



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Research Article

Design, Development and Analysis of *In-Situ* Gel of Ketoconazole for Sustained Ocular Delivery

Shubham Durgawale*

Rajarambapu College of Pharmacy, Kasegaon, Shivaji university, Maharashtra, 415404, India.

ARTICLE INFO

Published: 06 Aug 2025

Keywords:

Ketoconazole; In-situ gel;
Ocular drug delivery;
Poloxamer 407; HPMC;
Thermoresponsive system;
Sustained release;
Antifungal activity

DOI:

10.5281/zenodo.16750877

ABSTRACT

Ocular drug delivery is a complex and challenging area due to various anatomical and physiological barriers that limit drug penetration and retention. Conventional eye drops, particularly for antifungal agents such as ketoconazole, suffer from low ocular bioavailability and rapid precorneal elimination, necessitating frequent dosing. The present study focuses on the formulation and evaluation of a thermosensitive in-situ gel for the ocular delivery of ketoconazole to overcome these limitations. The gel was developed using Poloxamer 407 as a temperature-responsive polymer, Hydroxypropyl Methylcellulose (HPMC) as a viscosity enhancer, citric acid for pH adjustment, and disodium hydrogen phosphate for buffering and isotonicity. Preformulation studies confirmed drug-polymer compatibility, and the optimized formulation exhibited satisfactory gelation temperature, clarity, and mucoadhesive Ness. In-vitro drug release studies revealed sustained release of ketoconazole for up to 12 hours. The formulation also demonstrated acceptable stability and antifungal efficacy. This approach holds promise for enhancing the therapeutic efficacy, bioavailability, and patient compliance in the treatment of ocular fungal infections.


INTRODUCTION

Ocular drug delivery is a complex and evolving domain due to the eye's unique anatomy and physiology, which significantly limit drug absorption and therapeutic retention. Conventional ocular dosage forms such as eye drops and ointments exhibit low bioavailability, primarily due to rapid tear turnover, blinking, nasolacrimal

drainage, and the corneal barrier. Studies indicate that less than 5% of the administered drug reaches intraocular tissues via topical routes. [1,2] Additionally, conventional formulations often require frequent dosing, reducing patient compliance and therapeutic efficiency. [3]. To address these limitations, several novel drug delivery strategies have been investigated. Among them, in-situ gelling systems have attracted

*Corresponding Author: Shubham Durgawale

Address: Rajarambapu College of Pharmacy, Kasegaon, Shivaji university, Maharashtra, 415404, India.

Email : shubhamdurgawale291@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



considerable attention for their ability to transition from liquid to gel upon exposure to physiological stimuli—such as temperature, pH, or ionic strength—thus enhancing residence time and bioavailability. [4,5] Thermosensitive in-situ gels, in particular, are advantageous as they remain in a fluid state at room temperature and gel upon contact with the ocular surface temperature (~34°C), enabling sustained release and ease of administration. [6,7]. Ketoconazole, an imidazole-

derived antifungal agent, demonstrates broad-spectrum activity against fungal pathogens responsible for ocular infections such as keratitis and conjunctivitis. [8] However, its poor aqueous solubility and rapid precorneal elimination reduce its therapeutic utility when formulated as standard eye drops. [9] In-situ gel systems offer a rational solution to improve solubility, precorneal retention, and sustained delivery of ketoconazole. [10]

