OChiPEG Micelles Proven to Facilitate the Transscleral Delivery of Rapamycin

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Rapamycin, like many other ophthalmological agents, has several therapeutic effects, yet its hydrophobic properties render it unsuitable for noninvasive topical administration. This experiment by Elsaid et al. was constructed to find a suitable way to deliver this drug to the eye that is safe, rapid, effective, and inexpensive.

Rapamycin, a lipophilic macroring triene antibiotic formerly used to treat Candida albicans, was also found to have immunosuppressive, cytostatic, and antiangiogenic properties. Although its use is appealing in multiple eye diseases as an anti-inflammatory and antiangiogenic agent, its hydrophilic properties resulted in its administration only via invasive routes.

As a trial to enhance drug absorption and bioavailability via the topical route, rapamycin was loaded on micelles. These are nanocarriers composed of O-octanoyl-chitosan, which was prepared as described by Huang et al., grafted to octanoyl and polyethylene glycol (PEG) molecules.

The experiment was carried out on porcine eyes, in which the sclera is dissected, cut, and then clamped into Ussing chambers. The diffusion and permeability coefficients were obtained routinely through use of precalibrated linear regression graphs.

The authors carried out various physicochemical tests to evaluate the properties of the micelles, both loaded and unloaded with rapamycin. A remarkable decline in the crystallinity of rapamycin was recorded via thermal analysis. This may be owing to the formation of intermolecular interactions between rapamycin and the core of the micelles. Chitosan was selected to promote scleral drug retention and permeation, and the PEG component also showed stability-enhancing effects. The critical micelle concentration (CMC) was found to be 16.6 μM at room temperature. This value was up to 1700-fold higher than that for the rapamycin-containing polymeric micelles of Lu et al. This may be attributed to the positive charge of the chitosan component.

The authors pioneered in using rapamycin-loaded micelles that were as small as 50 nm. This size seems to be ideal, as the particles are small enough to permeate across the sclera but large enough to enhance bioavailability. Moreover, this optimum size reduces immune-mediated attack, a factor further reduced by particle PEGylation.

The aim of the work was to solubilize the drug, prolonging its ocular residence time and also enhancing its permeation. I believe that the aim was met through preparation of these OChiPEG micelles, which proved to have high drug entrapment efficiency and scleral retention properties.

I suggest that several experiments like this using different carrier micelles be carried out so that we can discover various vehicles to safely and efficiently deliver essential therapeutic agents that still need an appropriate mode of delivery rather than unwanted hazardous intravitreal injection.

References

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