CHAPTER 7

SUMMARY AND CONCLUSION

Losartan, an angiotensin II receptor (type AT1) antagonist used to treat hypertension was selected for the fabrication of transdermal delivery system as it complies with physicochemical and pharmacokinetic parameters suitable for skin penetration.

The pre formulation studies involving description, solubility and all other parameters of the drug were found to be comparable with the standard. The patches were prepared by solvent evaporation method. All the evaluation parameters of losartan patch within the limits.

F1 which is containing HPMC E-15 alone showed better drug release, but lasts for only 7 hrs. Formulation F2 containing HPMC E-15: Eudragit RS 100 (2:1) shows comparable release with F1 but it lasts for 12 hrs. The formulation F3 containing HPMC E-15: Eudragit RS 100 (1:1) shows extended release up to 24 hrs when compared to formulations F1 and F2. The patches F4 to F6 were prepared by incorporating permeation enhancers, which showed promising result. The patches containing oleic acid shows near complete release followed by DMSO and DMF.

For F3 formulations were found 85.53±2.403% of Losartan was released at the end of 24 hrs. Even though sustained effect was achieved to a greater extent but it lacks complete drug release at 24 hrs. So it necessitates further study to release the complete drug from the prepared formulations. Different class of enhancers acts by various mechanisms which are described briefly in introduction. The permeation enhancers choose for the studies were oleic acid, DMSO and DMF in formulations F4, F5 and F6 respectively. In the formulation F4, oleic acid was used as a permeation enhancer and the drug release response was studied. The drug release from this patch was found to be
97.626±1.142%. The result depicts oleic acid significantly increased the release, when compared to the formulation without enhancer i.e. F3. DMSO was tried in the formulation F5, drug release shows 96.37±1.117% at 24 hrs. DMF was tried in the formulation F6, drug release shows 94.573±0.534% at 24 hrs. By comparing all the patches which is sustained for 24 hrs, the patch containing oleic acid as a enhancer, shows maximum release at the end of 24 hrs and emerges as a best formulation.

From the above results, it is acknowledged that present work was an adequate preliminary study of improving bioavailability of Losartan by transdermal patches using HPMC E-15 and eudragit RS 100. Further detailed investigations and elaborate in-vivo studies need to be carried out and an in vitro-in vivo correlation need to be established to guarantee the efficiency and bioavailability of the formulation. Further studies on improving bioavailability have to be carried out with different polymers.

Atenolol, a synthetic, beta1-selective (cardioselective) adrenoreceptor blocking agent, used for antihypertensive treatment was selected as a model drug in the preparation of transdermal delivery system as it complies the physicochemical and pharmacokinetic parameters required to permeate through skin. The pre formulation studies involving description, solubility and all other parameters of the drug were found to be comparable with the standard. The patches were prepared by solvent evaporation method. All the evaluation parameters of Atenolol patch within the limits. Based on all these results, the transdermal drug delivery system C1 which is containing EVA alone showed drug release of 53.5% for 24 hrs. Formulation C2 containing Eudragit RS alone showed drug release of 38.41 % for 24 hrs. The formulation C3 containing Eudragit RL: Eudragit RS (1:1) shows better extended release up to 24 hrs when compared to formulations C1 and C2 but the drug is not completely released at the end of 24 hrs and showed drug release of 62.53 % for 24 hrs. The formulation C4 containing Ethyl cellulose: Polyvinyl Pyrrolidine (2:3) shows better extended release up to 24 hrs when compared to formulations C1, C2, and C3
but the drug is not completely released at the end of 24 hrs and showed drug release of 73.27 % for 24 hrs. The formulation C5 containing Eudragit RL: Hydroxy propyl methyl cellulose (2:3) shows better extended release up to 24 hrs when compared to formulations C1, C2, C3 and C4 but the drug is not completely released at the end of 24 hrs and showed drug release of 83.73 % for 24 hrs. The formulation C5 containing Eudragit RL: Hydroxy propyl methyl cellulose (3:3) shows better extended release up to 24 hrs when compared to formulations C1, C2, C3, C4 and C5 but the drug is completely released at the end of 24 hrs and showed drug release of 88.7 % for 24 hrs.

From the above discussions it can be concluded that C6 Showed prolonged drug release and it concluded as a better formulation. The release kinetics was evaluated by making by use of zero order, first order, Higuchi’s diffusion and Korsemeyer Peppas equation. The study of drug release kinetics showed that majority of the formulations were governed by Peppas model and to see whether the drug release is by diffusion, by swelling or by erosion mechanism, the data was plotted according to Higuchi’s equation. The release kinetics data are represented. The coefficient of determination indicated that the release data for formulation C1 followed zero order release kinetics with diffusion mechanism, while formulation C2 to C6 followed first order release kinetics with diffusion mechanism. Higuchi equation explains the diffusion release mechanism. The diffusion exponent ‘n’ values were found to be in the range of 0.5 to 1 indicating Non-Fickian mechanism.