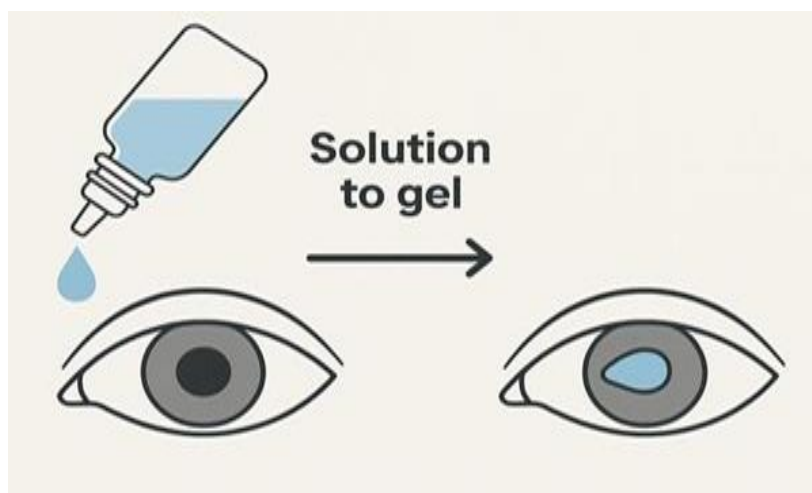


Fig no. 1: In-situ gelling system

In this study, a thermosensitive in-situ gel formulation of ketoconazole was developed using Poloxamer 407 as the primary temperature-sensitive polymer, and Hydroxypropyl Methylcellulose (HPMC) as a secondary polymer to enhance viscosity and Mucoadhesion. [11,12] Additionally, citric acid and disodium hydrogen phosphate were incorporated as buffering agents to maintain physiological pH and formulation stability. [13,14] The formulation was evaluated for its physicochemical properties, rheological behaviour, gelation temperature, drug release kinetics, and antifungal efficacy. The study aims to develop a stable, patient-friendly, and effective ocular formulation that overcomes the challenges of conventional antifungal therapy and improves treatment outcomes in ocular fungal infections.

2. MATERIALS AND METHODS

2.1 MATERIALS

Ketoconazole, the active pharmaceutical ingredient used in this study, was obtained from Aarti Pharmed Labs Ltd., Mumbai. The thermosensitive polymer Poloxamer 407, responsible for sol-to-gel transition at physiological temperatures, was sourced from Monachem Additives Pvt. Ltd. To enhance the viscosity and mucoadhesive properties of the formulation, Hydroxypropyl Methylcellulose (HPMC) was procured from Research Lab Fine Chem Pvt. Ltd., Mumbai. For buffering and pH adjustment, citric acid and disodium hydrogen phosphate were used, both obtained from Research Lab Fine Chem Pvt. Ltd., Mumbai. Additionally,

sodium hydroxide was employed for pH fine-tuning, while sodium chloride was incorporated to maintain isotonicity; both were also procured from Research Lab Fine Chem Pvt. Ltd., Mumbai. All excipients and chemicals used were of analytical grade and used as received, without further purification.

2.2 Methodology

2.2.1 Formulation Design

Methods

Formulation Approach: Cold Method

The formulation of ketoconazole ocular in-situ gel was carried out using the cold method, a widely used technique for temperature-sensitive systems. This method is especially suitable for poloxamer-based gels, ensuring the stability of thermoresponsive polymers throughout the preparation process. In this method, the required amount of Poloxamer 407 was slowly added to cold distilled water maintained at approximately 4°C, under continuous magnetic stirring to avoid clumping and ensure uniform dispersion. The solution was kept under refrigeration overnight to allow complete hydration and dissolution of the polymer. This step ensured that premature gelation was avoided and the sol remained stable at low temperatures. After complete dissolution of Poloxamer 407, the active pharmaceutical ingredient (Ketoconazole) was accurately weighed and added to the cold solution. Subsequently, Hydroxypropyl Methylcellulose (HPMC), used as a viscosity enhancer, was dispersed uniformly under slow stirring. Citric acid, disodium hydrogen phosphate, sodium hydroxide, and sodium chloride were then incorporated to adjust the pH, maintain isotonicity, and provide buffering

capacity. The final formulation was mixed thoroughly to achieve a homogeneous sol. The in-situ gel solutions were then stored in sterile, amber-colored glass containers at refrigerated temperature (2–8°C) until further evaluation. This preparation method preserved the thermosensitive properties of the gel, enabling a sol-to-gel transition upon instillation into the ocular cavity, triggered by body temperature (~34°C), thereby improving ocular residence time and bioavailability of ketoconazole.

Design of Experiment

The development of the thermosensitive ocular in-situ gel formulation of Ketoconazole was carried out using a structured experimental design approach to optimize the concentrations of key polymers and assess their effect on critical formulation characteristics. Poloxamer 407 was selected as the primary thermoresponsive polymer due to its reversible sol-to-gel transition at physiological temperatures. Hydroxypropyl Methylcellulose (HPMC) was incorporated as a secondary polymer to enhance viscosity and mucoadhesion, influencing gel strength and residence time. A 3² full factorial design was employed to investigate the effect of two independent formulation variables—Poloxamer 407 (X₁) and HPMC (X₂)—on key response variables: gelation temperature (°C) (Y₁) and gelling time (sec) (Y₂). Both polymers were evaluated at three levels: low (-1), medium (0), and high (+1), leading to a total of nine experimental runs (F1 to F9). The levels of the independent variables and their corresponding formulation batches are summarized in Table 1. The observed responses for gelation temperature and gelling time are detailed in Table 2.

