

New Formulation for Dry Eye Treatment based on Liposomes and Biodhesive Polymers

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Purpose: Dry eye syndrome can be considered as a group of diseases related to tear film disorders. Evaporative dry eye is one of the most frequent causes of this condition. The lipid layer plays a major role in avoiding the evaporation of the aqueous components of the ocular surface. Treatments directed to replace a disturbed lipid layer may have therapeutic benefits for dry eye patients. These formulations might contain lipid and aqueous components. Moreover these constituents must present film-forming properties. The aim of this work is to evaluate a new formulation based on liposomes and a bioadhesive polymer (hyaluronic acid) destined to topical administration for dry eye treatment.

Materials and Methods: Phospholipon 90G containing > 95% of phosphatidilcholine (PC) purified from soy lecithin was purchased from Phospholipid GmbH (Cologne, Germany). Cholesterol, vitamin E (α -tocopherol), Hyaluronic acid Ophthalmic grade (Mw 400.000-800.000Da) was acquired from Abarán Materias Primas, Barcelona, Spain.

A preservative free formulation containing aqueous and lipid constituents was developed. Liposomes were prepared according to the technique described by Bangham and Benitez and col. (ARVO 2007) by employing PC (200mg), Cholesterol(25mg) and vitamin E (2mg). After extrusion, the vesicles were dispersed in a hypotonic solution of hyaluronic acid. The tonicity of formulation was adjusted by addition of trehalose.

Size of the lipid droplets and *in-vitro* properties of the solutions such as surface tension, osmolarity, and pH were evaluated. The mean particle size and size distribution of liposomes were performed by photon correlation spectroscopy (PCS). Tolerance of the formulation was evaluated in macrophages by the mitochondrial-dependent reduction of the (tetrazolium salt 3(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) [MTT] to formazan. Studies were carried out at exposures of 15 minutes and 1 hour. Viability was set as 100% in untreated cells.

Results: The sizes of the liposomes were smaller than 1 μ m (392nm-478.5nm). Particles higher than 1 μ m were practically absent in the formulation (<2%). The surface tension value was 25.5 (\pm 0.3) mN/m. The final solution was hypotonic (188.5 \pm 0.4 mOsm/l) with a pH value of 7.04 (\pm 0.5). The formulation based on liposomes resulted in cell viability values higher than 90% at the exposure times assayed.

Conclusions: The new formulation based on liposomes could be useful for the treatment of dry eye.

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