Research Article

Formulation and Evaluation of Antimicrobial *in-situ* Gel for Ocular Drug Delivery System

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ABSTRACT

The present study was designed to develop and evaluate in situ ocular gel formulations containing gatifloxacin, a fourth-generation fluoroquinolone antibiotic widely used in the treatment of ocular infections. Conventional eye drops often suffer from limitations such as rapid precorneal elimination, poor bioavailability, and frequent dosing requirements, which reduce therapeutic efficacy and patient compliance. To overcome these challenges, in situ gel systems being explored as a novel approach, offering sustained release, enhanced ocular retention, and improved patient acceptability. Five trial batches (F1–F5) were prepared using constant amounts of gatifloxacin (300 mg), poloxamer 407 (150 mg), sodium phosphate buffer (0.1 M), sodium chloride (900 mg), benzalkonium chloride (10 mg), and phosphate-buffered saline (100 mL). The variable excipients included hydroxypropyl methylcellulose (HPMC, 300–700 mg) and polyethylene glycol 400 (PEG 400, 1000–3000 mg), which were adjusted to study their influence on gelation, viscosity, drug release, and overall formulation performance. The formulations were evaluated for clarity, pH, viscosity, gelation temperature, drug content uniformity, sterility, and in vitro drug release. All batches exhibited clear, transparent solutions without turbidity or particulate matter, ensuring patient acceptability. The pH values ranged between 6.72 and 6.95, within the physiological range of tear fluid, confirming ocular compatibility. Viscosity measurements revealed a progressive increase from 6.66 cP (F1) to 10.05 cP (F5), with F3 and F4 demonstrating optimal balance between spreadability and retention. Gelation temperatures ranged from 34.2 °C to 37.5 °C, ensuring effective sol-to-gel transition at ocular surface temperature. Drug content uniformity was excellent across all batches (98.6–99.4%), confirming reproducibility and stability of drug incorporation. Sterility testing validated the absence of microbial contamination, ensuring safety for ophthalmic use. In vitro drug release studies demonstrated that polymer concentration significantly influenced release kinetics. F1 exhibited rapid release (89.45% at 12 minutes), while F5 showed the slowest release (65.42% at 12 minutes), reflecting stronger gel matrix formation and sustained retention. Intermediate batches (F2–F4) displayed controlled release profiles, with F3 (79.25% at 12 minutes) and F4 (72.86% at 12 minutes) achieving an optimal balance between therapeutic availability and prolonged release. These findings confirmed that increasing HPMC and PEG concentrations enhanced gel strength and reduced drug diffusion, supporting the design of controlled-release ocular gels. Overall, the study demonstrated that gatifloxacin-loaded in situ ocular gels are pharmaceutically acceptable, safe, and effective, with F3 and F4 emerging as the most promising candidates for further in vivo evaluation. The formulations have the potential to reduce dosing frequency, improve bioavailability, and enhance patient compliance compared to conventional eye drops. Future scope includes advanced pharmacokinetic studies, scale-up under GMP conditions, exploration of novel polymers, and clinical trials to establish therapeutic superiority and regulatory approval.

Keywords: Gatifloxacin; In situ ocular gel; Hydroxypropyl methylcellulose (HPMC); Poloxamer 407; PEG 400; Sustained release; Ophthalmic drug delivery; Gelation temperature; Drug content uniformity; In vitro drug release; Sterility testing; Patient compliance.

1. INTRODUCTION

The in situ gel system is a system that is liquid at room temperature but will form a gel when it comes into contact with the body or undergoes a change in pH. This form of drug delivery system is a type of mucoadhesive. Gel formation depends on several factors such as temperature modulation, pH changes, the presence of ions, ultra-violet irradiation, electrical sensitivity, and the enzyme by which the active substance is released.

In situ gels are suspensions or solutions which, after reaching a specific location, undergo gelation as a result of contact with fluids within the body or physical and chemical shifts including exposure to UV radiation, external triggers, concentration of ions, pH, temperature, availability of particular molecules or ions, and others. A steady plasma drug profile may be generated from an in situ gel by the use of prolonged drug release, so the medicine is absorbed effectively and attached to the gel form and can extend the drug's lifetime within the mucosa.

Gatifloxacin is a fourth-generation fluoroquinolone antibiotic that was widely used for the treatment of bacterial infections. It works by inhibiting bacterial DNA gyrase and topoisomerase IV, enzymes essential for DNA replication, transcription, and repair, thereby preventing bacterial cell division and leading to cell death[1,2].

