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Nose to Brain Delivery of Dimethyl Fumarate Loaded in Carvacrol Based Nanoemulsion for the Treatment of Multiple Sclerosis

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ABSTRACT

Dimethyl fumarate (DMF) is a first line oral medication for the treatment of multiple sclerosis (MS), associated with several adverse events. Intranasal delivery of drug could potentially alleviate the adverse events and enhance the therapeutic efficacy. The current study aimed to formulate an oil in water (o/w) nanoemulsion (NE) by solvent evaporation self-nanoemulsification method. NEs encapsulating DMF with carvacrol (CV), a neuroprotective essential oil, for synergistic therapeutic effect were intended for intranasal administration. Chitosan was employed as a surfactant, owing to its mucoadhesive properties. FT-IR and TGA analyses revealed an increased stability of DMF due to the presence of CV. Response surface methodology was used for the optimization of NEs by applying Central Composite Design model. Surfactant concentration, oil to surfactant ratio, and probe sonication time were set as independent variables whereas, mean droplet size, PDI, and zeta potential were set as dependent variables. The selected formulation out of 15, had a mean size below 250 nm and a PDI less than 0.5 that was sustained at refrigerated temperatures for over 3 months. Drug content of selected formulation was found to be more than 65% despite the volatile nature of DMF and CV. Moreover, 50uM concentration of NEs showed good cell viability in MTT assay mediated cell viability studies. Permeability studies on RPMI 2650 nasal cell lines revealed the permeation of 86% of DMF in 3 hours. It was concluded that DMF-CV NEs are a promising therapeutic cocktail for MS that could reduce the adverse events related to DMF, enhancing therapeutic efficacy as well as patient compliance and medication adherence.

Keywords: Drug Delivery, Essential Oil, Intranasal, Nanomedicine, Neuroprotective