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Formulation and Characterization of pH-Induced *In Situ* Gel Containing Posaconazole for Ocular Drug Delivery

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Abstract

Objective: To create and evaluate an *in situ* medication delivery system for the eyes to improve its residence duration and hence its bioavailability in the ocular mucosa.

Methods: Carbopol is a pH-dependent water soluble *in situ* polymer. When the pH was alkaline, the carbopol polymer formulations stayed as a solution at acidic pH and formed a low-viscosity gel. The sol-gel transition happens nearly instantaneously due to the pH difference between carbopol-containing formulations and human tear fluid. Clarity, pH measurement, gelling capacity, drug content estimation, rheological research, *in vitro* diffusion study, *ex vivo* permeation study, stability study, ocular irritation study, and FTIR investigation were all performed on the formulations.

Results: The produced formulations showed continuous drug release from the formulation over 7 hours, extending the drug's residence length. Under accelerated stability conditions, the developed, optimized formulation was clear and stable after 90 days of storage. The improved formulations were evaluated for ocular irritation on Hen's egg chorioallantoic membrane. There was no eye injury or aberrant clinical symptoms in the cornea, iris, or conjunctiva, and the formulations were determined to be non-irritating.

Conclusion: Posaconazole-loaded *in situ* gels might be a potential technique for ocular medication administration in individuals with impaired immune systems to treat invasive Aspergillus and Candida infections.

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Introduction

Blindness and visual impairment are among the most serious worldwide health issues, posing a significant economic and social impact. Because of the peculiar structure of the eye, which prevents drug molecules from entering the intended spot, ocular drug administration has been one of the most difficult challenges for a pharmaceutical chemist [1]. More than 90 percent of ophthalmic medications on the market are eye drops. However, distinct elimination processes wash them away from the eye, resulting in limited ocular bioavailability (5%) following topical treatment. The limited bioavailability of drugs delivered by traditional routes is due to a large amount of precorneal drug loss due to nasolachrymal drainage [2]. This might lead to an elevated risk of unfavorable systemic toxic consequences. Achieving and maintaining adequate drug concentration at the target site of action in the eye is one of the major limitations of ocular medication administration. To extend the ocular residence time of medications following topical administration to the eye, several ophthalmic dosage forms such as ointments, eye drop solutions, gels, and ocular inserts have been studied [3].The corneal contact duration has been enhanced to some extent with these formulations. However, they have not been entirely accepted due to impaired vision and poor patient compliance caused by ointments and inserts, respectively [4].

In situ gelling has been one of the most promising techniques for improving medication retention time on the ocular surface in recent decades [5]. After instilling an aqueous solution containing stimuli-responsive polymers such as pH-sensitive polymers, thermos-sensitive polymers, and ion-sensitive polymers onto the eye surface, viscous and mucoadhesive gels form on the eye surface, improving ocular retention time and ocular bioavailability of ophthalmic drugs [6]. In today's hospitalized patients, fungal infections are still a major source of morbidity and mortality. Infections produced by Candida species are currently more frequent in critical care unit patients than in individuals with weakened immune systems. In recent years, there has been a surge in the number of infections caused by non-albicans Candida species. Posaconazole is a new second-generation Triazole antifungal medication that is taken orally. In immune-compromised individuals, it is extremely helpful in preventing invasive fungal infections. Invasive fungal infections such as aspergillosis or pharyngeal and esophageal candidiasis are treated with it as a first-line and salvage therapy [7]. It has a low risk of side effects. These characteristics make posaconazole a useful addition to the family of antifungal drugs, given the increased frequency of invasive fungal infections due to the HIV pandemic and medical improvements in transplantation and cancer therapy.

At present, four classes of antifungal agents are approved for use in IFI: Polyenes (e.g., Amphotericin B), azoles (e.g., itraconazole, fluconazole, and voriconazole), flucytosine, and echinocandins are the four types of antifungal medicines currently licensed for use in IFI (e.g., caspofungin, anidula fungin). The failure rate of these agents is considerable, ranging from 40% to 70% [8]. Furthermore, as these agents have become more widely used, resistance to them has emerged. Posaconazole, a second-generation triazole with broad-spectrum and robust action against common as well as rare but developing fungal diseases resistant to traditional antifungal therapy, is a welcome addition to the battery of available antifungal drugs in this circumstance [9]. Posaconazole, an antifungal and highly lipophilic agent with a broad spectrum, has been used topically as an off-label in treating ocular fungal infections due to its highly lipophilic character. *In situ*, gel carriers can potentially improve the solubility of lipophilic drugs and overcome ocular barriers [10]. Posaconazole is more effective against Candida albicans and Cryptococcus neoformans than itraconazole and fluconazole [11]. Its antifungal activity is equivalent to that of voriconazole. It inhibits the growth of Candida albicans (excluding Candida glabarta and Candida pelliculosa) and Crytococcus neoformans isolates resistant to fluconazole. Posaconazole has also been shown to have antifungal properties against rhodortula and trichosporon species [12].

