# FORMULATION AND EVALUATION OF OFLOXACIN LOADED INSITU OCULAR GEL



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## Abstract

**Objective:** During the process of this research, pH-triggered in-situ gels designed for the purpose of delivering ofloxacin to the eye were created, and their efficacy was assessed. In the treatment of bacterial eye infections, ofloxacin ophthalmic solution is utilized generally.

**Material & Methods:** Both hydroxypropyl methylcellulose (HPMC) E15LV and carbopol 934 were utilised as gelling agents in the in-situ gelling systems. The former was used to raise the viscosity of the systems, and the latter was used as a gelling agent. Because of this, the finished product had the perfect viscosity for its intended use. After the formulations had been created, they were put through a series of tests to evaluate several aspects of their makeup, including their general look, clarity, pH level, gelling potential, rheological testing, and pharmaceutical concentration. The formulation that was developed was successful from a therapeutic standpoint and was also reliable.

**Result & Discussion:** A technique utilising HPLC for determining the concentration of OFX has been devised and shown to be accurate. Researchers determined that the retention duration for OFX was 2.9 minutes (max= 242 nm). In methanol, a stock solution of OFX at a concentration of 1 mg/ml was made, and in the mobile phase, a variety of calibration standards with concentrations ranging from 0.39 to 50 g/ml were generated.

**Conclusion:** Visual inspection at room temperature revealed that the dispersion of OFX-ISG was transparent; however, after being diluted with simulated tear fluid, the substance took on the appearance of a gel (STF). When the ofloxacin nanomicelles were disseminated in gellan gum, they seemed to be whole. Based on the first findings acquired from our inquiry, it appears that OFX-ISG has the potential to be exploited as a delivery method for administering ofloxacin, which can be used to treat inflammations of the anterior portion of the eye.



**Keywords:** In-situ gels, Carbopol 934, HPMC E15LV, Ofloxacin

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## Introduction

The human eye is an organ that is responsible for detecting light and transmitting messages to the brain via the optic nerve. The eye is a multi-component organ that has many different elements, all of which work together to allow a person to see. The eye is said to be one of the most complicated organs in the body. The eyes are the most prominent parts of the visual system. They provide living things the ability to see, as well as the capacity to absorb and interpret visual detail, and they also enable certain photo response functions that are not dependent on the organism's ability to see[1]. Light that is taken in by the eyes causes a cascade of electrochemical events to take place in the neurons. The function of the eye is to take in light from its surrounding environment, regulate the amount of light entering the eye by means of a diaphragm, create an image by focusing light with a lens assembly that is capable of being adjusted, convert the image into electrical signals, and then send these signals to the brain via neural pathways that connect the optic nerve to the visual cortex and other regions of the brain. The majority of animal species possess sophisticated optical systems, including 10 fundamentally distinct types of eyes that are capable of producing images with a high level of resolution. Mollusks, chordates, and arthropods all have eyes that are capable of seeing images in high resolution[2-3]. Pit eyes are eye-spots that have been inserted into pits in order to lessen the angle of light that comes into the pit and has an effect on the eye-spot. As a consequence of this, the organism is able to determine the source of the light that is penetrating it. In eyes with a higher level of complexity, the retino hypothalamic tract is responsible for transmitting signals from the retina to the suprachiasmatic nuclei, where they are used to control the circadian rhythm, and to the pretectal region. Both of these processes are controlled by the brain. Ofloxacin, often known as OFX, is a fluoroquinolone antibiotic that is considered to be of the second generation and is effective against both gram-positive and gram-negative bacteria[4]. After topical administration of OFX eye drops containing 0.3 percent, reports indicated that the mean concentration of OFX in the aqueous humour surpassed the minimum inhibitory concentration for 90 percent (MIC90) of the frequently prevalent gram-positive and gram-negative bacteria. OFX produced the greatest aqueous humour concentration out of all of the fluoroquinolones that were administered topically. Because of the production of the zwitterionic form at the physiologic pH, corneal precipitations caused by topically administered fluoroquinolones are common. These precipitations are caused by the fluoroquinolones. Because of this, their solubility is decreased, and as a result, precipitation is possible at this pH[5]. Despite the fact that OFX eye drops have not been shown to produce precipitation as of yet, deposits may form. In situ-forming hydrogels are liquids that, following instillation, go through a phase transition to become a viscoelastic gel in reaction to the physiological circumstances that are present in the cul-de-sac. A change in temperature, a change in pH, or a change in the electrolyte composition can all bring about a phase transition. These are the three sorts of physiological changes that can bring about a phase transition. Ocular residence duration is lengthened as a direct consequence of the increase in viscosity that occurs following instillation[7-8]. It is preferable to employ in situ gels due to the fact that they are liquids that can be readily placed into the eye. In addition to this, in comparison to the instillation of prepared gels, they make it possible to provide exact amounts in a consistent manner[6].

