Formulation and evaluation of in situ ophthalmic gel of moxifloxacin hydrochloride

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Abstract

The field of Ocular drug delivery is one of the interesting and challenging endeavors facing the pharmaceutical scientist. The most frequently used dosage forms i.e. ophthalmic solutions and suspensions are compromised in their effectiveness by several limitations, leading poor ocular bioavailability. In situ hydrogels are instilled as drops into the eye and undergoes a sol to gel transition in the cul-de-sac, improved ocular bioavailability by increasing the duration of contact with corneal tissue, thereby reducing the frequency of administration. The purpose of the present work was to develop pH-triggered an ophthalmic drug delivery system using combination of gelling agents with different mechanisms for in situ gelation of Moxifloxacin hydrochloride, a fluoroquinolone antibiotic. In situ gels were prepared by simple dispersion method using carbopol along with HPMC in factorial design and then evaluated for pH, gelling capacity, drug content, rheological, gel strength and in-vitro diffusion studies and comparison with marketed eye drop formulation along with statistical studies. Among formulation batches F1 - F9; optimized formulation F6 imparted sustained release property to the gel formed in situ and effective other evaluation parameters. The developed formulations were therapeutically efficacious, stable, non-irritant and provided sustained release of the drug overcoming conventional drawbacks leading to better patient acceptance.

Keywords: In situ-forming systems; ophthalmic hydrogel; Moxifloxacin Hydrochloride; carbopol, HPMC.

1. Introduction

Eye is most interesting organ due to its drug disposition characteristics. Topical administration of anti-infective drug is the treatment of choice for diseases of anterior segments of the eye. When a drug solution is dropped into the eye, effective tear drainage and blinking result in a 10-fold reduction of drug concentration in 4-20 minutes. The limited permeability and rapid elimination results in low absorption and short duration of the therapeutic regimen [1] Ocular therapy could be significantly improved if the pre-corneal residence time of drugs could be increased.

Various ophthalmic vehicles such as inserts, ointments, suspensions, and aqueous gels lengthen the residence time of instilled dose but have some drawbacks such as blurred vision from ointments or low patient compliance from inserts [40]. This problem can be overcome by using in situ gel forming ophthalmic drug delivery systems prepared from polymers that exhibit reversible phase transitions and pseudoplastic behavior to minimize interference with blinking [2].

Depending on the method employed to cause sol to gel phase transition on the ocular surface, the following three types of systems have been recognized: pH-triggered - The polymers used in this system are Pseudolatexes - Carbomer (carbopol), Cellulose acetate phthalate latex (CAP-latex), Temperature-dependent - Poloxamers (Pluronic, Tetronics), Cellulose derivatives (MCHPMC), Xyloglucan, Ion-activated induced - Alginites, Gelrite® (Gellan gum).

Such a system can be formulated as liquid as solution upon exposure to physiological pH condition of eye, shifts to gel phase which has a higher viscosity thus increasing the pre-corneal residence and can improve patient compliance. [2]

With the advent of new generation of flouroquinolones such as Moxifloxacin HCl, the treatment of gram positive bacterial infections has been achieved. This drug shows increased potency than all other topical antibiotics making it able to eradicate methicillin-resistant Staphylococcus
species. Moxifloxacin HCl penetrates at very high level into ocular tissues including the tear film, cornea, anterior chamber, and ciliary body due to its biphasic nature i.e. soluble in both lipid and aqueous solutions. Therefore, it can achieve very high concentration in the eye \[3\]. Hence, it was thought of combining the benefits of the drug with pH sensitive/mucoadhesive polymers such as carbopol and hydroxypropyl methylcellulose (viscosity enhancing agent) to come out with a formulation, which might outperform the conventional eye drops of the same drug. The formulation would be useful to treat external infections of the eye such as acute and subacute conjunctivitis, bacterial keratitis, bacterial endophthalmitis, and keratoconjunctivitis.