Triazole posaconazole is the most effective against filamentous fungus. It is 4 to 16 times more effective against Aspergillus fungigatus resistant to itraconazole, voriconazole, and amphotericin B than amphotericin B. Fusarium species are also susceptible to posaconazole. In zycomycosis, it is less effective than amphotericin B, but more effective than voriconazole and equivalent to itraconazole. *In vitro*, posaconazole has much efficacy against Histoplasma capsulatum, Blastomyces dermatidis, and Coccidioides, but not so much against Sporothrix schenckii. Patients on posaconazole prophylaxis have been shown to develop resistant fungus isolates (namely Candida and Aspergillus spp.). These isolates had a lower sensitivity to other triazoles, indicating cross-resistance, and they should be investigated further [13,14]. This study proposes an *in situ* gel using posaconazole, employing a biocompatible and biodegradable polymer matrix that can undergo sol-gel transition at physiological temperature. The developed formulation's physicochemical properties, gelation characteristics, rheological behavior, drug release kinetics, and ocular tolerability will be comprehensively evaluated (Figure 1).

Materials and methods

Posaconazole was a gifted sample from Alastir Pvt Ltd, Chennai. Carbopol 940 and HPMC (Low and High viscous) were obtained from Sigma Aldrich Chemicals, Bangalore. The chemicals like β-cyclodextrin, sodium chloride, methylparaben, and propylparaben were acquired from Fischer Chemicals, Chennai. All of the polymers were pharmaceutical grade and utilized just as they were. The rest of the components and solvents were of analytical quality. Using glass distillation equipment, distilled water was created in the lab.

Analytical method development

Determination of λ max of posaconazole

By weighing 100 mg (0.1 g) of the drug, dissolving it in 100 ml of the volumetric flask, and then adjusting the volume with phosphate buffer to the target (7.4), a stock solution (1000 µg/ml) was prepared to estimate absorption maxima. To manufacture 100 g/ml of posaconazole, 10 ml of standard stock solution was placed in a 100 ml volumetric flask and filled to the mark with phosphate buffer (7.4). Transfer 0.2, 0.4, 0.6, 0.8, and 1.0 ml of the stock solution into a 10 ml volumetric flask and make up the volume with phosphate buffer 7.4 up to the mark to create serial dilutions with concentrations of 2, 4, 6, 8, and 10 µg/ml (Figure 2). Shimadzu's UV-visible spectrophotometer UV 1780 was used to scan the resultant solution between 262 nm.

Preparation of *in situ* gel

In situ gel formulations were created using the dispersion approach, including various concentrations of HPMC of low and high-viscosity cellulose derivatives in conjunction with Carbopol

940 (Table 1). To dissolve methyl and propylparaben, 75 mL of distilled water was heated to 70°C, and then sodium chloride (NaCl), HPMC, and Carbopol were added to the solution. The mixture was kept at room temperature overnight to allow the polymer to hydrate. Posaconazole was dissolved separately in 25mL phosphate buffer (pH 7.4) containing β-cyclodextrin. It was added to the polymeric solution above and agitated until it became homogeneous. The finished product was placed in sterile bottles and sterilized in an autoclave for 15 minutes at 121°C [15].

Characterization studies

Appearance and clarity, pH, and drug content

For the existence of any particle matter in the formulation, the appearance and clarity of the formulations were visually examined against a black-and-white backdrop. A pH meter was used to determine the pH of formulations to verify that they did not cause eye irritation in the patient after delivery. To evaluate the drug concentration in the formulations, 1 ml of the formulation was dissolved in 100 ml of simulated tear fluid (STF, pH 7.4) and diluted with the same medium before being measured using a UV-Visible spectrophotometer at a wavelength of 262 nm. The composition of STF pH 7.4 is as follows: 0.670 g of NaCl, 0.200 g of $NaHCO_3$, 0.008 g of $CaCl_2$. $2H_2O$ and distilled water up to 100 ml. The samples were measured in triplicate [17].