Table 1: Independent variables and their levels used in the factorial design

Levels	Poloxamer 407 (g) – X ₁	HPMC (mg) – X ₂
--------	------------------------------------	----------------------------



Low (-1)	3	1000
Medium (0)	4	1750
High (+1)	5	2500

Table 2: Experimental design and observed responses

Batch	Poloxamer 407 (g)	HPMC (mg)	Gelation Temperature (°C) – Y ₁	Gelling Time (sec) – Y ₂
F1	3	1000	30	96
F2	3	1750	29	105
F3	3	2500	34	111
F4	4	1000	37	93
F5	4	1750	28	102
F6	4	2500	41	117
F7	5	1000	40	97
F8	5	1750	27	104
F9	5	2500	38	115

All formulations were evaluated for their gelation behavior and transition temperature under simulated physiological conditions. The data were analyzed to identify trends and interactions between the polymer concentrations and response parameters. The factorial design facilitated the optimization of polymer concentrations for achieving ideal gelation characteristics suitable for ocular application.

2.2.2 Evaluation Parameters

Evaluation of Formulations

The developed ocular in-situ gel formulations of Ketoconazole were subjected to comprehensive physicochemical and biological evaluations to ensure their quality, performance, and therapeutic potential. The following parameters were assessed:

Visual Appearance and Clarity

Formulations were visually inspected against white and black backgrounds for color, clarity, and particulate matter. An ideal in-situ gel should be “colorless to slightly opalescent”, transparent, and free from visible impurities to ensure patient comfort and confidence. Clarity was qualitatively

graded using a standard notation system (+ to +++) to represent increasing transparency and elegance of appearance.

pH Determination

The pH of the formulations was measured using a “calibrated digital pH meter” (Figure 1). Ideal pH values ranged between “6.5 and 7.5”, which is compatible with the natural tear fluid, to prevent ocular irritation and maintain drug stability during administration and storage.

Viscosity Measurement

Viscosity was determined using a “Brookfield Viscometer” at ambient and ocular temperatures to simulate in-use conditions. An optimal formulation should exhibit low viscosity at room temperature for easy instillation and increased viscosity at body temperature for prolonged retention on the ocular surface.

Drug Content Uniformity

Drug content was quantified using UV-Visible spectrophotometry, ensuring uniform distribution of Ketoconazole across the formulation. All batches were analyzed in triplicate, and acceptable



drug content ranged between 85% to 95% of the label claim.

Gelation Temperature

The gelation temperature—the point at which sol-to-gel transition occurs—was recorded using the visual tube inversion method under controlled heating. Ideal gelation occurred between 27–41°C, suitable for ocular application and patient comfort.

Gelling Time

Gelling time was assessed as the duration required for the formulation to convert into gel upon exposure to simulated ocular temperature. Short gelling times (<120 seconds) were considered optimal to ensure rapid in-situ transformation and minimal drainage post-administration.

Gelling Capacity

Formulations were evaluated for their gel strength and retention behavior under simulated tear conditions. Gelling capacity was qualitatively rated as + (poor), ++ (moderate), or +++ (excellent), with emphasis on sustained ocular retention without inducing discomfort or blurred vision.

Spreading Coefficient

Spreading behaviour was determined using a glass slide method. The spreading coefficient (S) was calculated using the formula:

$$S = ML/T, \text{ where } M = \text{weight (g), } L = \text{slide length (cm), and } T = \text{time (sec).}$$

Higher values indicated better Spreadability and uniform ocular surface coverage, essential for consistent therapeutic effect.

Statistical Data Analysis

All experimental data were statistically analyzed using ANOVA and regression models via Design-Expert® software (Version 13). Significance was assessed at $p < 0.05$. The factorial design enabled identification of key formulation variables affecting gelation temperature and gelling time, with 3D surface and contour plots used for interpretation.

