ABSTRACT

Modified drug delivery systems stand in the global markets with unique advantages over conventional dosage forms. Current products are available with advanced concept of drug delivery from a simple pill to programmable smart designs. When the drug delivery systems meant for highly water soluble drugs it is always a challenge for formulation scientists to achieve constant drug release profile. The present study was aimed to develop and characterize novel modified release dosage forms for model, a highly water soluble drug Milnacipran HCl. Milnacipran HCl (MH), is an antidepressant drug having short half life and high aqueous solubility.

Various approaches including Porosity Controlled Osmotic Pump, Tablet in Tablet, Oral In Situ, Solid Dispersion and Matrix Molded Tablets were used to achieve the target. Novel herbal polymer was extracted from seeds of *Lepidium sativum* and was further characterized for release retardant. Aquarius coating system EKX-19102 was employed to formulate porous film in design of osmotic pump. A blend of hydrophilic polymer Benecel® and hydrophobic polymer Compritol ATO 888 was used in design of tablet in tablet. Low melting polymers were used to design matrix molded tablet.

All formulations were characterized for in house specification and in vitro drug release study as per official methods. Fourier transform infrared spectroscopy, differential scanning calorimetry, X ray diffraction and scanning electron microscopy were performed wherever necessary to characterize the dosage forms developed.

All formulations were submitted to short term stability study as per ICH guidelines. Zero order drug release was targeted to achieve from all formulations and this desirability was fulfilled by only Porosity Controlled Osmotic Pump. Further in vivo pharmacokinetics study of optimized Porosity Controlled Osmotic Pump was performed in rabbits and pharmacokinetics parameters were resolved. Level A in vivo in vitro correlation was carried out and good IVIVC was established.

**Key words:** Water soluble drug, Milnacipran HCl, Zero order drug release, Porosity controlled osmotic pump, Pharmacokinetics study