Viscosity

Brookfield viscometer DV2T model was used to do the viscosity measurements. In the sampler tube, the *in situ* gel formulations were put. Before each measurement, the samples were evaluated at 37°C 0.5°C in a circulating bath linked to the viscometer adapter. The spindle's angular velocity was raised one to four times, and the viscosity of the formulation was measured [17].

Gelling capacity

The created formulations were tested for gelling capacity to determine the composition suitable for use as an *in situ* gelling system. The gelling ability was assessed by adding 1 mL of the prepared formulation to a test tube containing 5 mL of STF pH 7.4 at 37°C. The time it took for the solution to change to gel and the created gel to disintegrate was visually observed. Based on the gelation duration and the period for which the created gel persists as such, the gelling capacity of the formulations was assessed in four groups: no gelation (-), poor (+), good (++), and excellent (+++) [18,19].

Drug content estimation

By diluting 1 ml of the formulation in 0.1N HcL and analyzing it at 262nm using a UV-visible spectrophotometer (Shimadzu UV-1780 PC, Shimadzu Corporation, Japan), the drug concentration was estimated [19].

***In-vitro* drug release studies**

The *in vitro* release of posaconazole from the manufactured formulations was examined using a modified diffusion testing apparatus. Freshly created synthetic tear fluid (pH 7.4) was used as the diffusion medium. After spending the night submerged in the diffusion medium, a semi-permeable membrane was attached to one end of a specially-made glass cylinder (open at both ends) with an inner diameter of 3.4 cm. Two millilitres of the mixture were piped into a glass cylinder in the donor chamber. When the cylinder was suspended in a beaker (Acceptor chamber) holding 100 ml of diffusion medium, the membrane barely brushed the surface of the diffusion medium. The acceptor chamber was maintained at 37 2°C with a stirring velocity of 50 rpm using the magnetic stirrer. 1 ml of the substance was removed and swapped out for an equivalent volume of fresh diffusion medium every hour. The aliquots were diluted in diffusion media before being measured at 262 nm with a UV spectrophotometer [20].

Hen's egg test on chorioallantoic membrane (HET-CAM)

The HET-CAM assay (Hen's egg chorioallantoic membrane test) investigated ocular discomfort. It's a non-animal ocular toxicity test employed in irritation research. The EPA has proposed the HET-CAM assay for rabbits as an alternative to the Draize test for ocular irritancy. Four viable eggs measuring 45–65 g were collected and examined under light. They were confirmed to be in good condition. The eggs were put in an upside-down position on a cotton-filled plate. These eggs were then incubated in an incubator for 10 days at a temperature of 37.5% relative humidity and a relative humidity of 55.7% for a total of 9 days. After every 12 hours, the eggs were manually turned gently. Using blunt forceps, eggs were gently removed towards the end of the 10th day, the egg shell was scratched off, and then the egg was sliced off.

The inner membrane was gently removed (CAM) to reveal the chorioallantoic membrane. Formulations (0.5 ml) were sprayed straight into the window and allowed to sit there for 5 minutes. The membranes were checked for vascular damage, and the time it took for the harm to occur was recorded, along with scores. Normal saline and 0.1 M NaOH were utilized as negative and positive controls. The compounds' ocular irritation potential was evaluated using three fundamental parameters: hyperaemia, haemorrhage, and coagulation [21,22].

Accelerated stability study

Stability testing was performed on the optimized sterile formulation. Glass vials were filled with sterile optimized ophthalmic formulation, which was then sealed with aluminium caps and grey butyl rubber closures. The vials containing the revised formulation were kept in a stability chamber for a month at a temperature of 40 2°C and 75 5% RH. Drug concentration, pH, aesthetic appearance, gelling ability, and *in vitro* drug release were all determined from weekly samples [23].

Evaluation of *in-vitro* release kinetics

The data collected were fitted using several kinetic models such as Zero-order reaction, first-order reaction, Higuchi's Kinetics model, Korsmeyer Peppas reaction, and Hixson Crowell erosion equation approach to analyze in-vitro release kinetics [24].

***Ex-vivo* permeation study**

The goat cornea was fresh from the slaughterhouse and put on modified Franz diffusion cell (FDC) equipment. STF fluid was kept at 37 ± 1ºC and constantly stirred in the receptor chamber. At regular intervals, 2 ml of test samples were obtained and replaced with new STF fluid. Each formulation was allowed to permeate for about 0.5-8 hours 34. The samples were also tested for Posaconazole concentration using a UV-Visible spectrophotometer set to 262 nm. The standard curve was used to determine the concentration of permeating medication at various time intervals [25,26].

