CHAPTER 3

OBJECTIVE AND SCOPE OF THE WORK

Losartan is an angiotensin-II competitive receptor antagonist drug and it dilates blood vessels, reduces mean systolic blood pressure (Ratha G.V., et al., 2010). It is used for the management of hypertension, congestive heart failure and post-myocardial infarction. Losartan is a BCS class II drug, exhibits low aqueous solubility <0.1 mg/mL with high log P value of 5.8 and low oral bioavailability (25-35%) due to first pass metabolism in liver due to its slow dissolution rate in the gastrointestinal tract. (Choi J.K., et al., 2010; Mukherjee, B., et al., 2005). In addition, the ideal properties of Losartan such as molecular weight of 422.911 g/mol, melting point of 184°C (Srikanth Reddy P., et al., 2014), and short oral half-life of 1.5-2 hrs has made the drug a suitable candidate for transdermal delivery (Rajesh Asija J., et al., 2015). The aim of the study was to prevent its first-pass metabolism and achieve control release by designing transdermal drug delivery system.

Atenolol is a beta-adrenergic blocking agent without membrane stabilizing or intrinsic sympathomimetic activity, which has been used for the treatment of hypertension (Hoffmann et al., 2001). Atenolol is a BCS class III drug, exhibits low permeability and high solubility 26.7 mg/mL with high log P value of 0.23 and low oral bioavailability (40%) due to first pass metabolism in liver. In addition, the ideal properties of Atenolol such as molecular weight of 266.3361 g/mol, melting point of 156°C, and short oral half-life of 6-7 hrs has made the drug a suitable candidate for transdermal delivery. The aim of the proposed study to design and evaluate transdermal patch formulations of Atenolol as another model drug in order to provide the delivery of the drug at a controlled rate across intact skin for improving the patient compliance.

To overcome the drawbacks of inconsistent in the oral plasma-drug concentration and poor compliance the present investigation was attempted to design and evaluate controlled release transdermal patches of two selected cardiovascular drugs such as Losartan and Atenolol.
1. To design and formulate matrix and membrane moderated based transdermal patch of Losartan by solvent evaporation method using a few selected polymers viz., HPMC E-15, PVA, PVP and Eudragit RS 100 in various proportions; permeation enhancers such as DMSO, DMF and Oleic acid for release retardant controlled release transdermal patch.

2. To design and formulate transdermal patch of Atenolol by mercury substrate method using a few selected polymers viz., HPMC, PVP, EVA, and Eudragit RS 100 in various proportions; Di-n-butyl Phthalate for the release retardant controlled release transdermal patch.