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FORMULATION AND EVALUATION OF pH TRIGGERED IN-SITU GEL FOR OCULAR TREATMENT

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ABSTRACT:

AIM: The purpose of this study is to construct and examine an in-situ gel using a pH-triggered method and a mixture of prednisolone and moxifloxacin. The ocular has a low bioavailability and a constrained efficacy in eye drops because of lacrimal fluids. The effectiveness of the in-situ gel-forming mechanism has diminished in the eyes and changed from sol to gel in the cul-de-sac. **Materials and procedures:** The crosslinked polyacrylic acid polymer in the pH-triggered in-situ gel containing Carbopol 940 has a broad-spectrum mechanism based on the addition of pathogens. The mucoadhesive polymer hydroxypropyl methylcellulose (HPMC) is used to increase viscosity. The pH was changed to 6.5 by using buffering agents in the proper amounts. Clarity, pH, gelation temperature, spreadability, and medication concentration were all assessed for each formulation. **CONCLUSION:** The pH-triggered in-situ gel was created, and evaluations of its transparency, gelation, and pH found them to be adequate. The continuous release of medication over long lengths of time made possible by this formulation of pH-triggered in-situ gel systems makes it more stable, non-irritating, and medically efficacious than conventional eye drops.

KEYWORDS: pH-triggered, eye drops, sol-to-gel, mucoadhesive, gelation temperature**.**

INTRODUCTION:

One of the most intriguing and demanding areas for pharmaceutical experts is ocular medication delivery. pharmaceuticals are often administered to the ocular system for local effects on the surface or interior of the eye, making the eye a challenging organ to research from the perspective of pharmaceuticals because it is an isolated organ. Because of how it disposes of drugs, the ocular system is particularly fascinating. One of the most difficult problems facing pharmaceutical researchers is how to deliver drugs to the eyes. Drug molecules are unable to reach the necessary location of action due to the particular anatomy of the eye. Anterior or posterior eye segments may be the focus of drug delivery to the eye. The relatively impermeable corneal epithelial membrane, tear dynamics, and nasolacrimal drainage are a few examples of the ocular anatomical and physiological restrictions that contribute to the low ocular medication bioavailability. Due to these circumstances, less than 5% of the medication that is delivered penetrates the eye. Additionally, traditional drug delivery methods including solutions, suspensions, and ointments are insufficient today to meet the demands of delivering a consistent flow of medication for a lengthy period of time. One of the primary causes of it is the medication's short length of residence at the site of action, which leads to low bioavailability. In situ, gel-forming systems are aqueous solutions that are liquid before delivery but gel under physiological circumstances. These delivery methods can be administered as eye drops, and as they come into contact with the eye, they immediately begin to gel.

In the current study, a mixture of Moxifloxacin and prednisolone ophthalmic was made into a gel using polymers Carbopol-940, HPMC, and a pH-triggered gelling system to increase contact time and controlled release, to decrease the frequency of administration, and to increase the therapeutic efficacy of the drug. Moxifloxacin is used to treat infection of the eye including bacterial conjunctitivs and prednisolone is used to treat inflammation of the eye, relieving symptoms such as swelling, redness and itching.

MATERIALS AND METHOD:

Moxifloxacin, Prednisolone, Carbopol 940, HPMC, citric acid, Di-sodium hydrogen phosphate and benzalkonium chloride

PREPARATION OF CITROPHOSPHATE BUFFER:

75ml of citrophosphate buffer pH 6.5 was prepared in distilled water by mixing 1.125gm disodium hydrogen phosphate and 0.407gm citric acid.

PREPARATION OF IN SITU GEL:

The detailed procedure for preparing the moxifloxacin and prednisolone situ gel-forming system as a pH-triggered system is outlined below. Formulation ingredients with their quantities were as given in Table. The buffer salt solution is prepared 75ml with citric acid 0.407g and disodium hydrogen phosphate 1.125g. HPMC (hydroxypropyl methylcellulose) and allowed to hydrate and Carbopol 940 was sprinkled over the HPMC and allowed to hydrate overnight. The solution was stirred with a magnetic stirrer for 30mins. Moxifloxacin and prednisolone were dissolved in water and benzalkonium chloride was added to this

solution. The drug was added to the polymeric solution and a sufficient quantity of 0.1M NaOH was added to the solution to get a clear solution.