Attenuated total reflectance Fourier transforms infrared spectroscopy (ATR FTIR)

The FT-IR spectra of pure drugs, polymers, and produced formulations were compared to characterize the functional groups. The samples were measured using ranging from 4000 to 400 cm-1 (Instrument JASCO 4100)(26).

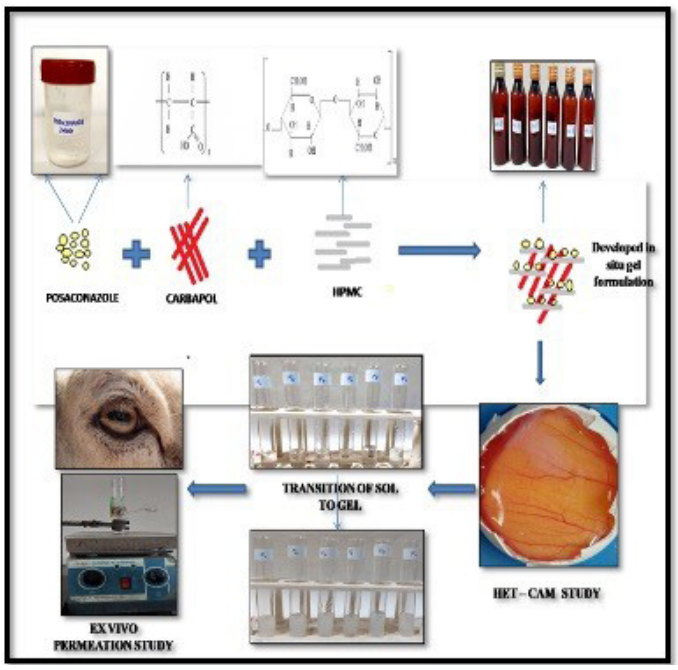

Figure 1: Schematic representation of the developed formulation in situ gel.

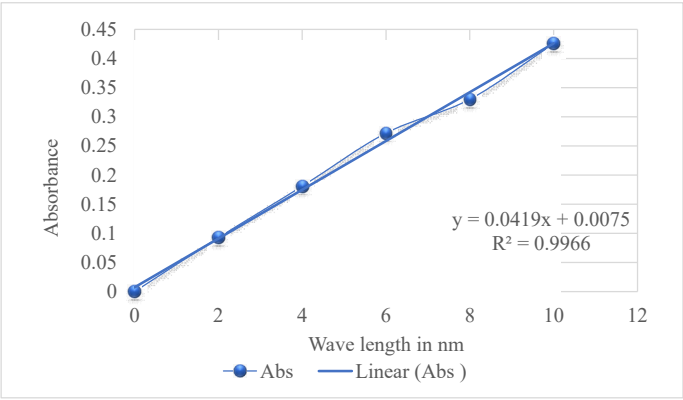

Figure 2: Linearity curve of posaconazole.

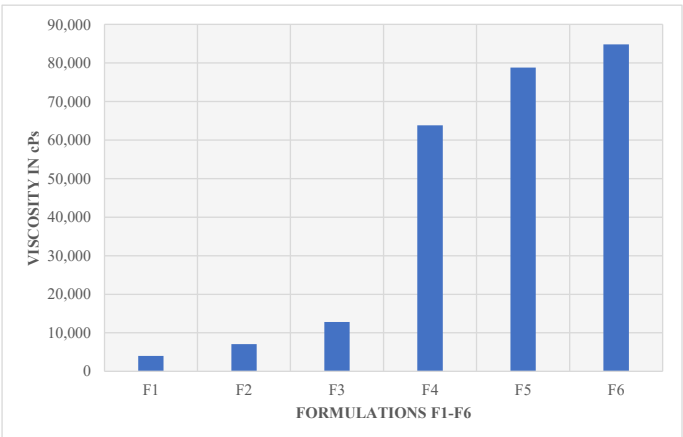

Figure 3: Viscosity of the developed formulations F1-F6.

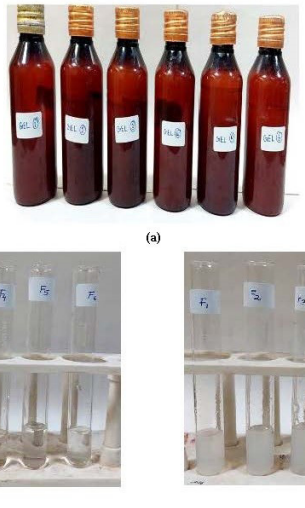

Figure 4: Gelation examination **(a)** Optimized formulation F1-F6; **(b)** STF fluid (pH 7.4); **(c)** Formation of gel structure.

