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Formulation and Evaluation of Ciprofloxacin Gel for Ophthalmic Drug Delivery

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ABSTRACT

Ciprofloxacin hydrochloride belongs to the fluoroquinolone group which is crystalline pale yellow powder. Ciprofloxacin hydrochloride acts as an antimicrobial agent for therapy of corneal ulcers due to bacterial strain. The main objective of present invention is to develop a framework for drug distribution to promote treatment adherence and dispensability is no exception. Thus, a topical drug transport system has been generated by using ointment formulation. In the present research a ciprofloxacin hydrochloride gel is developed using active pharmaceutical drugs, xanthan gum and HydroxyPropyl Methylcellulose (HPMC). Transparency, pH calculation, chelating ability, drug content, rheological analysis, and drug dissolution study were assessed for the prepared formulation.

Keywords: Antibacterial Infection, Ciprofloxacin, HPMC, *In Situ* Gel, Ophthalmic Delivery, Sol–gel Conversion, Xanthan Gum

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INTRODUCTION

A achievement and preservation of appropriate drug content at the target site inside the eye has become one of the main barriers encountered in ophthalmic administration. In an strive to advance the ocular way of deposition period of drugs for topical therapy to the eye, various ophthalmic delivery types such as formulations, creams, gels and polymeric implants have been researched. Owing to their frequent wash out during lacrimation in eyes, the eye drops have very poor absorption. Many of the formulations are used as solutions or injections. These can be resolved by manufacturing the medication as a formulation following ophthalmic implementation that undergoes immediate on site gel formation.

Ciprofloxacin hydrochloride belongs to the fluoroquinolone group which is crystalline pale yellow powder. The 2-D and 3-D structure of ciprofloxacin hydrochloride is given in Figure 1, 2. Ciprofloxacin hydrochloride acts as an antimicrobial agent for therapy of corneal ulcers due to bacterial strain. The antimicrobial activity of ciprofloxacin is due to interaction with the DNA gyrase enzyme that is required for microbial DNA replication. *In situ* gel formulations consist of polymers that in the cul-de-sac exhibit solution to gel phase transformations that enhance patient acceptance due to changes in particular physicochemical properties such as pH, heat and redox potential in the area [1].

Xanthan gum is a common thickening and suspending agent obtained from xanthomas campestris, a single-cell species which develops xanthan gum by process of fermentation in cabbage, broccoli, and other leafy vegetables. Xanthan gum acts as a suspension agent, an exceptional thickener even if it is present in small amounts. Xanthan gum provides great consistency and is cost effective. Xanthan gum is accessible in different grades to satisfy unique criteria for hydration, diffusion, and clarity. Further to help achieve continuous drug

delivery, HydroxyPropylMethylCellulose (HPMC) is integrated as a viscosity stimulator. HPMC is a semi-synthetic, stable, viscoelastic non-ionic non-toxic polymer, a strong pharmaceutical carrier with higher loading potential [2,3]. Figure 2 illustrates 2D structure of ciprofloxacin hydrochloride.

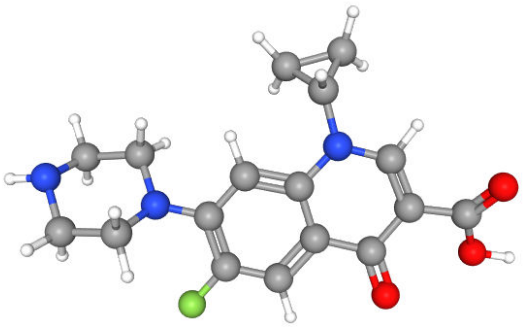

Figure 1: 3D structure of ciprofloxacin hydrochloride using ball and sticks.

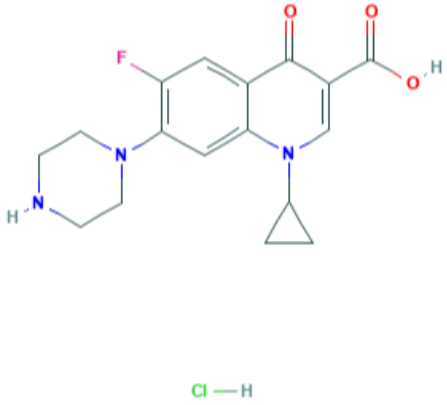

Figure 2: 2D structure of ciprofloxacin hydrochloride.