**Material & Methods**

**Material**

OFX (Liva Healthcare Pvt. Ltd.) Amino Acids such as alanine, arginine, asparagine, aspartic acid, cysteine glutamine, glutamic acid, HCL acid, water, ethanol, sodium phosphate, and calcium carbonate are all included in this compound. Weighing Balance, PH Scale, Hot Plate, Thermometer, UV Spectroscopy, and TLC were among the pieces of equipment utilised during the experiment.

**Method**

**Preparation of 0.1% OFX mixed nanomicelles**

OFX ( Liva Healthcare Pvt. Ltd.) Amino Acids such as alanine, arginine, asparagine, aspartic acid, cysteine glutamine, glutamic acid, HCL acid, Water, Ethanol, Sodium Phosphate, and Calcium Carbonate are all included in this compound. During the course of the experiment, the following pieces of apparatus were utilised: a thermometer, a weighing balance, a PH scale, a hot plate, and a thermometer.

**Preparation of Standard Ofloxacin Opthalmic Preparation**

In order to manufacture the standard ophthalmic solution of ofloxacin, the pure medication oflaxacin was combined with a number of various additives. A preservative that included benzalkonium chloride was utilised. The chelating agent that was utilised was EDTA, and sodium chloride was used to maintain the solution's isotonicity. Hydrochloric acid and sodium hydroxide were used to regulate the solution's pH.



**Study of Gelation**

This nanomicelle-loaded in situ gel was gelled with 100 ml of distilled deionized water and a simulated tear fluid (STF) composed of sodium chloride (0.6 kg), sodium bicarbonate (0.2 kg), and calcium chloride dehydrate (0.8 kg). The temperature was maintained at 34 degrees Celsius throughout the experiment to mimic the conditions in the eye. To dilute the gel, the nanomicelles were mixed with STF in a ratio of 7.8 to 2.2. The gelation of the dispersion was examined visually to see if STF was present.

**In-Vitro Drug Release**

There were nanomicelles in situ gels, and the gelation was carried out with 100 ml of deionized, distilled water, which contained sodium chloride, sodium bicarbonate, and calcium chloride dihydrate, to resemble tear fluid (STF). For the experiment, the temperature was maintained at 34 degrees Celsius to mimic the conditions in the eye. A 7.8:2.2 dilution of STF was used to dilute the nanomicelles-loaded in situ gel. In order to determine whether or not the dispersion gelled due to the presence of STF, a visual inspection was used.

## Result & Discussion

Using sodium chloride, sodium bicarbonate, and calcium chloride dehydrate in 100 ml of distilled deionized water, an in situ gel containing nanomicelles was gelled in the presence of STF. An eye chamber was created with a constant temperature of 34 degrees Celsius to mimic the eye's natural temperature range. In situ gel rich in nanomicelles was diluted with a 7.8:2.2 STF ratio. Visual inspection was the preferred way for identifying whether or not STF caused gel formation.

### Gelation Study

The OFX dispersion was clearly visible to the naked eye at room temperature. In Figs. 1 (a) and 3.1 (b) at 34°C, the dispersion shows the sol-gel transition when diluted 23:7 with STF. A viscoelastic gel is formed in the presence of tear fluids upon application of OFX.

