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Memantine Loaded Biodegradable Polymeric Nanoparticles for Glaucoma Treatment

E Sánchez, M.A Egea, M Espina, S Bonilla, ML García
University of Barcelona
Av. Joan XXIII s/n, 08028. Barcelona
esanchezlopez@ub.edu

Extended Abstract

Recent studies have shown that treatment with Memantine (MEM) protected retinal ganglion cells in monkey models of glaucoma, reducing ganglion cell loss during treatment with this drug (Hare et al, 2009).

An important goal is the development of a safe and effective formulation for delivery of Memantine to the eye posterior segment. In this way, biodegradable polyesters such as poly (lactic-co-glycolic acid) (PLGA) had demonstrated to be safe as drug delivery systems. Moreover, poliethilenglicol coating could increase the ocular residential time of the particles. For these reason in this work new MEM-PLGA-PEG nanoparticles had been developed in order to accomplish the quality standards for ocular drug delivery. (Vega et al, 2012)

MEM-PLGA-PEG nanoparticles were prepared by double emulsion method. Briefly, the first step consisted on the preparation of a w/o emulsion and ultrasound energy was applied. Then, a second water phase was added and a second sonication was done obtaining $w_1/o/w_2$ emulsion. Finally a slight amount of surfactant was added and nanoparticles were stirred overnight in order to eliminate organic solvent. (Zambaux et al, 1998).

Different factorial designs were carried out in order to determine the formulation critical factors involved in double emulsion method. In these assays, the effect of concentration of formulation compounds, sonication parameters, pH and volume phase ratios on size, polydispersion index, zeta potential and encapsulation efficiency was studied.

NPs characterization was performed by dynamic light scattering (DLS), showing an average size smaller than 200 nm and a monodisperse population, both confirmed by transmission electron microscopy (TEM). Surface charge of the formulation has been found to be negative being encapsulation efficiency higher than 50 %.

Short-term stability studies were carried out at 25ºC during the first 3 months. Backscattering profile showed no significant modifications due to particle size agregation suggesting that nanoparticles would be stable.

In vitro Hen´s Egg Test-Chorioallantoid Membrane (HET-CAM) was carried out showing optimal ocular tolerance of the nanoparticles in contrast with the free drug which was found to be irritating. These agree with in vivo Draize test results.

In conclusion, the association MEM loaded PLGA-PEG nanoparticles provides a new and stable ocular drug delivery system which had demonstrated to be less irritating than the free drug.

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