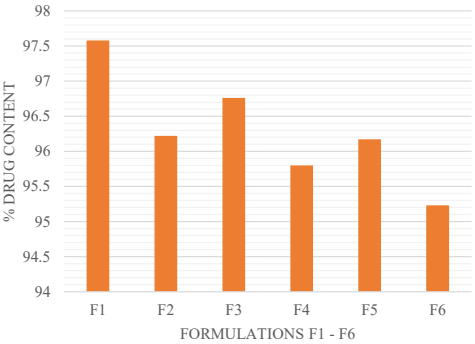

Figure 5: Drug content of the prepared formulations F1-F6.

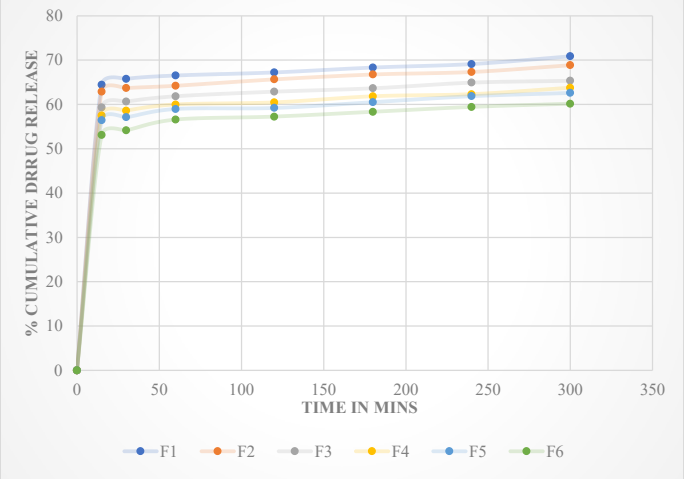

Figure 6: Cumulative drug release of developed formulations F1-F6.

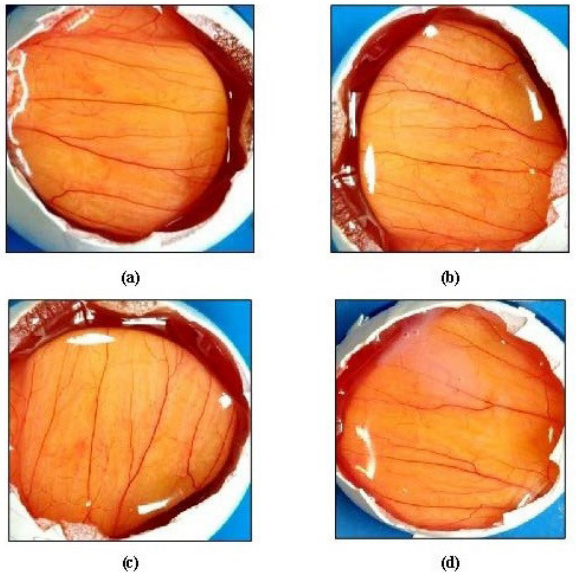

Figure 7: HET-CAM study. **(a)** Fertilized egg; **(b)** negative control (NaCl); **(c)** positive control (NaOH); **(d)** Optimized formulation F1.

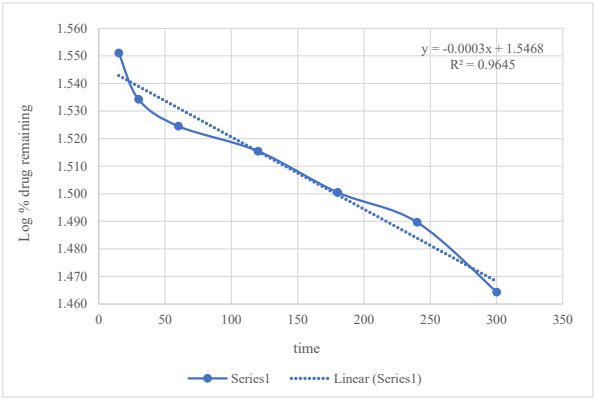

Figure 8: *In-vitro* release kinetics - First order model (F1).