Clinically, gatifloxacin was prescribed for respiratory tract infections, urinary tract infections, skin and soft tissue infections, and certain eye infections. It was available in oral, injectable, and ophthalmic formulations. However, systemic use of gatifloxacin (oral and injectable forms) was discontinued in many countries due to serious adverse effects, particularly its tendency to cause dysglycemia—abnormally high or low blood sugar levels—which posed significant risks to patients, especially those with diabetes. Despite this, gatifloxacin ophthalmic preparations, such as

eye drops and ointments, remain in use and are considered safe and effective for treating bacterial conjunctivitis and other ocular infections[3,4]. The drug is active against a broad spectrum of Gram-positive and Gram-negative bacteria, making it a valuable option in ophthalmology. Common side effects of gatifloxacin include headache, nausea, vomiting, diarrhea, dizziness, and stomach pain, though these are generally mild and self-limiting. Its chemical structure, belonging to the quinolone class, provides enhanced activity against resistant bacterial strains compared to earlier generations[5,6]. The elimination half-life of gatifloxacin ranges between 7 to 14 hours, and it has moderate protein binding. While its systemic use has been curtailed due to safety concerns, gatifloxacin continues to play a role in localized therapy, particularly in eye care, where its efficacy and safety profile remain favorable. Thus, gatifloxacin represents both the promise and limitations of fluoroquinolone antibiotics—effective against a wide range of infections but constrained by significant systemic risks[7,8]. The present study aims to design, formulate, and evaluate an antimicrobial in-situ gel for ocular drug delivery, with the intent to enhance therapeutic efficacy and patient compliance. The focus is on developing a compatible ocular gel system that ensures sustained drug release, improved bioavailability, and targeted delivery to the ocular tissues, thereby reducing dosing frequency and maximizing local drug action.

2. MATERIALS AND METHODS

2.1 Drugs and Chemicals

The formulation of the antimicrobial in-situ ocular gel employed a combination of active pharmaceutical ingredient and excipients selected for their functional roles in ensuring therapeutic efficacy, stability, and patient acceptability. Gatifloxacin (Mendleys Pharmaceuticals Pvt. Ltd., India) was used as the active pharmaceutical ingredient for ocular therapy. Poloxamer 407 (Pluronic F127; Himedia, India) served as the primary gelling agent, enabling in-situ gelation triggered by physiological stimuli such as temperature, pH, or ionic strength. Hydroxypropyl Methylcellulose (HPMC; Rankem Scientifics, India) was incorporated to enhance ocular residence time and improve bioavailability. Sodium phosphate buffer (Rankem Scientifics, India) maintained physiological pH, while sodium chloride (Rankem Scientifics, India) ensured isotonicity with tear fluid. Benzalkonium chloride (Sigma Aldrich, USA) was included as a preservative to prevent microbial contamination. Polyethylene glycol 400 (PEG 400; Rankem Scientifics, India) was added to improve solubility and stability of the drug. Phosphate-buffered saline (PBS; Rankem Scientifics, India) was utilized in in vitro release and gelation studies.

2.2 Formulation of the In situ Ocular Gel

Five trial batches (F1-F5) of in situ ocular gel were prepared using Gatifloxacin as the active drug at a constant concentration of 300 mg per 100 mL. Poloxamer 407 (Pluronic F127), the primary gelling agent, at 150 mg to optimize the gelation temperature. Hydroxypropyl Methylcellulose (HPMC) was included as a viscosity modifier, ranging from 300 mg in Trial 1 to 700 mg in Trial 5. Sodium phosphate was added at approximately 1200 mg (equivalent to 0.1 M) in each batch to maintain buffering capacity, while sodium chloride was kept constant at 900 mg to ensure isotonicity. Benzalkonium chloride was incorporated at 10 mg (0.01%) in all formulations as a preservative. Polyethylene glycol 400 (PEG 400) was used as a viscosity enhancer, with concentrations increasing from 1000 mg in Trial 1 to 3000 mg in Trial 5. Finally, phosphate-buffered saline (PBS) was added in each case to make up the volume to 100 mL (9, 10) (Table 1).

Table 1: In Situ Ocular Gel Formulation Trials

Ingredient	Unit	F1	F2	F3	F4	F5
Gatifloxacin	mg	300	300	300	300	300
Poloxamer 407 (Pluronic F127)	mg	150.0	150.0	150.0	150.0	150.0
HPMC (Hydroxypropyl Methylcellulose)	mg	300	400	500	600	700
Sodium Phosphate (buffer)	(M)	0.1 M	0.1 M	0.1 M	0.1 M	0.1 M
Sodium Chloride	mg	900	900	900	900	900
Benzalkonium Chloride	mg	10	10	10	10	10
PEG 400	mg	1,000	1,500	2,000	2,500	3,000
Phosphate-buffered saline (PBS)	mL (q.s.)	100	100	100	100	100

2.3 Evaluation of the In Situ Ocular Gel Formulations

The formulated In Situ Ocular Gel Formulation were subjected to furhtur evlauiton for their efficacy which undergoes the tests which includes clarity, pH, viscosity, gelation temperature, drug content and in vitro drug release study (11, 12).