The current study explains the composition and assessment of onsite ophthalmic formulation gel comprising ciprofloxacin hydrochloride [3,4]. At the moment of insertion, the active ingredient is in the solution process and soon after making link with the calcium ion having pH of 7.4, it becomes a clear deposit gel. Therefore all solutions and gels benefit from this method of formulation, which can enhance the shelf life of the composition and also the medication, precision and ease of application [4,5]. Figure 3 shows different method for sol-to-gel transformation.

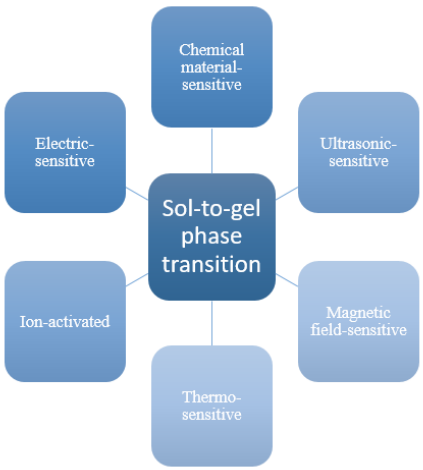

Figure 3: Different method for sol-to-gel transformation.

LITERATURE SURVEY

A research paper has discussed preparation of ophthalmic gel for ciprofloxacin hydrochloride. The prepared gel comprises polyacrylic acid as a phase changing polymer, HPMC as a release retarding agent, and ion exchange polymer as a complex forming compound. The prepared drug showed in vitro drug release activity of 98% within 24 hours [6]. Another research paper by H. R. Bakhsheshi-Rad used electrospinning method to develop Gel-Cip nanofibers coating. This coating was applied bone regeneration [7]. A research paper has developed drug using xanthum. Another research paper discuss preparation of ciprofloxacin hydrochloride drug using hydrophobic ethyl cellulose [8].

The present research depends upon pH activated system and ion triggered system. The topical drug delivery system comprises active pharmaceutical ingredients, excipients, polymer and copolymer. In the present paper, Xanthan gum is selected as polymer for gel formation, HydroxyPropyl Methylcellulose (HPMC) is selected as copolymer. HydroxyPropyl MethylCellulose (HPMC) as a viscosity inducer is coordinated to further assist in achieving continuous drug delivery.

METHODOLOGY

Formulating composition and assessment

The formulation of ciprofloxacin HCl is given in tabulated form in Table 1. The method of preparation gel is pictorially represented in Figure 4.

Table 1: Formulation of ciprofloxacin gel.

Sl. No.	Ingredients	F1	F2	F3	F4
1.	Ciprofloxacin HCl (g)	0.3	0.3	0.3	0.3
2.	Xanthan gum (g)	0.5	1.0	1.5	0.5

3.	HP Methyl Cellulose (g)	0.5	0.5	0.5	-
4.	Distilled water (g)	100	100	100	100

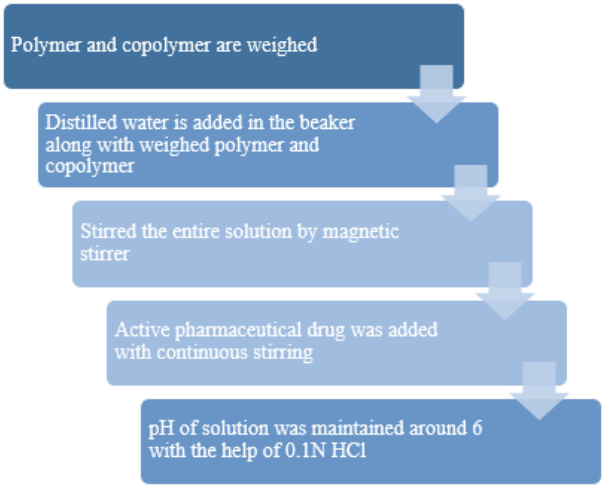

Figure 4: Method for preparing formulated gel.

Characterization of formulation

Clarity: Visual examination under a better light, presented against a monochrome backdrop with the contents put into action with a spinning movement, provided a clarity test. The development of cloudiness or any unrequired substances scattered in the synthesized solution was also reported.

Gelling capacity: The gel forming ability of the composition is calculated by putting a pinch of the formulated gel in a beaker having capacity of 50 ml of freshly obtained CaCl solution and examined during the emulsifying phase by the naked eyes. The rating of gelling capacity is outlined in Table 2.

