ABSTRACT

Lercanidipine is a vasoselective dihydropyridine calcium antagonist, mainly used for the treatment of hypertension and angina pectoris. However, it suffers from food dependent absorption, poor solubility, low permeability and considerable first pass metabolism, resulting in highly variable and low bioavailability of 10%. In present research work, attempt has made to develop fast dissolving films and thermo-responsive nasal gel incorporated with lercanidipine nanoparticles. Nanoparticles of lercanidipine were incorporated in fast dissolving oral films and thermo-responsive nasal gel via preparation of nanosuspension by evaporative antisolvent precipitation method. Prepared nanosuspensions were incorporated in formulations without lyophilizing or spray drying. Two nanosuspensions containing PEG 400 and TPGS 1000 as stabilizers, selected further for incorporation in fast dissolving oral films. Physicochemical and mechanical properties of the optimised films were observed to be within acceptance criteria. SEM images as well as FTIR chemical images of oral films show uniform distribution of nanoparticles in polymeric matrix. The DSC and XRD results proved the poorly crystalline nature of lercanidipine. However thermal processing of film induces crystallinity in hypromellose which results in embedding of amorphous drug nanoparticles in semicrystalline polymeric matrix. Superior dissolution and permeability properties of nanoparticles were confirmed by in-vitro dissolution studies and about 4.5 folds higher ex vivo drug permeation was observed from formulation through porcine buccal mucosa. Same way nanosuspension of lercanidipine was prepared by using poloxamer and TPGS as nanosuspension stabilizers. Formulated nanosuspension was incorporated in thermo-responsive nasal gelling composition which was made up of 14.5% poloxamer, 1% TPGS and 0.1% chitosan lactate. Thermoresponsible nasal gel containing nanoparticles exhibits gelling temperature at 29°C. Mucoadhesive strength of gel formulations was determined by texture analyzer. Incorporation of cationic drug increases the mucoadhesive strength of the gel. In situ gel formulation containing lercanidipine nanoparticles showed 6.5 folds higher permeation through goat nasal mucosa compared to plain drug. Nanonization of the drug, trans-mucosal administration of lercanidipine along with formulation considerations resulted into around 2.5 and 1.2 folds increase in the relative bioavailability for nasal and oral-transmucosal formulation respectively over oral administration of lercanidipine.