Table 1

Formulation table of In-situ gel:

INGREDIENTS	F1	F2	F3	F4	F5	F6
Moxifloxacin	0.5	0.5	0.5	0.5	0.5	0.5
Prednisolone	0.5	0.5	0.5	0.5	0.5	0.5
HPMC	0.1	0.1	0.1	0.1	0.1	0.1
Carbopol	0.3	0.4	0.5	0.3	0.4	0.5
Benzalkonium chloride	0.01	0.01	0.01	0.01	0.01	0.01
Citric acid	0.405	0.405	0.405	0.405	0.405	0.405
Disodium hydrogen phosphate	1.125	1.125	1.125	1.125	1.125	1.125

EVALUATION OF INSITU GEL:

Clarity and Visual Appearance:

One of the most crucial qualities of ophthalmic preparations is clarity. Visual inspection of all produced formulations against a black-and-white backdrop was used to assess each one for clarity.

Determination of pH:

In ocular formulations, pH serves as one of the most crucial factors. Solubility and stability are the two crucial areas where pH has an impact. When administering an ophthalmic formulation, the pH should be such that the patient is not irritated while yet ensuring formulation stability. An ideal pH range for ophthalmic preparations is 5.8 to 7. A pH metre was used to test the developed formulations for pH.

Gelling capacity:

To determine if the compositions were suitable for use as in situ gelling systems, all formulations were tested for gelling capability, time, and viscosity. By putting a drop of the system in a vial with 2 mL of newly made simulated tear fluid, equilibrated at 37 °C, and visually examining the gel formation, as well as recording the time for gelation and the time needed for the gel created to dissolve, the gelling capacity was ascertained.

Drug content:

1 ml of the produced formulation was diluted in 100 ml of phosphate buffer (pH 7.4) and the aliquot was spectrophotometrically estimated to measure drug concentration.

RESULTS AND DISCUSSION:

The ability of Carbopol 940 aqueous solutions to change into stiff gels when the pH is increased justifies its usage in situ gel-forming devices. The viscosity of the formulation was

increased by using hydroxypropyl methylcellulose (HPMC). In the pH-triggered gelling method, the citrophosphate buffer was utilised as a carrier.

EVALUATION PARAMETERS:

Clarity and Visual Appearance:

As indicated in Table 2, the clarity of all formulations was considered to be satisfactory. All of the produced formulations were free-flowing liquids at room temperature, transparent, and devoid of particle matter. The original clarity will be regained after over a night. Visual appearance is also transparent in the black and white background.

pH:

The pH of all the formulations was satisfactory given in table 2. The pH of the formulation ranges between 5.8 to 7. The formulation is to be liquid at room temperature.

Gelling capacity:

The formulation should have an optimal viscosity to allow for simple instillation into the eye as a liquid (drops), but also to allow for a quick sol-to-gel transition. the gelling ability of all formulations, which is shown as + gel forms in 60 seconds and dissolves quickly, ++ gel forms in 60 seconds and is stable for 3 hours, and +++ gel forms in 60 seconds and remains stable for 6 hours. Gelling capability rises with increasing gelling agent concentration at higher and lower concentrations. All formulation was satisfactorily given in Table 2.

Drug content:

The drug content of the ophthalmic formulations of Moxifloxacin and Prednisolone in situ gel was found satisfactory. Moxifloxacin and Prednisolone concentration was then determined at 265 nm using a UV-Visible spectrophotometer.

Table 2

Evaluation parameter of formulation:

S.no	**Evaluation parameters**	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
1.	Visual appearance	Transparent	Transparent	Transparent	Transparent	Transparent	Transparent
2.	Clarity	Clear	Clear	Clear	Clear	Clear	Clear
3.	pH	5.9	6.7	6.54	6.48	6.62	6.62
4.	Gelling capacity	+	++	++	++	++	++

CONCLUSION:

Moxifloxacin hydrochloride, a broad-spectrum antibacterial agent used in the treatment of ocular infections, and prednisolone, an anti-inflammatory agent used in the treatment of ocular infections, were successfully formulated as in situ gel-forming using Carbopol 940 as

a gelling agent of providing high viscosity and HPMC as a viscosity-enhancing agent. As a result, the proposed formulation is a feasible alternative to traditional eye drops due to its potential to improve bioavailability via a longer precorneal residence period and capacity to maintain drug release and improved patient acceptability due to the simplicity of administration and decreased frequency of administration. All evaluation parameters are satisfactory.

BENEFITS OF IN-SITU GEL:

- Better stability.
- Ocular bioavailability.
- Sustaining drug release.

DRAWBACKS OF THE IN-SITU GEL:

- Making blurred vision.
- Leaving residue in the eyelids.

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CONFLICT OF INTEREST:

Authors declare no conflict of interest

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