ABSTRACT

Glaucoma is the second most leading cause of blindness globally. Several studies were proved that free radicals are one of the major reasons for increasing glaucoma patient by increasing intra ocular pressure (IOP). Hence, potent anti-oxidants are suitable and focused for the prevention/ treatment of glaucoma. Resveratrol (RES) and quercetin (QUR) are the most attracting polyphenolic anti-oxidant molecules and also showed efficiency in reducing IOP. But they showed stumpy efficiency due to low solubility and permeability. Therefore, focused on novel approaches might improve the therapeutic efficacy of these compounds. Hence, the aim of the present study is to develop and characterize RES/QUR loaded polyethylene glycol (PEG) modified chitosan (CS) nanoparticles (NPs) and RES loaded biodegradable temperature-pH responsive pluronic F-127-grafted-peptide P₁₁ nanodispersion (ND) to reduce the IOP for the treatment of glaucoma.

Formulated PEG modified CS NPs showed controlled release, iso-osmolar, and improved permeation of drugs. Ocular tolerance of the NPs was evaluated using Hen’s egg test on the chorioallantoic membrane and it showed that the NPs were non-irritant. FITC loaded PEG modified CS NPs crossed the cornea and reached upto retinal choroid. RES/QUR loaded PEG modified CS NPs reduced the IOP by 4.3±0.5 mmHg and 3.7±0.5 mmHg respectively upto 8hr in normotensive rabbits. The developed NPs have efficient delivery of RES/QUR for the treatment of glaucoma.
The stimuli responsive hybrid temperature and pH system of pluronic F-127 and peptide P$_{11}$ was synthesized by the activation of pluronic F-127 followed by conjugation with the peptide P$_{11}$ (Gln-Gln-Arg-Phe-Glu-Trp-Glu-Phe-Glu-Gln-Gln - QQRFEWFEQQ) This hybrid pluronic F-127-g-P$_{11}$ conjugation was confirmed using the FTIR, TEM and NMR study. RES was incorporated in the hybrid pluronic F-127-g-P$_{11}$ system and formation of NDs using solvent evaporation method. The RES loaded ND was non-irritant, iso-osmolar in nature, showed controlled release and improved corneal permeation. The NDs effectively reduced IOP (4.7±0.5mmHg) in normotensive rabbits compared to RES dispersion (2.5±0.5mmHg). The results indicated that the pluronic F-127-g-P$_{11}$ conjugated NDs can be used as vehicle for the effective delivery of RES and successfully reduced the IOP for the treatment of glaucoma. Hence the present study results proved that showed that the NDs are comparatively better than NPs to reducing IOP.

**Key words:** Chitosan, PEG, Pluronic F-127, P$_{11}$ peptide, Quercetin, Resveratrol and Glaucoma