ABSTRACT

Candesartan Cilexetil (CC) is a selective angiotensin II receptor antagonist and it is widely used in the treatment of hypertension, heart failure, myocardial infarction and diabetic nephropathy. The water solubility of the candesartan cilexetil is very poor and its oral bioavailability is only 15%.

The main goal of the study is to improve the in vitro dissolution of poorly soluble candesartan cilexetil, by using novel carriers which is called microsponge drug delivery system which is a special type of microspheres formed by suitable polymer under specific conditions.

Candesartan cilexetil loaded microsponges were fabricated by adopting quasi emulsion solvent diffusion method (QESD), by using Eudragit E100 as pH-dependent soluble carrier in different ratio in which dichloromethane was used as highly volatile porogenic solvent in different volume and polyvinyl alcohol as good emulsifying agent within the dispersion medium in different ratio also effect of other factors like stirring speed and temperature was studied. The best selected formula was formulated at (1:2) drug: polymer ratio, the volume of dichloromethane was (10 ml) and the ratio pf polyvinyl alcohol is 1% (2 gm / 200 ml of water).

The selected formula was clearly formed microsponges of porous structure with production yield (95%) and encapsulation efficiency (91%) with particle size range between (65-69 µm). The selected formula was subjected to in vitro dissolution study at (0.1 N) Hcl (pH 1.2) for 60 minutes, and showed dissolution rate about (80%) at first 30 minutes and the model of kinetics release was obeyed to Korsmeyer –peppas model and a fickian diffusion mechanism. The scanning electron microscope images showed porous microsponges which drug was

distributed within channels and on the surface. The selected formula was subjected to compatibility studies including DSC and FTIR studies , all these studies showed a good compatibility and was no interaction between drug and excipients. XRD study showed absence of characteristics peaks and the drug was in amorphous form. The selected formula was filled into hard gelatin capsules using spry dried lactose as diluent. The content uniformity study for filled capsules was within accepted range according to USP.

The stability study for filled capsules was established through storing at temperatures 40, 50 and 60°C for four months. The calculated shelf life 25°C using Arrhenius method was approximately 2 year.