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Bioengineered PLGA-chitosan nanoparticles for brain targeted intranasal delivery of antiepileptic TRH analogues

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Abstract

The bio-engineering of nanoparticles for the transportation of various therapeutic agents specifically to brain has sparked a rapidly growing interest in the field of material chemistry. In this study, L-pGlu-(1-benzyl)–L-His–L-ProNH_2 (NP-355) and L-pGlu-(2-propyl)–L-His–L-ProNH_2 (NP-647) were synthesized and encapsulated in biodegradable poly-lactide-co-glycolide (PLGA) nanoparticles which were further decorated with mucoadhesive surface coating of chitosan. NP-355 and NP-647 which are analogues of thyrotropin releasing hormone, have been reported to demonstrate potential antiepileptic properties against various animal models of seizures. However, their applicability is limited by their short lives due to rapid metabolism and blood brain barrier. The treatment of disorders associated with central nervous system such as epilepsy has been a major challenge for several decades due to difficulty in delivery of drug molecules and imaging agents to brain. To overcome these issues, development of sustained release delivery system for these neuropeptides is proposed which can be administered directly from nose to brain utilizing olfactory nerve channels. The synthesized nanoparticles were evaluated for their physicochemical properties, sustained release properties, toxicity and antiepileptic potential following intranasal administration. The ability of these nanoparticles to reach the brain was evaluated by utilizing quantum dots as fluorescent probes. Our results proved that the polymeric nanoparticles can be used for successful delivery of neurological drugs to the brain.

Keywords: Modified polymeric nanoparticles; TRH analogues; antiepileptic; PLGA; chitosan; brain delivery; intranasal; quantum dots.