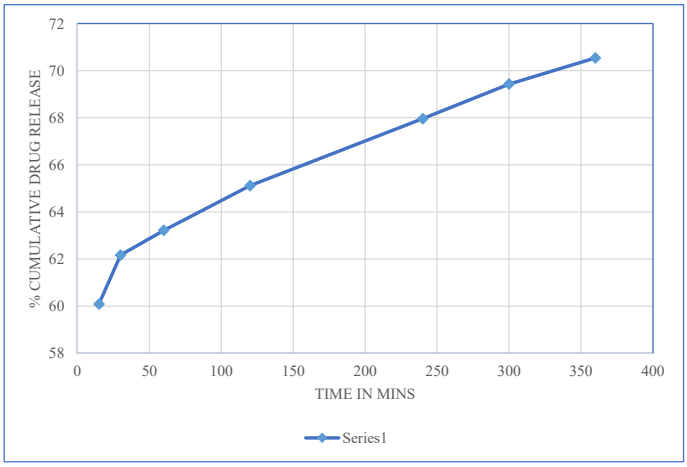

Figure 9: Ex-vivo study of cumulative percent drug release for the optimized formulation F1.

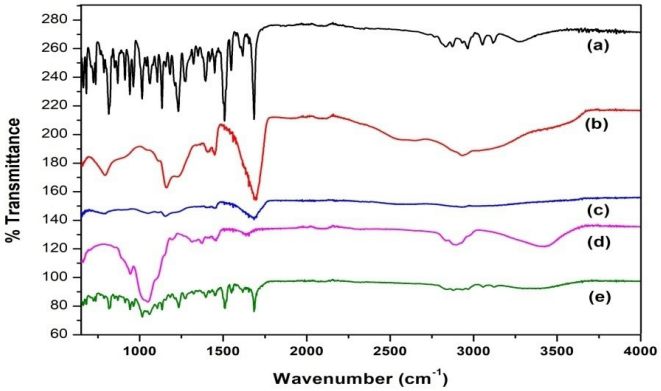

Figure 10: FT-IR spectra of pure drug, polymer and their physical mixture. **a)** Posaconazole **b)** Carbopol 940 **c)** HPMC (low viscous) **d)** HPMC K200M e) Physical mixtures of drugs and polymers.

Table 1: Optimization of formulations (F1 - F6).

S.NO	Ingredients	F1	F2	F3	F4	F5	F6
1.	Posaconazole	100	100	100	100	100	100
2.	Carbopol 940	0.3	0.4	0.5	0.6	0.7	0.8
3.	HPMC (high viscous)	0.6	0.7	0.8	1.0	1.5	2.0
4.	HPMC (low viscous)	0.2	0.4	0.6	0.8	1.0	1.5
5.	Sodium chloride	0.9	0.9	0.9	0.9	0.9	0.9
6.	Methyl paraben	0.1	0.1	0.1	0.1	0.1	0.1
7.	Propyl paraben	0.005	0.005	0.005	0.005	0.005	0.005
8.	Distilled water	100	100	100	100	100	100

Table 2: Results of physicochemical characterization of in situ gel formulations.

Formulation	Clarity	pH	Viscosity (cPs)	Drug content	Gelling capacity
F1	Clear solution	6.3	4,032	97.58	++
F2	Clear solution	6.2	7,056	96.22	++
F3	Clear solution	6.5	12,792	96.76	+++
F4	Clear solution	6.3	63,840	95.80	+++
F5	Clear solution	6.7	73,840	96.17	+++
F6	Clear solution	6.8	84,321	95.23	++

(++) - good; (+++) – excellent.

Table 3: HET-CAM test.

Sample	Score formulations							
	Time in (mins)							
	0	5	15	30	60	120	240	300
SODIUM hydroxide and normal saline as control (positive and negative)								
EGG 1	0	0	0	0	0	0	0	0
EGG 2	0	0	0	0	0	0	0	0
EGG3	0	0	0	0	0	0	0	0
AVERAGE	0	0	0	0	0	0	0	0
Developed in situ gel formulation (F1)								
EGG 1	0	0	0	0	0	0	0	0
EGG 2	0	0	0	0	0	0	0	0
EGG3	0	0	0	0	0	0	0	0
AVERAGE	0	0	0	0	0	0	0	0

Score test - 0-3 is normal, 3-5 is a mild irritant, 5-9 is a moderate irritant, and 9-11 is a severe irritant.

Table 4: Stability studies of the formulations F1-F6 as per ICH guidelines for 0-6 months.