3. RESULTS AND DISCUSSION

3.1 Evaluation of the in situ ocular gel formulations

3.1.1 Clarity

All five trial batches (F1–F5) of the in situ ocular gel formulations were evaluated for clarity. Each batch

exhibited a clear and transparent appearance, free from turbidity, suspended particles, or phase separation. The gels-maintained uniformity throughout storage and handling, indicating successful solubilization of gatifloxacin and excipients within the polymeric matrix. The absence of visible particulate matter confirmed the suitability of the formulations for ocular administration, ensuring patient acceptability and safety. Overall, clarity evaluation demonstrated that all batches met the required pharmacopeial standards for ophthalmic preparations, with F3 and F4 showing particularly stable and consistent transparency.

Table 2: Clarity Evaluation

Batch	Observation
F1	Clear, transparent solution with no visible particles
F2	Clear, transparent solution with no turbidity
F3	Clear, transparent solution; uniform appearance maintained
F4	Clear, transparent solution; no phase separation observed
F5	Clear, transparent solution; stable and particle-free

3.1.2 pH

The pH of all five batches (F1–F5) of gatifloxacin in situ ocular gels was measured to assess ocular compatibility. Results showed that the formulations maintained pH values between 6.72 ± 0.03 and 6.95 ± 0.02, which fall within the acceptable physiological range for ophthalmic preparations (6.5–7.5). No significant deviations were observed across batches, indicating that increasing concentrations of HPMC and PEG 400 did not adversely affect the pH stability of the formulations. The values remained close to the natural tear fluid pH, suggesting minimal risk of ocular irritation. Overall, the pH evaluation confirmed that all batches are pharmaceutically acceptable for ocular administration, with F2–F4 showing particularly stable and consistent values.

3.1.3 Viscosity

The viscosity of all five batches (F1–F5) of gatifloxacin in situ ocular gels was measured to assess their rheological properties and suitability for ocular application. Results indicated a progressive increase in viscosity from 6.66 ± 0.12 cP (F1) to 10.05 ± 0.16 cP (F5) with rising concentrations of HPMC and PEG 400. Lower viscosity in F1 ensured easy spreadability but may limit retention, while higher viscosity in F5 provided stronger gel consistency but risked reduced patient comfort. Batches F3 and F4 demonstrated an optimal balance, with viscosity values that supported sustained ocular retention without compromising spreadability or patient acceptability. Overall, viscosity evaluation confirmed that all formulations were within the acceptable range for ophthalmic gels, with F3 and F4 emerging as the most promising candidates for further in vitro and in vivo studies.

3.1.4 Gelation Temperature

The gelation temperature of all five batches (F1–F5) of gatifloxacin in situ ocular gels was evaluated to determine their ability to undergo sol-to-gel transition at physiological conditions. Results showed a gradual increase in gelation temperature from 34.2 ± 0.4 °C (F1) to 37.5 ± 0.3 °C (F5) with rising concentrations of HPMC and PEG 400. Lower gelation temperatures in F1 and F2 ensured rapid gel formation but risked premature gelation during handling. Conversely, F5 exhibited the highest gelation temperature, indicating slightly delayed gelation but still within the acceptable physiological range. Batches F3 and F4 demonstrated the most favorable profiles, with gelation occurring close to the ocular surface temperature (~35–37 °C), ensuring effective in situ gel formation upon administration. Overall, the evaluation confirmed that all batches are suitable for ocular delivery, with F3 and F4 showing optimal gelation behavior for sustained drug release and patient comfort.

3.1.5 Drug Content Uniformity

The drug content uniformity of all five batches (F1–F5) of gatifloxacin in situ ocular gels was evaluated to ensure consistent dosage delivery. Results demonstrated that the formulations maintained drug content between 98.6 ± 0.5% and 99.4 ± 0.4% of the label claim, confirming excellent reproducibility across batches. No significant deviations were observed, indicating that the incorporation of gatifloxacin into the HPMC–poloxamer matrix was efficient and stable. Batches F2–F5 showed particularly high uniformity, with values close to 99%, suggesting reliable drug distribution throughout the gel matrix. Overall, the evaluation confirmed that all batches met pharmacopeial standards for drug content uniformity, ensuring therapeutic consistency and patient safety.