In-vitro Drug Release (Optimized Batch)

The optimized formulation (F4) underwent in-vitro release studies using a Franz diffusion cell containing simulated tear fluid (pH 7.4, 37°C). Aliquots were collected at specific time intervals and analyzed spectrophotometrically to determine cumulative drug release. The batch exhibited sustained release up to 12 hours, indicating suitability for controlled ocular delivery.

Kinetic Modelling of Drug Release

Drug release data were fitted into zero-order, first-order, Higuchi, and Korsmeyer-Peppas models to elucidate the release mechanism. The best-fitting model was selected based on the correlation coefficient (R^2) values. The results suggested a diffusion-controlled release pattern, confirming the effectiveness of the gel matrix.

Stability Studies

Stability of the optimized batch was evaluated under accelerated conditions ($40 \pm 2^\circ\text{C} / 75 \pm 5\% \text{RH}$) for 3 months. Parameters such as pH, viscosity, drug content, clarity, and gelation behavior were monitored at predetermined intervals. The formulation showed no significant changes, indicating satisfactory stability.

Anti-fungal Activity (Optimized Batch)

Antifungal efficacy was determined using the agar diffusion method against 'Candida albicans. The

optimized formulation produced a prominent zone of inhibition, confirming that the drug retained its biological activity and was effectively released from the gel matrix.

3. RESULTS AND DISCUSSION

Preformulation Studies

Preformulation studies are crucial in the rational development of pharmaceutical dosage forms. Ketoconazole was observed as an amorphous, white, odorless powder with a melting point ranging between 148°C to 154°C. Solubility

testing showed the drug to be soluble in ethanol and methanol but insoluble in water. These characteristics supported further formulation into ocular gels.

FT-IR Spectroscopic Analysis

FT-IR analysis confirmed the identity and purity of Ketoconazole and excipients (HPMC, Poloxamer 407, Citric acid, Disodium hydrogen phosphate). No significant interaction was observed in the overlay spectra, suggesting compatibility of the drug with all excipients.

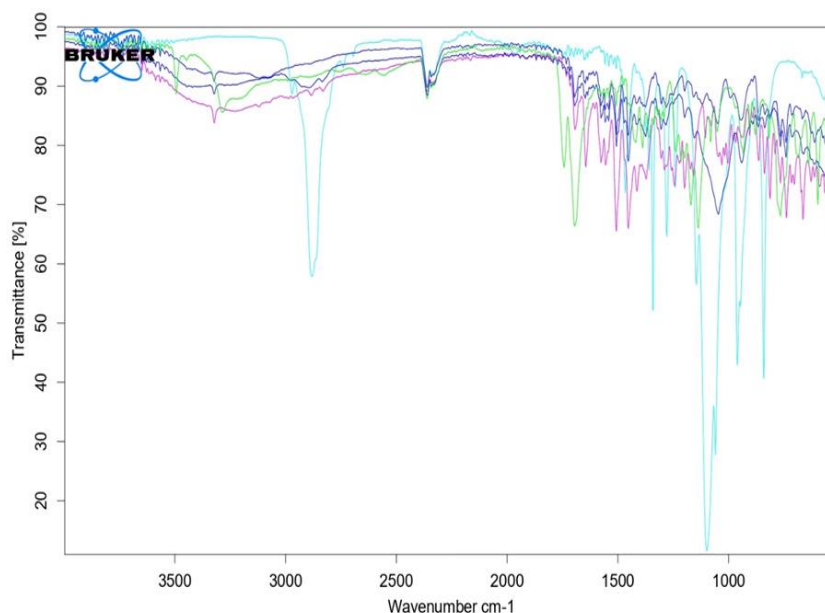


Fig no. 2: Overlay plot of drug and Excipients

Differential Scanning Calorimetry (DSC)

DSC thermograms demonstrated that there were no significant shifts in melting points in the

formulation, confirming the absence of drug–excipient interactions.