2. Materials and Method


2.1 Methods

i. Selection of Drug and Polymers

Moxifloxacin HCl, the most recent fourth generation fluoroquinolone antibiotic with least chances of developing resistance owing to its action on both bacterial DNA gyrase And topoisomerase IV, has extended activity against gram positive microorganisms. In addition, good water solubility, higher penetration efficacy at tear fluid pH makes it a suitable drug candidate for formulating as in situ gelling system \[3\]. Carbopol has dual property of pH responsiveness and mucoadhesiveness both of which, contribute equally in the improvement of retention of formulation in the eye, whereas HPMC is a viscosity builder and also acts as a drug release retardant.

ii. Determination of Absorbance Maxima of Moxifloxacin HCl by UV Spectrophotometer

A drug solution of 8 g/ml in simulated tear fluid (pH 7.4) was prepared, scanned and UV spectrum was recorded in range of 200-400 nm.

iii. Calibration Curve of Moxifloxacin HCl in Simulated Tear Fluid (pH 7.4)

The stock solution was prepared by dissolving 100 mg of drug in 100 ml of STF to get 1 mg/ml concentration solution. From the above solution, adequate aliquots were removed and diluted suitably to acquire final concentration from 1 to 10 g/ml. All the solutions were scanned through UV Spectrophotometer and absorbances were taken against a blank of STF at max of 287 nm.

iv. Interaction Studies \[4\]

The proper design and formulation of a dosage form requires consideration of the physical, chemical and biological characteristics of all drug substances and excipients to be used in the formulation of the product. The drug and excipients must be compatible with one another to produce a stable, efficacious, and safe product. The interaction study of prepared in situ gel formulations was carried out using infrared spectroscopy following KBR dispersion method. The spectrum of dried mixture of drug and potassium bromide was then run followed by drug with excipients in the wavelength region between 4000 and 400 cm\(^{-1}\). The drug-polymers compatibility was confirmed by differential scanning calorimetric (DSC), which was carried out by heating drug and the physical mixture of drug with polymers separately from 25 \(^\circ\)C to 275 \(^\circ\)C at the heating rate of 10 \(^\circ\)C/min in a nitrogen environment. The instrument used was METTLER differential scanning calorimeter with Star\(^{\circ}\) SW 8.10 software.

2.2 Formulation

i. Selection of Vehicle \[5\]

Before preparing in situ gelling system, selection of appropriate vehicle is essential. Therefore, polymer dispersions were prepared in different buffer solutions like acetate buffer I.P. (pH 4.0, 5.0), citrophosphate buffer I.P. (pH 5.0, 6.0) and phosphate buffer I.P. (pH 6.0). Based on visual appearance and solubility at the dosage level desired (0.5%, w/v); citrophosphate buffer pH 5.0 was chosen as it gave clear solutions while, others showed fine precipitates or fibres in them.

ii. Preparation of pH-induced in Situ Gelling System \[6\]

PH sensitive polymers like carbomers form gel upon change in their environment (pH). Carbopol 934P is a polyacrylic acid, which undergoes sol-to-gel transition in aqueous solution when the pH is raised above its pKa value of about 5.5. Hence, carbopol 934P was selected for preparation of pH induced in situ gelling system. The intended work was divided into two parts so as to optimize the polymer concentration: Optimization of polymers concentration Incorporation of active ingredients in optimized polymer ratio

iii. Optimization of Carbopol for In Situ Gelling Capacity

Carbopol 934P in various concentrations (0.1 to 0.5% w/v), was uniformly dispersed in beakers containing required quantity of citrophosphate buffer (pH 5.0), and allowed to hydrate overnight. Subsequently, stirring was done by magnetic stirrer. These solutions were evaluated for clarity, gelling capacity and viscosity at nonphysiological (pH 5.0) conditions. The results were considered while selecting an optimum polymer concentration.

iv. Optimization of Carbopol and HPMC Combination for In Situ Gelling System \[6\]

Carbopol in less concentrations forms low viscosity solutions and is unable to form stiff gel upon instillation in the eye. However, high concentration makes the solution highly acidic, not easily neutralized by the buffering action of the tear fluid. A reduction in the carbopol concentration without compromising the in situ gelling properties as well as the overall rheological behaviour of the system can be achieved by adding a suitable viscosity-enhancing polymer such as hydroxypropyl methylcellulose (HPMC). Therefore, HPMC K4M (4000-5600 cps) was used in formulation.

