

Strategic Development of Duloxetine Loaded Nanospheres for Prolonged Release: An Explorative In-vitro and In-vivo Investigation for Depression

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Abstract:

Duloxetine (DLX) is an antidepressant belongs to the class selective serotonin and norepinephrine reuptake inhibitor (SNRI). Its inadequate bioavailability is the result of its low permeability and first-pass metabolism. The current study sought to prepare DLX nanospheres for parenteral delivery using (polylacticglycolic acid) (PLG) F1 and Polycaprolactone (PCL) F2 for long acting and sustained release. Entrapment efficiency, zeta potential, particle size, differential scanning calorimetry (DSC) and X-ray diffraction (XRD) studies were performed to characterize the formulation which was formulated by emulsion solvent evaporation technique. Nanospheres were assessed for toxicological and pharmacokinetic investigation. Nanospheres size ranges from 149.3 to 448 nm and 119.5 to 381 nm for F1 and F2 respectively and had entrapment efficiency ranging from 56–71% for F1 and 54–68% for F2. DSC analysis showed broadening in the drug peak and a shift for the polymer peak, may be due to physical interaction. XRD studies revealed reduction in crystallinity of DLX. In vitro release of F1 showed long and sustained release upto 21 days in comparison with F2. F1 restored the 5HT at higher extent than F2 and Oral DLX suspension. In vivo pharmacokinetic results proved that after 21 days of dosing, the estimated brain concentration of DLX was significantly higher in F1 i.e., 1.25 times than F2 and 2.5 times than daily dose of oral DLX suspension. Therefore, it would be effective in improving the treatment of central nervous system (CNS) disorders.