In vivo gene delivery into ocular tissues by eye drops of poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide)(PEO-PPO-PEO) polymeric micelles.

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Abstract

The primary objective of this study was to investigate the feasibility of using PEO-PPO-PEO non-ionic copolymeric micelles as a carrier for eye-drop gene delivery of plasmid DNA with lacZ gene in vivo. Using pyrene fluorescence probe methods, zeta potential, and dynamic light scattering test (DLS), the ability of micelle formation of these block copolymers with plasmid was studied. Gene expressions were visualized by both the quality of enzymatic color reaction using X-gal staining and by the quantification of the substrate chlorophenol red galactopyranoside (CPRG) in enucleated eyes on day 2 after gene transfer. In addition, microscopy to identify the types of cell showing uptake and expression of the transferred gene was used. We found that the block polymeric micelles were formed above 0.1% (w/v) of block copolymer with a size of 160 nm and a zeta potential of -4.4 mV. After 2 days of topically delivery three times a day, the most intense gene expression was observed on days 2 and 3. Reporter expression was detected around the iris, sclera, conjunctiva, and lateral rectus muscle of rabbit eyes and also in the intraocular tissues of nude mice upon in vivo topical application for 48 h with a DNA/polymeric micelle formulation. Furthermore, after two enhancement treatments, the transport mechanisms of the block copolymeric micelles were found through endocytosis in tissues by enhancement through the tight junction pathway. Thus, efficient and stable transfer of the functional gene could be achieved with PEO-PPO-PEO polymeric micelles through topical delivery in mice and rabbits. These in vivo experiments indicate the possible potential use of block copolymers for DNA transfer.