2.3 Procedure

A number of formulations were designed containing various combinations of grade of HPMC with carbopol in order to select the appropriate polymer combination. Buffer solutions was distributed equally in beakers and to it HPMC K4M (0.2 to 0.6% w/v) was dispersed with continuous stirring. Carbopol 934P ranging from 0.3 to 0.5% w/v was sprinkled over all the
solutions, and set aside for overnight hydration. Subsequently, the solutions were stirred with magnetic stirrer to get uniform solution. These different solutions were observed for clarity, gelling capacity and viscosity at non-physiological (pH 5.0) conditions by using Brookfield viscometer.

2.3.1 Incorporation of Moxifloxacin HCl in the Optimized Polymer Ratio

A) Factorial Design

A 3² full factorial design (FFD) was constructed where the amounts of carbopol (X1) and HPMC (X2) were selected as the factors. The levels of the two factors were selected on the basis of the preliminary studies carried out before implementing the experimental design. All other formulation and processing variables were kept invariant throughout the study. Table 1 gives the translation of the coded levels to the experimental units and 9 formulation batches were prepared as per design.

B) Preparation of in Situ Gelling System

The citrophosphate buffer of pH 5.0 was prepared in double distilled water; HPMC K4M was added and kept for some time to hydrate. Carbopol 934P was sprinkled over this solution and allowed to hydrate overnight. The solution was stirred with magnetic stirrer. The drug solution was prepared by dissolving Moxifloxacin HCl in double distilled water and pH was adjusted with 0.5 M sodium hydroxide solution. Benzalkonium chloride was then added and the solution was filtered through 0.22 μm cellulose acetate membrane filter. The drug solution was incorporated to the polymer solution with constant stirring until a uniform solution was observed. The final volume was made up to 100 ml. The formulations, in their final containers were sterilized by autoclaving at 121 °C and 15 p.s.i. for 20 min. The contents of the developed in situ gelling system are given in table 2.

Table 1: Amount of variables in 3² factorial design batches

<table>
<thead>
<tr>
<th>Coded Values</th>
<th>Actual Values (% w/v)</th>
</tr>
</thead>
<tbody>
<tr>
<td>X1</td>
<td>X2</td>
</tr>
<tr>
<td>-1</td>
<td>0.3</td>
</tr>
<tr>
<td>0</td>
<td>0.4</td>
</tr>
<tr>
<td>+1</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Table 2: Contents of formulations

<table>
<thead>
<tr>
<th>Sr. no.</th>
<th>Ingredients</th>
<th>Formulations*</th>
<th>Formulations*</th>
<th>Formulations*</th>
<th>Formulations*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Moxifloxacin HCl</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>2</td>
<td>Carbopol 934P</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>3</td>
<td>HPMC K4M</td>
<td>0.3</td>
<td>0.4</td>
<td>0.5</td>
<td>0.3</td>
</tr>
<tr>
<td>4</td>
<td>Sodium chloride</td>
<td>0.9</td>
<td>0.9</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>5</td>
<td>Benzalkonium chloride</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
<td>0.01</td>
</tr>
<tr>
<td>6</td>
<td>Citrophosphate buffer(pH 5.0)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

*All quantities are expressed as % w/v

3. Evaluation of Prepared In-Situ Gelling System

3.1 Visual Appearance and Clarity

Clarity is one of the most important characteristic features of ophthalmic preparations. The formulations were examined for visual appearance and clarity by visual observation against a white and black background to check the presence of any particulate matter.

3.2 pH

The preparation to be instilled into eye should be non-irritating to the eye. To ensure that the preparation has same pH as that of lacrimal fluid, the pH of the prepared in-situ gelling system after addition of all the ingredients was measured using digital pH meter.

3.3 Drug Content Uniformity

The vials (n=3) containing the preparation were shaken for 2-3 min and 1 ml of preparation was transferred to 100 ml volumetric flask and volume was made up with simulated tear fluid pH 7.4. Aliquot of sample was withdrawn and further diluted to 10 ml with same simulated tear fluid pH 7.4. The concentration of Moxifloxacin HCl was determined at 287 nm by using UV-Visible spectrophotometer (Pharmspec, 1700, Shimadzu, Japan).