Table 2: Rating for the gel forming ability.

Observation	Rating
No gel formation	1
Gel formation took only a few minutes and lasted for a few hours.	2
Gel formation occurs quickly and lasts for a few hours.	3
Gel formation is instants and lasts for a long time.	4
Very stiff gel	5

Rheological studies: The key aim of the research work is significant research and development initiatives to construct improved topical drug delivery systems. The purpose of the research is to develop an gel exhibit colloidal suspension behavior, so that physiochemical research needs to be conducted. The viscosity assays of the formulation were performed by using a u-tube viscometer. The viscosity of the formulation is noted.

Measurement of pH: The pH was calculated using a pH meter for each formulated sample, which was subsequently measured using standard pH 4 - 7 buffers according to the existing method.

Drug composition: 1 ml of the formula produced was diluted in a phosphate buffer of 100 ml(pH= 7.4), accompanied by spectroscopic aliquot calculation to evaluate drug concentration.

Drug release study: A phosphate buffer of 100 ml pH= 7.4) was dissolved with 1 ml of the formula made, followed by spectroscopic aliquot measurement for drug concentration assessment. With the rotation speed kept at 100rpm, the temperature was regulated. The samples were extracted and spectrophotometrically tested for the drug substance at various time intervals.

RESULT AND DISCUSSION

Gelling capacity

According to the given result, it was observed that formulation F3 shows immediate gelling and for prolongs time. The general appearance, drug content, gel forming ability and drug composition of the formulation is presented in Table 3.

Table 3: Physicochemical properties of ciprofloxacin gel.

Sl. No.	Batch No.	Color	pH	Gel forming capacity ratings	Drug content %
1	F1	Transparent solution	6.3	2	83.1
2	F2	Transparent solution	6.23	2	88
3	F3	Transparent solution	6.37	3	91.11
4	F4	Transparent solution	6.3	1	89.1

Rheological studies

The viscosity is based upon the formulations containing polymeric material. Compared to the F4 batch without HPMC viscosity obtained was more as the addition of HP Methyl Cellulose led to an improvement in the consistency of formulations and led to more pseudo-plasticity (F1-F3). F3 proved to be better formulated than others due to the higher concentration of xanthan gum and HP methyl cellulose. An appropriate solution must have proper viscosity in order to intillate it in eyes for rapid transformation of sol to gel. Table 4 shows data on rheological study of formulation.

Table 4: Rheological study of formulation.

Batch no.	Viscosity Solution (Pas	Viscosity of gel (Pas
F1	0.018	88.5
F2	0.0474	254
F3	0.19	876
F4	0.00366	0.132

Drug release study

The maintained delivering nature of Ciprofloxacin HCl gel is indicated by the in vitro dissolution test. Percentage of the drug release in gel Ciprofloxacin HCl was established to be 78.02% release in 24h. Dissolution study of the drug is graphically presented in Figure 5.

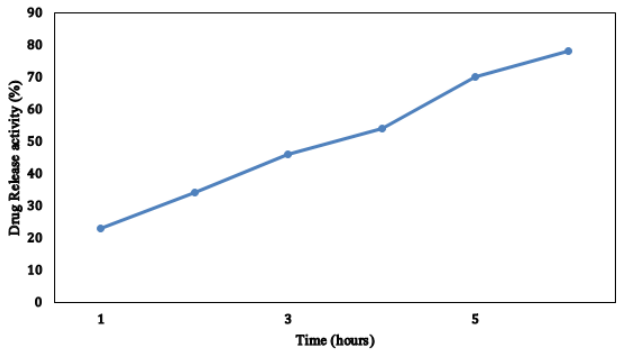

Figure 5: Drug release activity.

CONCLUSION

Ciprofloxacin hydrochloride has been successfully implemented using xanthan gum and HPMC as on site gel-forming eye drops. Therefore the above findings show that the combination of xanthan gum and HPMC could be used as an *in situ* gelling agent to elevate eye absorption rate and therapeutic response. The dissolution experiments and physical and chemical features of the generated formulation (IG3) revealed that it could be a good option to eye drops and creams with respect to ease of application, with the additional benefit of a better drug dissolution profile, which could lead to better therapeutic efficacy. The ciprofloxacin gel will be more acceptable and efficient to the patients.

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