

## Effect of additives on gelation of methylcellulose based ophthalmic thermoresponsive *in situ* gels

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The poor bioavailability and therapeutic response exhibited by conventional ophthalmic solutions have driven explorations in the design of novel formulation. *In situ* gel forming DDS are, in principle, capable of releasing the drug in a controlled manner. The ocular cavity provides a natural reservoir, which is easily

accessible for the application of *in situ* gel. In the present study, the development of an *in situ* gelling vehicle for ophthalmic DDS based on methylcellulose (MC) was studied. The influence of different additives on the gelation, rheology, mechanical and drug release of *in situ* gel based on MC was studied. The gel temperature of various grades of MC (A<sub>4</sub>C, A<sub>15</sub>C and A<sub>4</sub>M) at 0.5% w/v was found 60°C-70°C in purified water. It was found that 0.5-1% w/v Sodium Borate, 0.01-0.012% w/v Benzodecumbromide, 2.5-5% w/v Mannitol and 0.5% w/v Hydroxyethylcellulose was capable of decreasing the gel temperature at physiological temperature, 37°C±2°C. Rheological studies indicated

shear thinning mechanism and increase in viscosity at physiological response with the addition of additives in MC solutions. All solutions were observed as clear solution and gel at their respective phase transition temperature. pH and Isotonicity of solutions were found between 5-6 and 290-310mOsm respectively. The extent of drug release from MC solution was 8-10hrs. Our results support that, by simply mixing with additives of interest, the novel thermo responsive *in situ* gel can be formed for controlled drug release which is a better alternative than conventional ophthalmic solutions to enhance the ocular bioavailability of the drug.

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