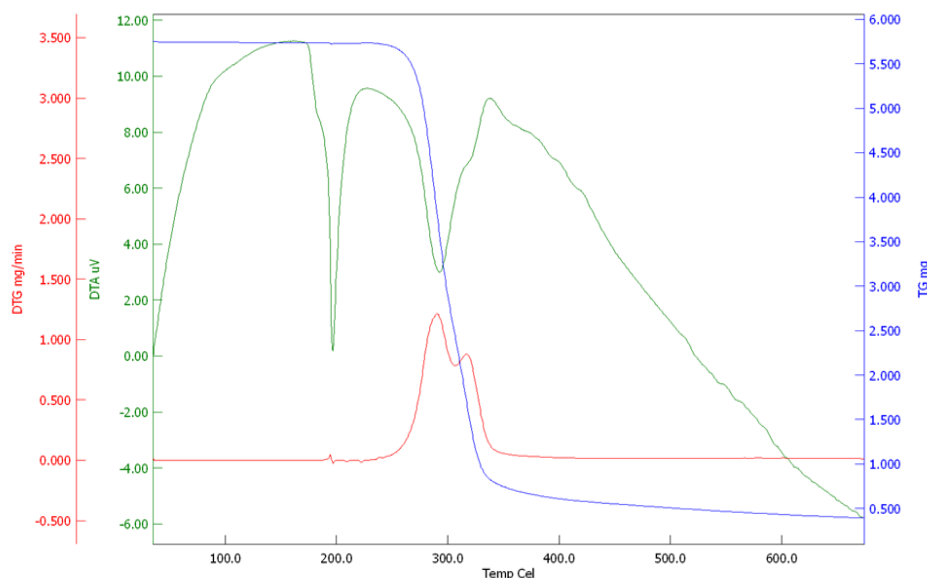


Fig no. 3: DSC of Ketoconazole with polymers

Calibration Curve

The calibration curve of Ketoconazole was constructed in distilled water, ethanol, and simulated tear fluid (STF) across 2–10 µg/mL concentrations. All standard curves showed excellent linearity with R² values of 0.9928 (distilled water), 0.9995 (ethanol), and 0.9994 (STF).

Table no. 3: Calibration curve of Ketoconazole in Distilled water

Concentration (µg/ml)	Absorbance (Abs.)
00	0.0
02	0.043
04	0.071
06	0.125
08	0.158
10	0.187

Table no. 4: Calibration curve of Ketoconazole in ethanol

Concentration (µg/ml)	Absorbance (Abs.)
00	0.0
02	0.039
04	0.072
06	0.111
08	0.145
10	0.184

Table no. 5: Calibration curve of Ketoconazole in STF

Concentration (µg/ml)	Absorbance (Abs.)
00	00
02	0.042
04	0.083
06	0.119
08	0.162
10	0.205

Formulation and Characterization of Thermoreversible In-situ Gel

Formulation of our in-situ gel of Ketoconazole of 9 batches were made by using 3² Factorial Design by the preparation method used in here is Cold Method.

Visual Appearance and pH

All formulations were cloudy with stable turbidity (++). pH values ranged from 4.7 to 7.1, falling within the acceptable ocular pH range.

Table no. 6: pH of all formulation batches

Sr. No.	Formulation Code	pH
1.	F1	6.2
2.	F2	6.5

3.	F3	7.1
4.	F4	5.5
5.	F5	5.9
6.	F6	6.9
7.	F7	4.7
8.	F8	5.0
9.	F9	6.8

Viscosity and Drug Content

Viscosity of the gels ranged from 2443 to 3914 cps, suitable for ocular administration. Drug content ranged between 82.09% to 93.45%, with formulation F4 showing the highest content (93.45%).

Table No. 7: Viscosity (cps) & Drug content of All Formulation Batches

Sr. No.	Formulation Code	Viscosity of Gel (cps)	Drug Content (%)
01.	F1	2868	89.72
02.	F2	3601	90.23
03.	F3	3914	82.09
04.	F4	3004	93.45
05.	F5	3598	87.90
06.	F6	3598	85.22
07.	F7	2443	88.86
08.	F8	2625	82.17
09.	F9	2959	85.01

Gelation Temperature and Gelling Time

Gelation temperature varied from 27°C to 41°C, while gelling time ranged from 93 to 117 seconds (Tables 8.6.5, 8.6.6). Formulation F4 showed optimal performance (37°C, 93 sec).

