Formulation development and pharmacological evaluation of intranasal Hesperetin formulation in experimental model of Parkinson's disease

Abstract

Objective: Hesperetin is a potent neuoprotective agent but due to its shorter half-life, poor oral bioavailability and rapid clearance its use is restricted. The objective was to develop intranasal formulation of hesperetin (hsp), study its nasal permeation and its efficacy on 6-hydroxydopamine (6-OHDA) lesioned rat's model of Parkinson's disease (PD).

Method: Hsp was formulated using co solvent (cohsp), micro emulsion (mehsp), and insitugel (ighsp). PD was developed in Wistar rats with a single intra cerebro-ventricular (icv) administration of 6-OHDA (4 µl) at a rate of 2µl/min. (AP:-2.5, L: +2, DV: -9). Post 14 days of surgery, the rats were divided into 8 groups (n=6). They were treated with either saline or L-dopa [(10 mg/kg, p.o.) + benserazide (2.5 mg/kg, p.o.)] or various formulations of hsp (100 µg/kg i.n). Three groups were kept as self control for each formulation that contained the additives without drug. Treatment was done for 14 days. Locomotion, catalepsy and rotation behavior parameters were carried out on day 0, 7, 14, 21. On day 21st, blood was withdrawn for estimations of oxidative and inflammatory markers. Brain and nose was removed for histopathological studies.

Result: 6-OHDA induced PD as evident by the locomotor, catalepsy, stepping test paradigm and rotational parameters from day 0 onwards ($p<0.001$). Administration of hsp normalized these behavioral changes significantly ($p<0.001$). 6-OHDA treated animals showed marked rise in the total protein content, NO, LPO and reduced GSH which was reversed by hsp formulations ($p<0.001$). Comparative evaluations of various formulation demonstrated, mehsp exhibited maximum protection.

Conclusion: Hesperetin microemulsion is an efficacious neuroprotective formulation.