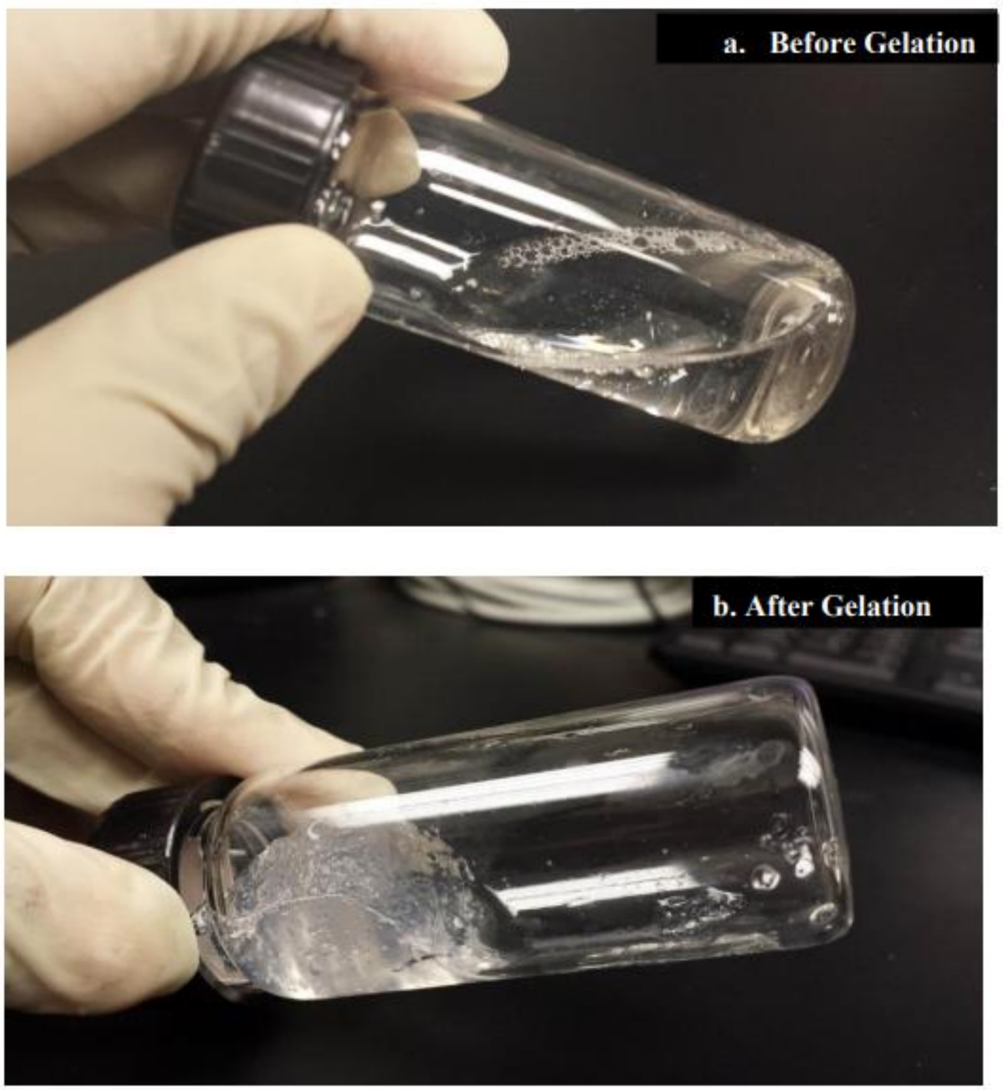


**Fig 1: (a) After being diluted with simulated tear fluids in the eye, a sol-gel transition of ofloxacin mixed nanomicelles that were disseminated in gellan gum (b) formulation was seen.**



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**HPLC Analysis**

A technique utilising HPLC for determining the concentration of OFX has been devised and shown to be accurate. Researchers determined that the retention duration for OFX was 2.9 minutes (max= 242 nm). In methanol, a stock solution of OFX at a concentration of 1 mg/ml was made, and in the mobile phase, a variety of calibration standards with concentrations ranging from 0.39 to 50 g/ml were generated. Each standard was examined three times, and the calibration curve was constructed by plotting the average peak area against the concentration of the sample[9-10]. A correlation coefficient value ($r^2$) of 1.00 was achieved, which resulted in the drawing of a straight line with the equation y = 1991x + 767. (Fig.2). In figure 3, you can see a representation of an OFX chromatogram sample.