Table No. 8. Gelation temperature & Gelling Time of All Formulation Batches

Sr. No.	Formulation Code	Gelation Temperature (°C)	Gelation Time (sec)
1.	F1	30	96
2.	F2	29	105
3.	F3	34	111
4.	F4	37	93
5.	F5	28	102
6.	F6	41	117
7.	F7	40	97
8.	F8	27	104
9.	F9	38	115

Gelling Capacity and Spreading Coefficient

Gelling capacity ranged from + to +++ and spreading coefficient from 81.48±1.43 to 89.52±1.41, indicating satisfactory gel formation and Spreadability.

Table No. 9: Gelling Capacity & Spreading Coefficient of All Formulation Batches

Sr. No.	Formulation Code	Gelling Capacity	Spreading Coefficient
1.	F1	++	81.81±0.89
2.	F2	+	88.86±0.89
3.	F3	++	84.37±1.07
4.	F4	+++	89.52±1.41

5.	F5	++	81.48±1.43
6.	F6	+	82.46±0.97
7.	F7	+	88.39±1.15
8.	F8	+++	84.13±1.28
9.	F9	++	88.37±1.78

Optimization by Statistical Design

Statistical analysis using ANOVA revealed significant influence of HPMC and Poloxamer 407 on gelation temperature ($p = 0.0283$) and gelling time ($p = 0.0093$). Response surface plots illustrated the interactive effects of formulation variables.

Data Analysis of Y1 Gelation temperature (cps):

Two-dimensional contour plots and 3D response surface plot for variables Y1 (Gelation temperature) are shown.

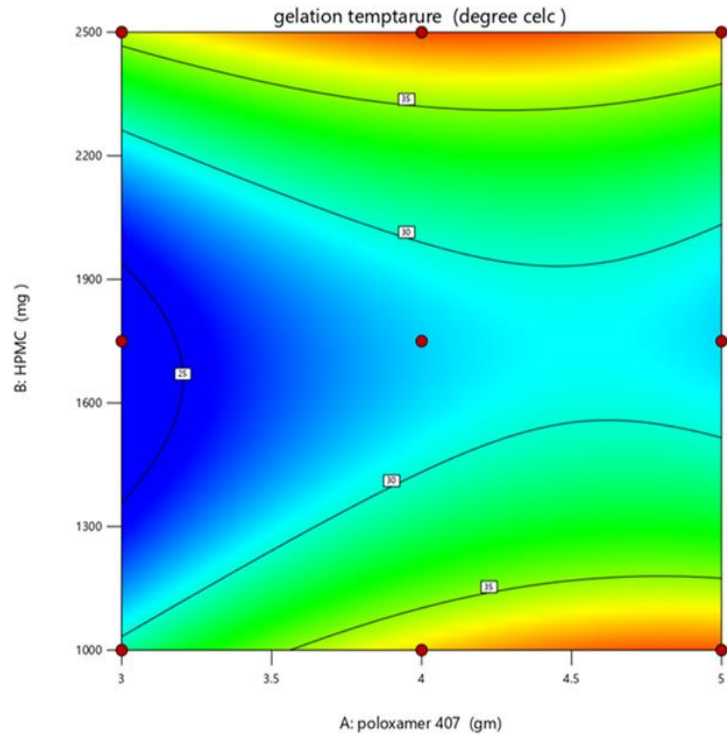


Figure No. 4: Contour Plot of Y1 (Gelation temperature)

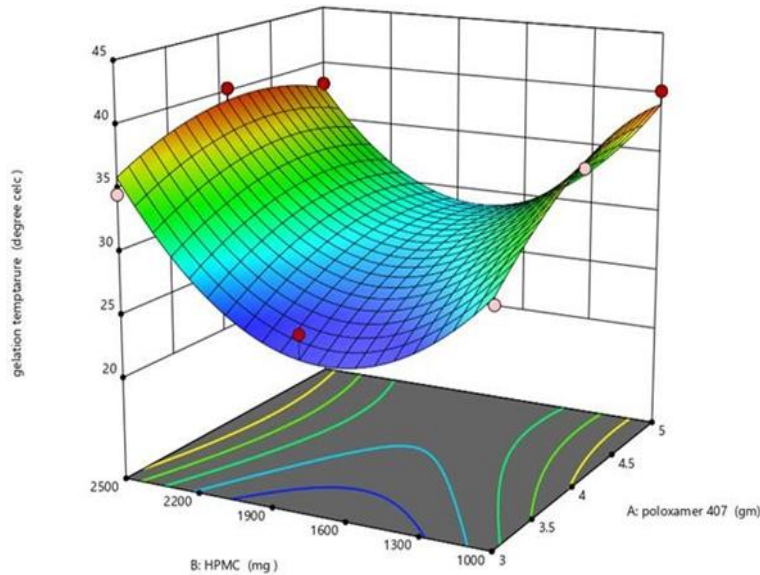


Figure No. 5: Surface Response Plot of Y1 (Gelation temperature)

