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A Concise Review The Ph Triggered Concept In Situ Ophthalmic Gel Of Sodium Cromoglycate, Diclofenac Sodium and Aceclofenac

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ABSTRACT

The ophthalmic solutions have a major problem that is the poor bioavailability, such as the attainment of optimal drug concentration at the site of action, which is compromised mainly due to precorneal loss resulting in only small fraction of the drug being ocularly absorbed. This is overcome by developing an in situ ophthalmic gel which increases the retention time of the drug. The present review describes the formulation and evaluation of in situ gel-forming ophthalmic drug delivery system of an anti allergy drug sodium cromoglycate, an anti-inflammatory drug diclofenac sodium and aceclofenac based on the pH triggered concept in situ gelation. All the formulations varies in concentration and the content used. Based on the results obtained, Sodium cromoglycate which has been formulated with gelrite and HPMC E15LV has the highest ocular residence time compared to the other two formulations.

Keywords: *Ophthalmic in situ gel,sodium cromoglycate, diclofenac sodium, aceclofenac, gelrite, HPMC E15LV*

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1. Introduction

Major problem in ocular therapeutics is the attainment of optimal drug concentration at the site of action, which is compromised mainly due to precorneal loss resulting in only small fraction of the drug being ocularly absorbed [1,2]. Ophthalmic preparations are defined in the USP as "sterile dosage forms, essentially free from foreign particles, suitably compounded and packed for instillation onto the eye" [3]. A new approach is to try to combine advantages of both solutions and gels, such as accuracy and facility of administration of the former and prolonged residence time of the latter [2,4]. Like ointments, gels are also difficult to administer for some patients. In this respect in-situ gels are intresting since these are conviently dropped as a solution onto the conjuctival sac, where they undergo a transition into a gel with its favorable residence [4]. The sol-gel-sol transition occurs as a result of chemical and physical change induced by the physiological environment [2,4].
Advantages of in situ forming gel [2,3,4]:

1. Generally more comfortable than insoluble or soluble insertion. Less blurred vision as compared to ointment.
2. Increased bioavailability due to – increased precorneal residence time, decreased nasolacrimal drainage of the drug which cause undesirable side effects arising due to systemic absorption of the drug through naso-lacrimal duct is reduced.
3. Drug effect is prolonged hence frequent instillation of drug is not required.
4. The principle advantage of this formulation is the possibility of administering accurate and reproducible quantities, in contrast to already gelled formulations and moreover promoting precorneal retention.

2. Materials and Methods

a. Material

Sodium cromoglycate, gelrite, HPMC E15LV gifted by Cipla R&D Mumbai India, Diclofenac sodium gifted by Yarrow chem..Products Mumbai, carbopol, sodium arginate (Ranbaxy chemical pvt ltd), Aceclofenac gifted by Unichem laboratories Mumbai India, HPMC purchased from Oxford laboratories Mumbai, Di sodium hydrogen phosphate procured from Qualigens chemicals Mumbai, Tween 80 and citric acid procured from Hyderabad. Carbopol 934 purchased from Reddy's laboratories Hyderabad. All other chemicals and solvents were of analytical grade.

3. Method

Preparation of *in situ* gel:
Sodium cromoglycate
The solubility, melting point, UV curve, IR spectrum and DSP graph was done to characterize the sodium cromoglycate. Then the ophthalmic *in situ* gel was prepared using different concentrations of gelrite ang HPMC E15LV.
Diclofenac sodium
Drug was dissolved in distilled water and then sodium chloride was added and stired until dissolved. Benzyl alcohol was added bas preservative, and then HPMC was added and allowed to swell. Carbopol was sprinkled and allowed for hydrating overnight. Adjusted to desirable pH and volume was made up. This formulation was made by using various polymeric agents like sodium alginate, HPMC, HPC, HEC and carbopol.

Aceclofenac

Disodium hydrogen phosphate and citric acid was dissolved in purified water then HPMC was added and carbopol 940 was sprinkled and allowed for hydrating overnight.. Aqueous solutions of varying concentration of Carbopols 940 (CP) and HPMC of different grades were used. Tween 80 was added and Benzalkonium chloride (BKC) was added into solution of Aceclofenac. These solution was added into the Carbopol-HPMC solution and volume was made up.

Evaluation of ophthalmic gel

General appearance[5] : Colour and clarity of solution

Drug content[5]: Determined by taking 1 ml of the formulation and diluting it to 100ml with distilled water. 5 ml was withdrawn and further diluted to 25 ml with distilled water. Concentration was determined at 200-400nm by using UV visible spectroscopy.

pH of the ophthalmic gels[4] : pH measurement by using pH meter.

In vitro diffiusion study[4] : in vitro release of drug was carried out in formulations with different concentrations of excipients using a dialysis membrane. The diffusion medium was taken as 100ml of stimulated tear fluid composition and stirred at 50rpm at 37^0C ± 0.5^0C. One end of the diffusion tube was covered by a dialysis membrane. The formulation was kept in that diffusion tube and the diffusion tube was kept in the diffusion medium so as the formulation come in contact with the stimulated tear fluid. The drug samples were withdrawn at the interval of 30 minutes for the period of 7 hours 30 minutes from diffusion medium and analyzed by a UV spectrophotometer using stimulated tear fluid as blank.

4. Result and Discussion

An *in situ* ophthalmic gelling system was formulated and evaluated by using different polymeric systems like sodium alginate, gelrite, hydroxyl propyl methyl cellulose, hydroxyl propyl cellulose, hydroxyl ethyl cellulose and carbopol. Then the formulations were evaluated on its general appearance, pH, in vitro diffusion studies and drug content. Clarity of all formulation was found to be satisfactory. All the formulations are within the pH range of tear fluids. The drug content was found to be in acceptable range for all formulations. In formulation of sodium cromoglycate, the viscosity of gel increases with the increase of gelrite from 0.4 to 0.6% and increase in HPMC E15LV from 1.0 to 2.0%. The increase in viscosity of ophthalmic solutions results in increased pre-corneal residence time for up to 12 hours. The increased in viscosity was achieved due to the inclusion of gelrite which undergoes gellation when it comes in contact with calcium and sodium ions of tear fluid[2]. Whereas in the formulation of diclofenac sodium, higher concentration of sodium alginate and HEC showed better sustaining effect amongst the other formulations which resulted in release of drug up to 8 hours. The formulation of Aceclofenac with varying concentrations of carbopol and different gardes of HPMC showed an increased residence time and sustained drug release by in vitro diffusion studies up to 8 hours[3].

5. Conclusion

An attempt of developing *in situ* gelling system of sodium cromoglycate, diclofenac sodium and aceclofenac with variety polymers with different grades and concentrations was carried out. All the formulations showed the desired pre-corneal residence time and sustained drug

release with the various types of polymers used for each formulation.

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