Development of Intranasal mucoadhesive microemulsions of Levodopa for the treatment of Parkinson's disease: in vitro and in vivo evaluations in rat model

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Abstract: Levodopa (L-DOPA) along with Carbidopa is widely prescribed drug for the treatment of Parkinson's disease. The major drawback is poor penetration of Levodopa through BBB. As nasal route of administration has direct access to brain via olfactory and trigeminal nerve pathways, in the present study intranasal micro emulsions (ME) and mucoadhesive microemulsions (MME) of L-DOPA were developed and evaluated. The microemulsions were prepared by water titration method. Pseudo ternary phase diagrams were constructed to identify optimal Smix ratio which yield greater microemulsion region. The microemulsions were characterized for size, PDI, Zeta potential, ex vivo permeation studies using porcine nasal mucosa. The optimal formulations were evaluated for Pharmacokinetics plasma and brain in rat model. Mucoadhesive agent Chitosan was added at 0.5%w/w concentration to optimal microemulsion formulation to get MME. The optimized ME formulation showed globule size of 96 nm, PDI 0.173, zeta potential -33.6 mV, flux 57.53 μg/cm^2/h and MME showed size 118 nm. The flux of MME was significantly higher than ME and drug solution. The pharmacokinetic studies, brain showed that Drug targeting efficiency (DTE) and Direct nose to brain transport (DTP%) of intranasal MME is significantly high (2.77 and 66.7%) when compared to drug solution (0.9 and 27.97%) given orally. Bioavailibity of MME, brain is 3.06 folds to oral solution 1.66 folds to ME formulation. The present study demonstrates significantly high brain targeting efficiency of nasal MME formulation over nasal ME, nasal solution and oral suspension.

Key words:Levodopa,Microemulsion, Intranasal, Mucoadhsive