ABSTRACT

Timolol Maleate is a beta-adrenergic blocker, widely effective in lowering intraocular pressure with open-angle glaucoma and aphakic glaucoma. The technique using 3^2-Full Factorial design for the in-situ gel formulation. In the present research work, Timolol Maleate *in-situ* gel systems were prepared using the optimized concentrations of Carbopol and HPMC E50LV. The formulations prepared were evaluated for several parameters like viscosity, drug-polymer interaction, visual appearance and clarity, pH measurement, drug content uniformity, sterility, *in vitro* drug release, and ocular safety or eye irritation. Drug diffusion data was fitted to various kinetic equations such as zero order, First Order, Higuchi and Peppa's exponential equation.

At pH 4.8, the formulations were in a liquid state and exhibited low viscosity. An increase in pH to 7.4 by addition of simulated tear fluid caused the solutions to transform into gels with high viscosity. Among the formulations two optimized formulations were taken OF1 and OF2 which fulfill in prolonged residence time which compared with marketed product.

Finally, the formulation was evaluated for ocular safety in rabbit by the procedure of modified Draize technique. The results of the study showed that the scores scored were less than the maximum total score indicating there was no irritation to the ocular tissues and hence the formulation was safe. Two months of stability study was carried out at room temperature for all three optimized formulations and results showed no significant changes in percentage drug entrapment efficiency and *in-vitro* drug diffusion study after stability study.

Keywords: Timolol maleate; *In-situ* gel systems; Viscosity; Carbopol; Glaucoma; Eye irritation.