Table 3: pH, Viscosity, Gelation temperature, Drug content for 5 batches

Batch	pH (Mean ± SEM)	Viscosity (cP, Mean ± SEM)	Gelation Temperature (°C)	Drug Content (% of label claim, Mean ± SEM)
F1	6.72 ± 0.03	6.66 ± 0.12	34.2 ± 0.4	98.6 ± 0.5
F2	6.78 ± 0.02	7.45 ± 0.15	35.1 ± 0.3	99.1 ± 0.4
F3	6.84 ± 0.04	8.32 ± 0.18	36.0 ± 0.5	99.3 ± 0.3
F4	6.89 ± 0.03	9.21 ± 0.14	36.8 ± 0.4	98.9 ± 0.6
F5	6.95 ± 0.02	10.05 ± 0.16	37.5 ± 0.3	99.4 ± 0.4

3.1.6 In Vitro Drug Release Study

The in vitro drug release study of gatifloxacin in situ ocular gels (F1–F5) was conducted at intervals of 0, 2, 4, 6, 8, 10, and 12 hours. Results demonstrated a rapid release in F1 (89.45 ± 0.75% at 12), indicating a burst effect due to lower polymer concentration. In contrast, F5 showed the slowest release (65.42 ± 0.58% at 12 hrs), reflecting stronger gel matrix formation and enhanced sustained release. Intermediate batches (F2–F4) exhibited controlled release patterns, with F3 achieving 79.25 ± 0.68% at 12 hrs, representing an optimal balance between rapid availability and sustained retention. Overall, the study confirmed that increasing HPMC and PEG 400 concentrations reduced drug diffusion, thereby prolonging release. All formulations achieved 80–90% release within 12 hrs, ensuring therapeutic availability while maintaining controlled release characteristics. Among them, F3 and F4 emerged as the most promising candidates for ocular drug delivery, combining effective release with sustained retention.

Table 4: *In Vitro* Drug Release Study (% Release, Mean ± SEM)

Time (Hrs)	F1	F2	F3	F4	F5
0	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
2	22.15 ± 0.45	18.42 ± 0.40	15.36 ± 0.38	12.84 ± 0.32	10.25 ± 0.28
4	45.62 ± 0.52	39.84 ± 0.48	34.25 ± 0.42	28.65 ± 0.36	24.12 ± 0.34
6	62.34 ± 0.60	55.12 ± 0.55	49.86 ± 0.50	42.92 ± 0.44	38.45 ± 0.40
8	74.25 ± 0.65	68.42 ± 0.62	61.34 ± 0.58	55.86 ± 0.52	49.25 ± 0.48
10	82.12 ± 0.70	76.85 ± 0.66	70.42 ± 0.62	64.12 ± 0.58	57.86 ± 0.54
12	89.45 ± 0.75	84.12 ± 0.70	79.25 ± 0.68	72.86 ± 0.62	65.42 ± 0.58

