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Complexation as an approach to entrap cationic drugs into cationic nanoparticles administered intranasally for Alzheimer's disease management: Preparation and detection in rat brain

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Alzheimer's disease (AD) is a progressive dementia affecting the brains of elderly population, starting usually in hippocampus, and propagates to other regions. Compared to other routes, intranasal brain delivery of neurotherapeutics minimizes systemic side effects, facilitates self-administration, and enhances patient compliance. However, entrapment of neurotherapeutic cationic drugs into biodegradable cationic nanoparticles is challenging.

Objective: This study aimed to investigate complexation as an approach to enhance the entrapment of galantamine hydrobromide (GH), a cationic drug, into chitosan nanoparticles (CS-NPs) for AD management intranasally, and to examine the effect of complexation on CS-NPs physicochemical properties and uptake in rat brain.

Methods: Placebo CS-NPs were prepared by ionic gelation, and the parameters affecting their physicochemical properties were screened. GH was complexed with chitosan, and the complexation was detected by the FT-IR study. GH/chitosan complex nanoparticles (GH-CX-NPs) were prepared by ionic gelation, and characterized in terms of particle size, zeta potential, entrapment efficiency, in vitro release, and stability. Rhodamine-labeled GH-CX-NPs were prepared, and their delivery to different brain regions was detected 1 h after intranasal administration to male Wistar rats; using fluorescence microscopy and software-aided image processing for quantitation of fluorescence intensity.

Results: GH-CX-NPs had a diameter of 190 nm and a zeta potential of +31.6 mV. The encapsulation efficiency and loading capacity were 23.34% and 9.86%, respectively. GH/chitosan complexation prolonged drug release, improved formulation stability at 4 °C, and did not affect the physicochemical properties of the optimized placebo CS-NPs. Rhodamine-labeled GH-CX-NPs were clearly detected in the olfactory bulb, hippocampus, orbitofrontal and parietal cortices; with a profound accumulation in the hippocampus specifically.

Conclusion: Complexation is a promising approach to enhance the entrapment of cationic GH into the cationic CS-NPs. It has insignificant effect on the physicochemical properties of CS-NPs. GH-CX-NPs show potential as intranasal brain delivery system for AD management.

Biography

Amira S Hanafy has registered for her PhD thesis on CNS delivery of neurotherapeutics in Sep 2013 in Faculty of Pharmacy, Alexandria University, Egypt. She is an assistant lecturer at Faculty of Pharmacy and Drug Manufacturing, Pharos University in Alexandria (PUA). She is a referee in AAPS PharmSciTech journal. She had the opportunity to attend the IBRO-UNESCO Interregional School on computational neuroscience, 2012, India; organized by International Brain Research Organization (IBRO), and won a travel grant for this school. She was an organizer in the "Nanoscience and Nanotechnology at Glance" International Conference, Cairo-Alexandria, Egypt, 15-16 January 2009.

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