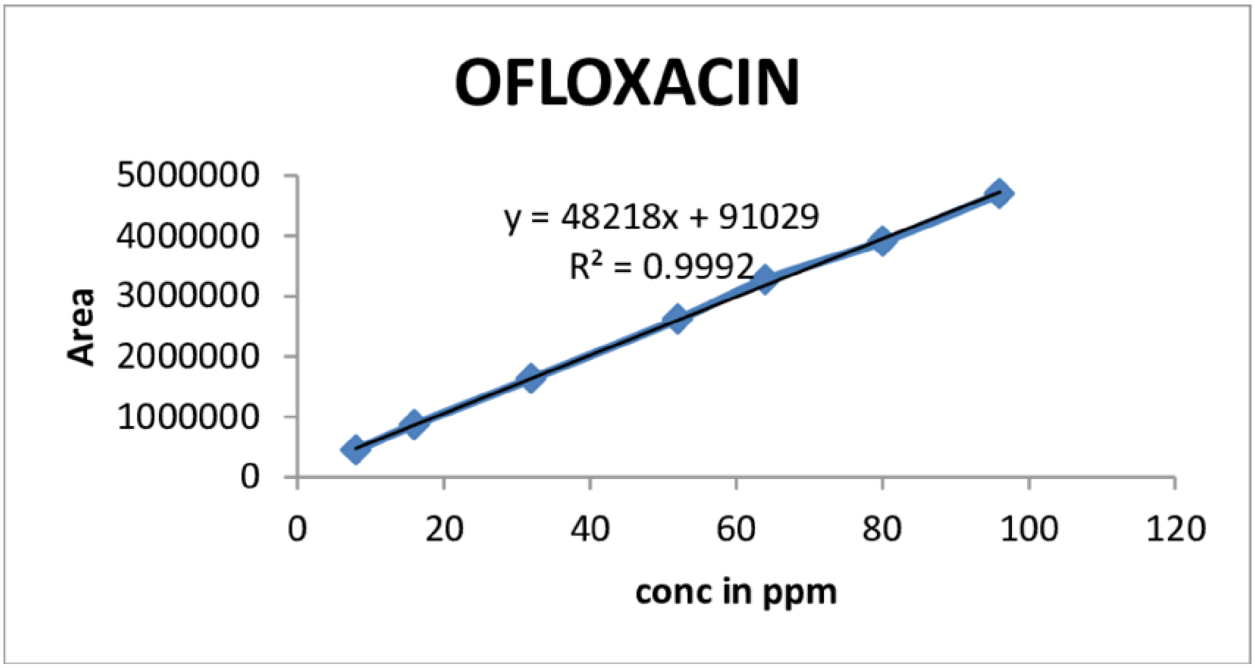


**Fig 2: Calibration Curve of Ofloxacin**

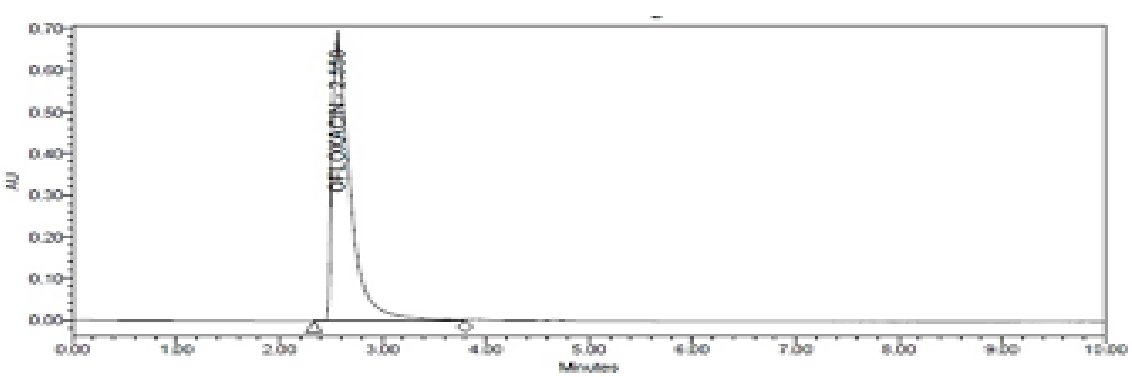


**Fig 3: Ofx HPLC chromatogram, showing the connection between the area under the curve (AUC) and the retention time (mins).**