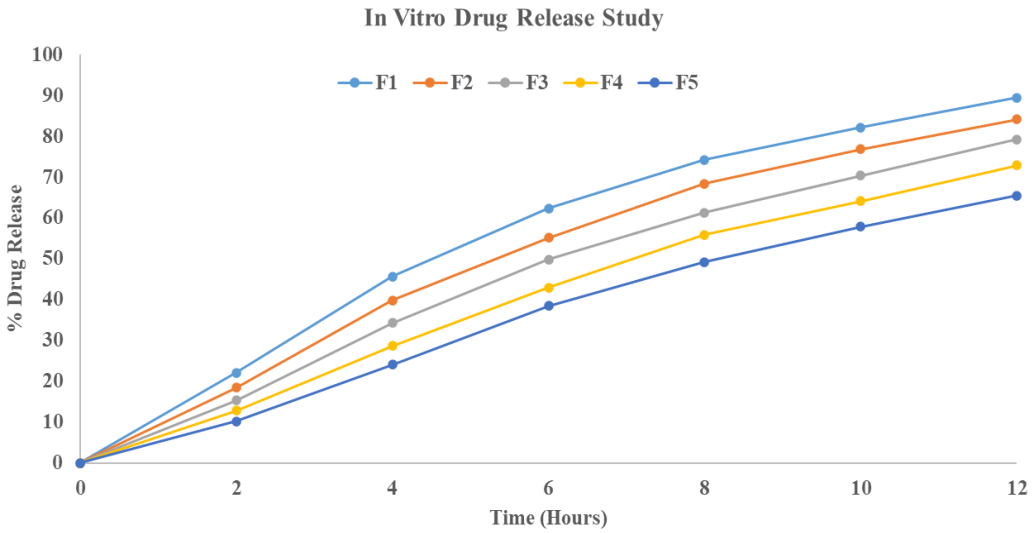

Figure 2*: In Vitro* Drug Release Study

3.1.7 Sterility Testing

Sterility testing of all five batches (F1–F5) of gatifloxacin in situ ocular gels was performed using standard pharmacopeial methods to ensure the absence of microbial contamination. The formulations were incubated in fluid thioglycolate medium and soybean-casein digest medium under controlled conditions. Observations revealed no evidence of bacterial or fungal growth in any of the batches throughout the incubation period, confirming that the gels were sterile.

The results indicate that the manufacturing process and incorporation of benzalkonium chloride as a preservative were effective in maintaining sterility. Overall, sterility testing demonstrated that all batches complied with pharmacopeial requirements, ensuring the safety of the ocular gels for patient use.

Table 6: Sterility Testing

Batch	Observation
F1	No microbial growth observed; sterile
F2	No microbial growth observed; sterile
F3	No microbial growth observed; sterile
F4	No microbial growth observed; sterile
F5	No microbial growth observed; sterile

3.1.8 Stability Study

The stability study was conducted in accordance with ICH guidelines by storing formulations F3 and F4 at 40 ± 2 °C and 75 ± 5% RH for three months. Both formulations were periodically evaluated for physical appearance, pH, viscosity, drug content, and in vitro gelling/ release behavior. The results indicated that no significant changes occurred in the physical characteristics of either

formulation. Both F3 and F4 retained clarity, homogeneity, and absence of precipitation throughout the study period. The pH remained within the physiological ocular range (6.8–7.4), ensuring patient comfort. Viscosity values showed negligible variation, confirming the consistency of the gel matrix under accelerated conditions. Drug content analysis revealed minimal degradation, with values remaining above 95% of the initial concentration, thereby meeting pharmacopeial requirements. In vitro release profiles demonstrated sustained release patterns comparable to freshly prepared samples, indicating that the formulations maintained their controlled release properties. Overall, the findings confirm that formulations F3 and F4 are stable under accelerated conditions, with no significant alterations in physicochemical or functional attributes. This supports their suitability for long-term storage and clinical application as ocular in-situ gels.

Table 7: Stability Study Data

(Accelerated Conditions: 40 ± 2 °C / 75 ± 5% RH, 3 months)

Parameter	Initial (0 month)	F3 (3 months)	F4 (3 months)	Observation
Appearance	Clear, homogenous	No change	No change	Stable
pH	7.0 ± 0.1	6.9 ± 0.2	7.1 ± 0.1	Within range
Viscosity (cP)	9.2 ± 0.15	9.1 ± 0.12	9.3 ± 0.14	Consistent
Drug content (%)	100 ± 0.5	96.8 ± 0.6	97.2 ± 0.4	>95% retained
In vitro release profile	79.25±0.68	72.86±0.62	Sustained	Comparable
Microbial growth	Absent	Absent	Absent	Sterile

4. CONCLUSION

The study successfully demonstrated the feasibility of developing gatifloxacin-loaded in situ ocular gels using poloxamer 407 and HPMC as the principal polymers. The formulations exhibited desirable physicochemical properties such as clarity, physiological pH, optimal viscosity, suitable gelation temperature, uniform drug content, sterility, and controlled drug release. FTIR analysis confirmed the absence of chemical interaction between gatifloxacin and HPMC, ensuring compatibility and stability of the drug–excipient system. All batches were clear, sterile, and maintained physiological pH, which supports patient safety and acceptability for ocular administration. The controlled release behaviour was evident, with increasing polymer concentration enhancing gel strength and reducing drug diffusion, thereby sustaining drug release. Among the trial batches, F3 and F4 emerged as the most promising formulations, offering effective drug release profiles suitable for prolonged therapeutic action. These optimized formulations demonstrated clinical potential by reducing dosing frequency, improving bioavailability, and enhancing patient compliance compared to conventional eye drops. The findings suggest that gatifloxacin in situ ocular gels represent a promising advancement in ophthalmic drug delivery, combining sustained release, enhanced ocular retention, and patient-friendly administration. Future studies should focus on in vivo evaluation to confirm therapeutic efficacy, ocular tolerance, and pharmacokinetic performance, alongside scale-up and extended stability studies under ICH guidelines to enable clinical translation. Overall, the study provides a strong foundation for the development and commercialization of in situ gel systems for effective management of ocular infections.

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