3.4 In Vitro Gelation Studies

The gelling capacity of the prepared system containing different concentrations of carbopol 934P and HPMC K4M was evaluated. It was performed by placing a drop of system in vials containing 1 ml of simulated tear fluid, freshly prepared and equilibrated at 37 °C, and visually assessing the gel formation and noting the time for gelation as well as time taken for the gel formed to dissolve.

3.5 Measurement of Gel Strength

A sample of 50 gm of gel was placed in a 100 ml graduated cylinder and gelled in with 0.5N NaOH at pH 7.4 at 37 °C. The apparatus for measuring gel strength (weigh or apparatus as shown in figure 12, weight 20 gm) was allowed to penetrate in insitu ophthalmic gel. The gels strength, which means the viscosity of the gels at physiological pH, was determined by the time (seconds), the apparatus was taken to sink 5cm down through the prepared gel.
3.6 Rheological Studies \[6, 10\]
Viscosity of instilled formulation is an important factor in determining residence time of drug in the eye. The rheological studies of the formulations were carried out with a Brookfield viscometer (RVDV II+ Pro model) using sample adaptor with spindle number (SC4-21), and angular velocity was increased gradually from 0.5 to 100 rpm. Then, the hierarchy of angular velocity was reversed (100 to 10 rpm). The average of two readings was used to calculate the viscosity. The pH of the formulations was raised from 5.0 to 7.4 by adding 0.5 N sodium hydroxide solution, and simultaneously the temperature was increased from 25°C to 37°C. The viscosity of samples was recorded before and after gellifying. (Both at physiological and non-physiological conditions.)

3.7 Sterility Testing \[11\]
Sterility testing was intended for detecting the presence of viable form of microorganisms and performed for aerobic/anaerobic bacteria and fungi by using fluid thioglycolate medium and soybean-casein digest medium, respectively as per the Indian Pharmacopoeia 1996. Both the media were observed every day for the presence or absence of turbidity and compared with a positive and negative control.

3.8 In Vitro Release Studies \[12\]
In vitro release rate of the Moxifloxacin Hydrochloride from the sol gel system for the corneal drug availability was determined by the diffusion process. 1 ml of the formulation was kept in the donor compartment over a dialysis membrane which was rinsed & soaked for the 24 hours in the diffusion medium. The donor compartment was immersed in the receptor compartment which was calibrated containing 25.38 ml of the simulated tear fluid 7.4. The beaker containing diffusion medium (receptor compartment) was maintained at 37±0.5°C with the constant stirring at 22 rpm using the magnetic stirrer. One ml aliquots were withdrawn from the diffusion medium every hour for the 8 hours & same quantity of fresh, diffusion medium was replaced for the amount withdrawn. The samples withdrawn was analysed spectrophotometrically at 287nm for the Moxifloxacin Hydrochloride using Shimadzu Double beam UV-Visible spectrophotometer. The comparison between drugs released from developed formulations with marketed (MOSI) eye drop was made.

3.9 Statistical Analyses \[13\]
The effect of formulation variables on the response variables were statistically evaluated by applying ANOVA at 0.05 levels using a commercially available software package Design-Expert® version 7.1.6 (Stat-Ease Inc.). To describe the response surface curvature, the design was evaluated by quadratic model, which bears the form of equation:

\[ Y = b_0 + b_1X_1 + b_2X_2 + b_3X_1^2 + b_4X_2^2 + b_5X_1X_2 \]

Where, Y is the response variable, b0 the constant and b1, b2, b3, b4, b5 the regression coefficients. X1 and X2 stand for the main effect; X1X2 are the interaction terms, and show how response changes when two factors are simultaneously changed. X1^2 and X2^2 are quadratic terms of the independent variables to evaluate the nonlinearity. The polynomial equation was established by applying ANOVA using Design Expert software.

4. Result and Discussion

4.1 Estimation of Moxifloxacin HCl by UV Spectrophotometer
The drug solution (8 µg/ml) was scanned for UV absorption between 200-400 nm. The spectrum was recorded, which showed the absorbance maxima (max) at 287 nm.

4.2 Construction of Calibration Curve of Moxifloxacin HCl
Calibration curve of the drug in simulated tear fluid (pH 7.4) was plotted by recording the absorbance of solutions of different concentrations (1-10 µg/ml). The Beers and Lamberts range was found to be in the range of 1-10 µg/ml and the coefficient of correlation was 0.99778 and slope 0.09975 as shown in fig.1.

