Topical administration of melatonin-loaded lipid-polymer hybrid nanoparticles for posterior segment eye diseases

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Melatonin is a pleiotropic neurohormone with several beneficial effects. This molecule is gaining increasing interest as a neuroprotective agent in glaucoma therapy [1]. Topical application of micromolar concentrations has been shown to be more effective and safer than high doses administered intravitreally. [2,3]. In order to increase the bioavailability of topical formulations, drug can be formulated to prolong the corneal retention time. [4]. In the following study, melatonin-loaded lipid-polymer hybrid nanoparticles (LPHNs) were designed and optimized via DoE (Design-Expert® from Stat-Ease) with 3 factors set at 3 levels. To increase corneal retention polymeric matrix was coated with two cationic lipids. The optimized nanocarriers were characterized by dynamic light scattering and UV spectrophotometry analyses that showed suitable size for ophthalmic administration (189.4 nm), homogeneous particle size distribution (PDI < 0.3), positive surface charge (+39.8 mV), high encapsulation efficiency (79.8 %), suitable pH (6.3) and osmolarity (296 mOsm/Kg) values. Systems showed good mucoadhesive properties and a sustained and controlled melatonin release profile. Calorimetric and spectroscopic analyses confirmed the encapsulation of melatonin in the systems and the interaction of lipids on the polymer matrix. Cytocompatibility studies on the retinal endothelial cell lines demonstrated the safety of nanocarriers at concentrations <1 µM. In vitro studies are on-going to assess the antioxidant role of melatonin. Further in vivo analyses will be required to confirm the safety of the hybrid nanoparticles and to validate them as a potential platform for topical melatonin delivery.

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