P 30

Preparation and evaluation of poly-ε-caprolactone nanoparticles as carriers for nose-to-brain delivery of Idebenone

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Background and purpose: Idebenone (IDB) is a short-chain benzoquinone, a coenzyme Q_{10} analogue with potent antioxidant activity. It is originally developed for the treatment of cognitive impairments, such as Alzheimer's disease. After oral administration, IDB is extensively metabolized in the liver with less than 1 % reaching the systemic circulation. However, to increase the distribution of IDB in the brain, alternative routes of administration can be used. For example, intranasal route can provide direct drug delivery via the olfactory and trigeminal nerve pathways (nose-to-brain). The present work is focused on the preparation of poly-ε-caprolactone (PCL)-based nanoparticles as drug delivery systems for nasal administration of IDB. **Experimental Approach:** The PCL nanoparticles were prepared by solvent evaporation technique. Polymers of molecular weight (Mw) 14, 000 g/mol and 80, 000 g/mol were used. Polysorbate 20 and Poloxamer 407, alone and in combination, were used at different concentrations to stabilize the dispersion. Emulsification was carried out under the following conditions: oil/water ratio 1:10, polymer concentration 0.25 %, homogenization speed 25,000 rpm. The molecular weight of the polymer and the type of the emulsifier were studied at three different levels. The nanoparticles were characterized by DLS, SEM, TEM, and FTIR. **Key Results:** The prepared particles were spherical in shape and the size distribution was found to be dependent on the type of the emulsifier. The mean particle size varied in the range 188 to 628 nm. The models prepared with the polymer of lower molecular weight had smaller average size, which was probably due to the lower viscosity of the polymer solution used in their preparation. A multimodal size distribution was found for models prepared with Poloxamer 407, whereas the models formulated using Polysorbate 20 demonstrated homogenous monomodal particle size distribution. The ζ-potential ranged from -5.3 to -17.9 mV. Three batches of IDB-loaded nanoparticles were prepared based on the optimized formulations of blank nanoparticles. Drug loading ranged from 21 % to nearly 30 %. Entrapment efficiency ranged from 53.33 % for models prepared with PCL Mw 14 kDa to 36.98 % for PCL Mw 80 kDa models. This may be due to the lower compatability between of IDB with PCL of higher molecular weight. The FTIR spectra showed successful incorporation of the drug in the polymer matrix. Within the 48 h of *in vitro* release study the percentage of the released drug varied from 50% to 60.07%. **Conclusion:** Idebenone-loaded PCL nanoparticles were successfully prepared by single emulsion solvent evaporation technique with high entrapment efficiency and optimal particle size for nose-to-brain delivery.

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