Intercept: - 0.03238
Slope: 0.09975

![Fig 1: Calibration curve of Moxifloxacin HCl in simulated tear fluid](image1)

4.3 Interaction Studies by IR Spectroscopy
The prepared in-situ gelling systems were evaluated for interaction studies to ensure that there is no interaction between drug and polymers. Fig.2 and 3.

![Fig 2: IR spectrum of Moxifloxacin HCl](image2)

![Fig 3: IR spectrum of a representative formulation](image3)
4.4 Formulation

4.4.1 Selection of Vehicle

The clarity and solubility of solution with citrophosphate buffer (pH 5.0) was relatively better as compared to other buffers and also upon addition to polymer solution it did not form any precipitate. Hence, citrophosphate buffer of pH 5.0 was selected as a vehicle for formulations.

4.4.2 Optimization of Carbopol Concentration

The carbopol solution of 0.3–0.5% w/v retained liquid state (free flow) at pH 5.0 and 25 °C and gelled upon exposure to physiological conditions. Accordingly, the optimum concentration of carbopol selected for in situ gel formulation system was to be used as the in situ gel forming agent is 0.3% (w/v); so carbopol concentrations 0.3-0.5% w/v were selected for formulating in situ gelling system.

4.4.3 Optimization of Carbopol and HPMC K4M Combination Concentrations

Optimum concentrations of HPMC K4M from 0.3-0.5% w/v were used along with carbopol 934P in optimized concentrations (0.3-0.5% w/v) for formulating in situ gelling system. The concentration of HPMC K4M above 0.5% forms gel at formulation pH so it can no longer be used.

4.5 Evaluation of Prepared In Situ Gelling System

4.5.1 Visual appearance, Clarity, and pH

The clarity of all formulations was found to be satisfactory. The formulations were light yellow in colour. Terminal sterilization with autoclaving had no effect on the physicochemical properties of the formulations. PH of the formulations did not vary considerably.

4.5.2 Drug Content Uniformity

The drug content was found to be in the acceptable range for all the formulations. Percent drug content for all nine formulations was in the range of 97.84-100.11% indicating uniform distribution of the drug. Table no.3.

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Drug content* (%)</th>
<th>Gelling capacity</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>98.4±0.90</td>
<td>+</td>
</tr>
<tr>
<td>F2</td>
<td>98.3±1.87</td>
<td>+</td>
</tr>
<tr>
<td>F3</td>
<td>97.8±2.42</td>
<td>+</td>
</tr>
<tr>
<td>F4</td>
<td>98.3±0.99</td>
<td>++</td>
</tr>
<tr>
<td>F5</td>
<td>98.1±0.34</td>
<td>++</td>
</tr>
<tr>
<td>F6</td>
<td>98.8±2.76</td>
<td>+++</td>
</tr>
<tr>
<td>F7</td>
<td>100.1±2.24</td>
<td>+++</td>
</tr>
<tr>
<td>F8</td>
<td>99.0±1.81</td>
<td>+++</td>
</tr>
<tr>
<td>F9</td>
<td>98.9±2.21</td>
<td>+++</td>
</tr>
</tbody>
</table>

5.5.3 In vitro Gelation Studies

F1, F2 and F3 exhibited very weak gelation. F4 and F5 showed more suitable gelling capacity, which completed the gelation immediately and remained for few hours, compared with the F6, F7, F8, and F9, which gelled instantaneously but remained for extended period of time. These can also be reflected in the viscosity F9 had greater viscosity, which would cause the gel difficult to spread out on cornea and would make vision blurring.

4.5.4 Gel Strength

At the physiological pH condition (pH 7.4) the viscosity of formulations were increased with increase in polymer concentrations and that causes increase in gel strength. The gel strength increases from F1-F9 batches. The highest gel strength was exhibited by the F9 batch that contain carbopol 934P 0.5% and HPMC K4M 0.5% and lowest gel strength was exhibited by the F1 batch that contains lowest concentration of both the polymers. Figure no.4.