Month	Formulation F1 at 25º C ± 2º / 5% RH			Formulation F1 at 40º C ± 2º / 5% RH		
	0	3	6	0	3	6
Appearance	Clear	Clear	Clear	Clear	Clear	Clear
pH	6.04	6.02	6.05	6.03	6.01	6..03
Drug content	97.67±0.11	96.71±0.87	96.63±0.53	95.54±0.59	94.87±0.32	95.21±0.89
Gelling studies	+++	+++	+++	+++	+++	+++

(+++) – excellent.

Table 5: Drug content evaluation of Formulations during stability studies.

Code	Drug content (%) at 0 month (n=3) ±S.D	Drug content (%) at 3 months (n=3) ± S.D		Drug content (%) at 6 months (n=3) ± S.D	
	25º C	25ºC	40ºC± 75%RH	25º C	40ºC±75%RH
F1	98.76 ± 0.85	97.31 ± 0.31	97.81 ± 0.79	96.69 ± 0.89	97.90 ± 0.91
F2	96.63 ± 0.23	98.45 ± 0.28	97.34 ± 0.65	96.48 ± 0.63	95.88 ± 0.85
F3	97.54 ± 0.53	96.75 ± 0.65	96.43 ± 0.42	95.76 ± 0.52	96.64 ± 0.34
F4	96.48 ± 0.71	95.41 ± 0.32	95.56 ± 0.67	95.82 ± 0.82	96.49 ± 0.23
F5	96.33 ± 0.64	97.54 ± 0.67	96.76 ± 0.38	97.75 ± 0.77	95.66 ± 0.69
F6	95.21 ± 0.29	95.37 ± 0.18	95.62 ± 0.49	96.86 ± 0.63	95.23 ± 0.62

Table 6: *In-vitro* release kinetics.

	Release kinetics				
	Zero	Higuchi	Peppas	First	Hixson Crowell
	1	2	3	4	5
	R(CvT)	R(CvRoot(T))	log T vs log C	Time vs log % remaining	Time Vs (Q1/3-Qt1/3)
Slope	0.019	0.438	0.301	-0.013	0.001
Correlation	0.9803	0.9691	0.5814	-0.9821	0.9816
R^2	0.9610	0.9391	0.3380	0.9645	0.9636

Table 7: Interpretation of FT-IR spectrum of drug, polymer and physical mixtures.

S.no	F1	Wave number (cm^{-1})	Vibrations
1.	Posaconazole	3116,3093,2964,2872,1684,1449, 1394,1322,1231,1014,962,941 890 and 850	OH, = C-H, C-H, C=N, C-O, C-N are stretching, R-C-H bending and CH rocking.
2.	Carbopol 940	3569,3072,2934,1636,1448, 1411,1225,1160 and 798	OH, =C-H, CH, C=O, C-O are stretching, R-C-H bending and CH rocking.
3.	HPMC (low viscous)	2930,1448,1152,1110 and 1050	CH, C-O are stretching, R-C-H bending.
4.	HPMC K200M	2896,1374,1313,1195,1048and 943	CH, C-O are stretching, R-C-H bending.
5.	Physical mixtures of drugs and polymers	3126,2967,1687,1510,1450,1395, 1274, 1057, 942 and 822	OH, CH, C=O, C-N, C-O are stretching, R-C-H bending, CH rocking.

Results and discussion

Determination of visual appearance, pH, clarity, and drug content

Posaconazole developed *in situ* gel was white in color, and all formulations were transparent. The formulations' appearance, clarity, pH, and medication concentration were unaffected by the autoclaving process used for terminal sterilization. At room temperature, the formulations were liquid, and the pH of the formulations was in the range of 6–7, with a quick transition to the gel phase noted at the pH of the tear fluid, i.e., pH 7.4. The drug content of all formulations was between 94.31 and 97.03 %, indicating that the drug was distributed uniformly in produced ophthalmic formulations (Table 2).

Viscosity

The viscosities of all created formulations F1-F6 were tested with a Brookfield Viscometer DV2T model and are shown in Figure 3. The findings revealed that when the polymer concentration was raised, the viscosities of the individual formulations increased. The produced formulations F1-F6 had viscosities in the 4032 – 8432 cPs range. Formulation F6 had the highest viscosity of all the formulations, measuring 84,321 cPs.

