70].

6. Rakesh Kumar Sharma et al., (2013), conducted a study on the solid lipid nanoparticles as carrier of Metformin for transdermal delivery. Evaluation was done for particle size, surface morphology and in vitro- in vivo release studies. Evaluation for patches was done by ex-vivo skin permeation studies. Solvent diffusion technique was used for the preparation of Metformin solid lipid
nanoparticles using polymethacrylic acid as polymer, propylene glycol as solvent and Soya lecithin as lipid base. Permeation of high cumulative amount of drug was observed with ex-vivo permeation studies. Finally, the authors concluded that for diabetes patients, transdermal delivery of Metformin solid lipid nanoparticles is pain less, safe and cost effective drug delivery system [71].

7. A.R. Gardouh et al., (2013), conducted a study on the Preparation of solid lipid nanoparticles of glyceryl mono stearate containing dibenzoyl peroxide, Erythromycin base and Triamcinolone acetonide as model drugs. High shear hot homogenization method was used for the preparation of solid lipid nanoparticles loaded with three model lipophilic drugs. By using different standard physical and imaging methods, the prepared solid lipid nanoparticles were evaluated. Infrared spectroscopy and thermal procedures were used for studying the stability of prepared formulae. When compared with the pure drugs and commercially available formulation, model drugs showed faster release patterns significantly (p<0.05). Finally, in this study they concluded that high encapsulation efficiency was observed with solid lipid nanoparticles with small particle size and relatively high loading capacity for Erythromycin base, Dibenzoyl peroxide and Triamcinolone acetonide as model drugs [72].

8. Praveen Kumar Gaur et al., (2013), conducted a study on the Diclofenac sodium loaded solid lipid nanoparticles using guggul lipid as major lipid component. Melt-emulsion sonication/low temperature solidification methods were used for the preparation of SLNs and characterized for in vitro drug release, physical parameters & accelerated stability studies and formulated into gel. The highest in vitro drug release was given by GMS nanoparticle 1 and stearic acid nanoparticle 1. When compared to commercial emulgel in receptor fluid, guggul lipid nanoparticle gel 3 exhibited 104.68 times higher drug content. It also showed higher C_max which is almost 8-12 times greater than commercial Emulgel at 4 hours. Finally, in this study, they concluded that SLN with guggul lipid showed good physical properties with acceptable stability and also a promising permeation profile [73].

9. Subhra Prakash Bhattacharyya et al., (2012), conducted a study on Flurbiprofen loaded solid lipid nanoparticles, formulation and optimization by using response surface methodology. Flurbiprofen is a non-steroidal anti-inflammatory drug which is poorly water soluble. Modified solvent injection
method was used for the preparation of Flurbiprofen solid lipid nanoparticles dispersions by using different ratio of tripalmitin and stearic acid a lipid and pluronic-F-68 in different amounts as emulsifier. To systematically optimize the drug entrapment efficiency, particle size and drug release, a central composite design for 2 factors at 3 levels each was employed. This study concluded that the effect of the 2 factors on different response variables helped in identifying the optimum formulation with excellent dissolution profile and stability [74].

10. **Panakanti Pavan Kumar et al., (2012)**, conducted a study on the formulation of Atorvastatin (ATR) loaded solid lipid nanoparticles by hot homogenization followed by ultra sonication technique and optimization of formulation and process parameters to formulate preferred SLN dispersion. In this study, the effects of composition of lipid materials, zeta potential, surfactant mixture & sonication time on particle size, invitro drug release behavior and drug entrapment efficiency were investigated. Transmission Electron Microscopy (TEM) was used to determine the shape and surface morphology which showed fairly spherical shape of nanoparticles. When compared to the dispersion of pure drug, the ATR-SLN formulation had controlled drug release over a period of 24 hrs was demonstrated by the in-vitro drug release study[75].

11. **Amulyaratna Behera et al., (2012)**, conducted a study on the formulation and evaluation of Glibenclamide loaded poly (lactic-co-glycolic) acid (PLGA) nanoparticles for controlled release. Solvent evaporation technique was used for the preparation of GB-loaded PLGA nanoparticles. The effect of stirring speed and drug: polymer ratio on particle size, zeta potential, size distribution, drug loading, drug release and encapsulation efficiency were studied. Without any incompatibility, stable NPs were prepared successfully. Finally, in this study the authors concluded that, by emulsification solvent evaporation method, controlled release biodegradable Glibenclamide nanoparticles can be prepared efficiently [76].

12. **Ekambaram P et al., (2011)**, conducted a study on the formulation and evaluation of solid lipid nanoparticles of Ramipril. In this study, in order to increase the Ramipril bioavailability and also to overcome the side effects by using the lipids like glyceryl mono oleate and glyceryl mono stearate along with the stabilizers like poloxamer 188, tween 80 and span 20, solid lipid nanoparticles of Ramipril were prepared. Evaluation for the prepared formulation was done in
the aspects of drug content, entrapment efficiency, particle size analysis, in-vitro drug release, stability, scanning electron spectroscopy and Fourier transform-infrared studies. When compared to the other formulations with different lipids and surfactants a formulation that contains glyceryl mono oleate which was stabilized with span 20 showed smaller particle size, narrow particle size distribution and prolonged drug release [77].

13. Udhumansha et al., (2007), investigated the effect of hydrophobic and hydrophilic matrix on in vitro and in vivo characteristics of Carvedilol transdermal patches. Solvent evaporation technique was used with different ratios of hydrophobic and hydrophilic polymeric combinations, the authors developed a matrix type transdermal therapeutic system containing Carvedilol. In comparison with oral administration, the bioavailability studies in rats showed that the Carvedilol transdermal patches provided steady state plasma concentration with minute fluctuations and enhanced bioavailability. Finally, the authors observed that the Carvedilol patches provided sustained and continued drug release for 24hrs and throughout the period the patches were able to control the hypertension [78].

14. Das MK et al., (2006), studied the effect of percutaneous absorption of Trazadone hydrochloride (TZN) by using essential oils that includes fennel oil, citronella oil, eucalyptus oil and mentha oil. When compared with transdermal devices, pretreatment of skin with essential oil showed increased flux values of TZN. Finally the authors concluded that fennel oil > eucalyptus oil > citronella oil > mentha oil was the order of penetration flux [79].

15. Manvi FV et al., (2003), formulated Ketotifen fumerate transdermal patches by using a combination of ethyl cellulose: hydroxy propyl methyl cellulose and L-100: hydroxy propyl methyl cellulose plasticized with poly ethylene glycol 400. By Keshary chein diffusion cell, the effect of permeation enhancers like propylene glycol and dimethyl sulfoxide at different concentration on skin permeation kinetics was studied. It was observed that with increase in the permeation enhancers concentration there was increase in permeation rate. When compared with the formulation without enhancers both the combination of EC: HPMC and EL-100: HPMC films enhanced the permeation rate with increase in concentration of enhancers and when compared to EL: HPMC film, EC: HPMC films showed higher drug release rate [80].