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**Table 3:** Drug content and gelling capacity of formulations

**Fig 4:** Plot of Gel Strength Vs Formulation Batches for F1-F9

4.5.5 Rheological Studies

Dynamic viscosity of formulations was measured as the change of shear rate under non-physiological (pH 5) and physiological (pH 7.4) conditions to investigate the rheology of these formulations. At pH 5.0 the formulations were in a liquid state and exhibited low viscosity. An increase in the pH to 7.4 caused the solutions to transform into gels with high viscosity. The formulations exhibited pseudo plastic rheology. Figure no. 5 & 6.
4.5.6 Sterility Testing
All the prepared in-situ gelling systems were evaluated for the sterility. After 7 days of incubation the results showed that no microbial growth was found in all formulations.

4.5.7 In vitro drug release study of formulation
These F1-F3 formulations exhibited these release at 6 hr and with slight increase up to 8hr i.e. they exhibited sustained release effects and this could be due to increase in HPMC concentration. F4, F5, and F6 showed 95.27%, 93.91%, and 90.54% drug release. 89.01% and 86.38% of the drug was released from F7 and F8. This more sustained release was seen due to higher concentration of both carbopol (0.5% w/v) and HPMCK4M. F9 showed least drug release (84.85%). 97.79% of drug was released in 3h from marketed eye drop (MOSI, FDC Ltd.) as shown in graph fig.no.7 The developed formulations obviously outperformed the marketed eye drop by releasing drug over a long period of time and lead to prolonged therapeutic activity.

4.5.8 Statistical Analyses \[4, 11\]
A 3\(^2\) full factorial design was selected and the 2 factors were evaluated at 3 levels. The amount of carbopol 934P (X1) and HPMC K4M (X2) were selected as independent variables and \(t_{50}\) and rel\(_{8h}\) were the dependent variables. The data was processed using Design Expert. 7.1.6 software and analyzed statistically using analysis of variance (ANOVA).

A. ANOVA Study
The model F-value of 35.31 implied that the model was significant. There was only a 0.72% chance that a “Model F-value” could occur due to noise. Values of “Prob>F” less than 0.05 indicate model terms are significant. In this case X1, X2, X1\(^2\) were significant model terms. Values greater than 0.1 indicate the model terms are not significant (Table 28). The final model for release in 8 h was as follows; \(R^2=0.9957\)

\[
\text{Rel}_{8h} = 93.35 - 4.75(X1) - 1.57(X2) - 0.91(X1) (X2) - 1.75(X1)^2 - 0.17(X2)^2
\]

the Model F-value of 20.37 implied the model was significant. Values of “Prob>F”indicated that X1, X2 were significant model terms. The final model for \(t_{50}\) was as follows;

\[
\text{t}_{50}\% = 2.09 + 0.77 (X1) + 0.28 (X2) - 0.12 (X1) (X2) + 0.17(X1)^2 - 0.083(X2)^2
\]

The time taken for release of 50% of drug from the formulations varied from 1.0 to 3.0 h. The results also indicated that the effect of concentration of carbopel was more significant than the effect of concentration of HPMC.

4.5.9 Response Surface and Contour Plot
The quadratic surface model obtained from the regression analyses was used to build up 3D surface and 2D contour plots in which the responses were represented by curvature surface as a function of independent variables. The relationship between the response and independent variables can be directly visualized from the response surface plots. Figure no.8 & 9.

Fig 8: 3D Response surface plot of carbopol and HPMC on rel8h

Fig 9: 3D Response surface plot of carbopol and HPMC on t50%

5. Conclusion
The optimized formulation (F6) contained 0.4% w/v carbopol 934 P and 0.5% w/v HPMC K4M wherein carbopol caused initial fast release of drug due to its hydrophilic nature later on hydroxypropyl methylcellulose imparted sustained release property to the gel formed in situ. The in situ gelling system will get good patient acceptance because it is easy to instill and gradually erodes by dissolution of the gel, avoiding the need for removal. Hence, it can be concluded that in situ gels are a viable alternative to conventional eye drops by providing sustained release of medicament resulting in decreased frequency of administration leading to better patient acceptance.

6. References
3. Lane SS. A fall update on the advantages of fourth-generation fluoroquinolones. www.eyeworld.org/supplements/vigamox%206pg%201-4r%20to%20print.pdf