Design, Development and Optimization of Donepezil loaded Nanoparticles

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Many neuroprotective agents like donepezil hydrochloride has poor penetration to brain after oral/systemic administration due to poor permeation through blood brain barrier. Thus, it is required to develop a novel drug delivery system that would provide the release of neuroprotective agents/drugs directly into brain avoiding blood brain barrier. Objectives: To develop a self mucoadhesive nanoparticulate drug delivery system and to optimize it for the effective delivery of drugs to brain through nasal route. Material and Methods: Donepezil hydrochloride loaded chitosan nanoparticles were developed and optimized using Design of Experiment approach. Results and Discussion: The optimized formulation has shown mean particle size (177.8 nm), drug payload (22.2 mg/100 mg of chitosan), process yield (91.96 %), zeta potential (+ 16.6 mV) and mucoadhesive strength (9.26 g). The in-vitro drug release (> 90 % in 24 hours) and ex-vivo diffusion (> 70 % in 24 hours) were promising. The delivery of drug to brain was estimated employing wistar rats. Approximately, three times more drug was estimated in brain with nanoparticles (nasal administration) vis-à-vis drug in solution (oral/nasal administration). Finally, confocal laser scanning microscopy confirm the localization of nanoparticles in different regions of brain. Conclusion: From the above results, it was concluded that the nose to brain delivery of neuroprotective drug loaded mucoadhesive nanoparticles has better potential as compared to other routes of brain drug delivery.

The purpose of the present study was to investigate the possibility of targeting an anti-Alzheimer's drug donepezil in the brain using polymeric nanoparticles. The Donepezil loaded chitosan nanoparticles were prepared by ionic gelation method to improve the bioavailability and enhance the uptake of donepezil to the brain via intranasal delivery. The formulations were optimized on the basis of response surface methodology. Donepezil loaded chitosan nanoparticles were developed and characterized for particle size, size distribution, zeta potential, entrapment efficiency, drug loading, *in vitro* drug release and *in vivo* studies using gamma scintigraphy techniques. The TEM and SEM images of the formulation suggested that particle size was within 100–200 nm and particles were spherical in shape with smooth morphology. The biodistribution studies after intranasal administered in rats showed higher percentage of radioactivity per gram in the brain for the donepezil loaded chitosan nanoparticles formulation as compared to donepezil solution ($p < 0.05$) which are indicative of direct nose to brain transport. The higher drug transport efficiency (191.398%) and direct transport percentage (1834.480%) were found with chitosan nanoparticles as compared to donepezil solution. These results suggest that intranasally administered chitosan nanoparticles have better brain targeting efficiency and are a promising approach for treatment of Alzheimer disease.