Gelling capacity

In the pH range of 6.20 to 6.80, all of the created formulations were found to be somewhat pale white dispersion, and after adding STF fluid pH 7.4, instantaneous stiff gelation was seen for formulations F1-F6, as shown in Figure 4 (a), (b) and (c). The change from sol to gel formation happens after adding 20-50 µl formulation to STF fluid. The gel that had developed lasted for around 8-10 hours. Based on the gelation time, the gelling capabilities of the produced formulations were examined and used for further investigation. Posaconazole, carbopol 940P, and both high and low-viscosity HPMC offer the highest gelling capacity of any formulation.

Drug content

A UV visible spectrophotometer set to 262 nm determined the drug concentration in the formed formulations F1-F6. For all developed formulations F1-F6, the drug content ranged from 95.20 % to 97.58 % (Figure 5).

In-vitro release study

In-vitro drug release and *in situ* gel formation results for all formulations are represented in Figure 6. All the formulations' drug release patterns have been demonstrated to increase over time. F1 had the highest percent cumulative drug release of all the formulations, at 70.87 %. For all of the created formulations F1-F6, the content ranged from 60.15 % to 70.87 %.

Hen's egg test on chorioallantoic membrane (HET-CAM)

HET-CAM test is an alternative to animal experiments for assaying corrosives/severe ocular irritants on the CAM of fertilized eggs. This test is useful for determining any CAM damage induced by the test drug. F1 was subjected to a HET-CAM (Hen's Egg Test - Chorioallantoic Membrane) investigation with appropriate positive and negative controls, as illustrated in Figure 7 (a), (b), and (c). The results revealed no substantial damage to the CAM membrane during the application of formulation F1 on CAM, and no irritations in the conjunctiva were seen (Figure 7(d) and Table.3).

Stability studies

According to ICH requirements, a stability analysis was conducted on the formulations. For 0- 6 months, formulas were kept in firmly wrapped amber-tinted glass vials sealed with aluminium foil at room temperature 25ºC ± 2ºC and 40ºC ± 75 percent RH. The samples were taken at regular intervals and vortexed for 3-5 minutes in deionised water. According to the stability analysis, the developed formulations were most stable in a room rather than at higher temperatures. As demonstrated in Table 4, almost 90% of the medication content was steady. After 6 months, the formulation preserved for stability studies was subjected to the test criteria of appearance, pH, gelling capability, and drug content, all of which yielded positive findings, as shown in Table.5

In-vitro release kinetics

The release data was fitted with multiple kinetic models to establish the extract re-lease process from the gel matrix. A kinetic study of the drug (extract) release data was done by creating a graph between the percent cumulative extract releases and the square root of time. It suggested that extract release was linearly related to time. To analyze the release kinetics, data from in-vitro experiments were fitted with a variety of kinetic models, including the Zero order reaction, Higuchi's Kinetics model, Korsmeyer Peppa's reaction, First order reaction, and Hixson Crowell erosion equation approaches. The first-order model is followed by the improved gel formulation (F1), with the maximum regression coefficient (R^2) value (Figure 8) & (Table 6). The regression coefficients' results confirmed that the extracellular matrix was released diffusion-dependent.

Ex-vivo transcorneal approach - permeation experiment

The improved formulation, F1, was tested ex-vivo by graphing cumulative percent drug release against time, as shown in Figure 9. At the end of 7 hours, formulation F1 had the highest percent drug release of 71.05 %. The created formulation F 1's permeability coefficient was measured to be Kp = 0.0058 cm/min.

Attenuated total reflectance Fourier transforms infrared spectroscopy (ATR FTIR)

FTIR was used to establish the existence of functional groups (Instrument - JASCO 4100). Using a KBr pellet method, measurements were obtained from 400 cm-1 to 4000 cm-1. For the medication and several excipients, an FT-IR analysis was conducted. The results revealed varied stretching, bending, and rocking vibrations based on the groups present. Figure 10 shows pure drug, polymer, and their physical mixture FT-IR spectra. The interpretations of FT-IR spectra for the respective compounds are given in Table 7.

Conclusion

Using carbopol and HPMC, posaconazole was effectively synthesized as *in situ* gel-forming eye drops. Consequently, as shown above, the carbopol and HPMC mixture may be utilized as an *in situ* gelling vehicle to improve ocular bioavailability and patient compliance. According to physicochemical characterization and in-vitro drug release studies, the developed formulation (F1) could be a viable alternative to traditional eye drops and ointment in terms of ease of administration, with the added benefit of sustained drug release, which could lead to improved patient compliance. To summarize, it is one of the most promising new delivery systems in the field of ocular therapies for the successful treatment of fungal diseases in the future.

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