**In-Vitro drug Release Study**

At a temperature of 34 degrees Celsius, the in vitro release of ofloxacin was investigated using OFX-ISG, and a comparison was made to OFX. The patterns for the release of OFX and OFX-ISG ofloxacin are depicted in Figure 4. Within the first several hours, the release of more than half of the drug was caused by OFX-ISG, which was responsible for the release. On the other hand, treatment with OFX-ISG was successful in eliminating all traces of ofloxacin from the body for up to 30 hours. The rapid release of ofloxacin from OFX can be attributed to two factors: the short relaxation time of nanomicelles (on the order of microseconds to seconds), and the rapid partitioning of ofloxacin into and out of micelles. Both of these factors contribute to the rapid release of ofloxacin from OFX. It was determined that the presence of gellan gum in OFX-ISG was responsible for the extended release of ofloxacin. To be more specific, this was the case with regard to the remaining 30 percent of the drug that was made available.



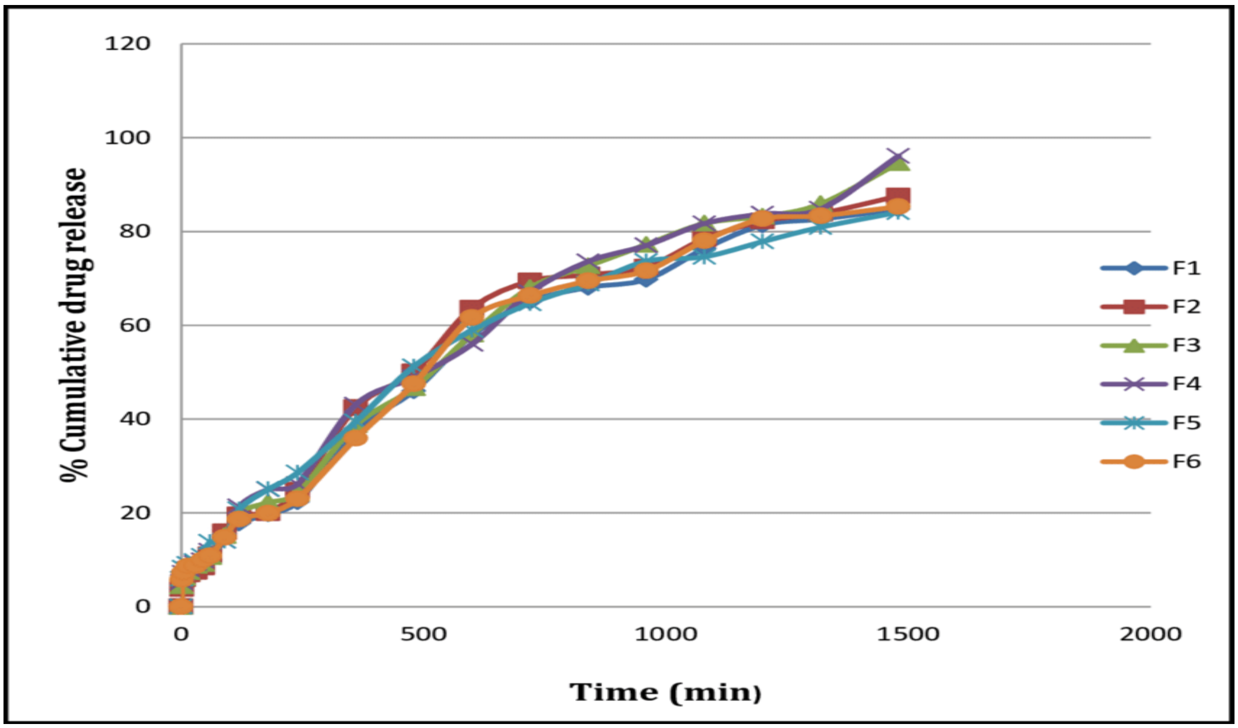


**Fig 4: In vitro release of Ofloxacin**

**Conclusion**

When looked at with the naked eye and inspected at room temperature, the dispersion of OFX-ISG after it had been diluted with simulated tear fluid seemed to be gel-like (STF). The ofloxacin nanomicelles appeared to be in their entirety in the gellan gum. Based on the preliminary findings of our investigation, OFX-ISG appears to have the potential to be utilised as a delivery system for ofloxacin, which is a medication that can be utilised to treat inflammations of the anterior part of the eye. It is essential to research the in vitro properties of OFX-in ISG as well as its capacity to treat eye inflammations following several doses.

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