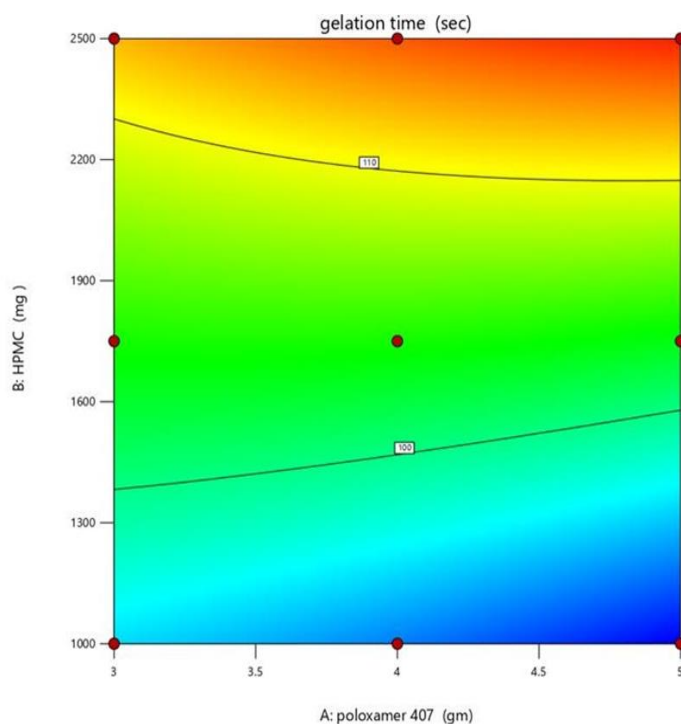


Figure No. 6: Contour Plot of Y2 (Gelling Time)

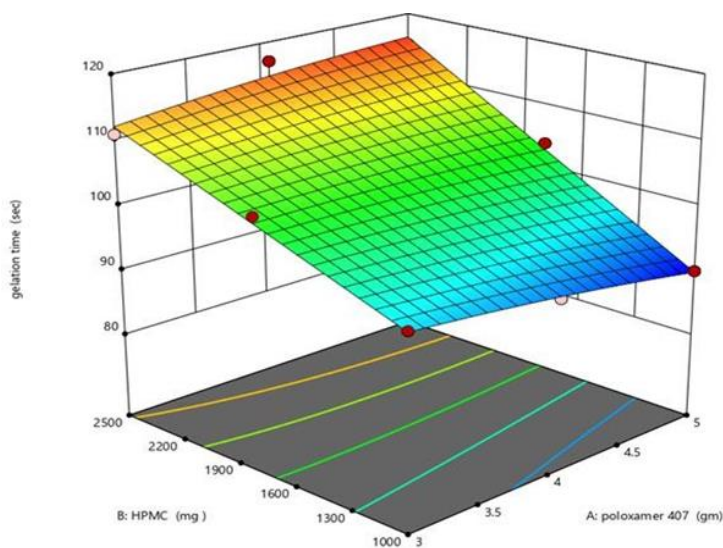


Figure No. 7: Surface Response Plot of Y2 (Gelling Time)

In-vitro Drug Diffusion

Formulation F4 exhibited sustained drug release with 88.94% cumulative drug diffused over 8 hours, indicating that the selected polymeric blend effectively controlled drug release.

Table No. 10: Percent Cumulative Drug Diffused of Optimized Batch (F4)

Sr. No.	Time (Min)	Average Percent Cumulative Drug Diffused \pm S.D.
1.	00	0.00
2.	15	16.02 \pm 1.78
3.	30	19.26 \pm 2.63
4.	60	25.31 \pm 1.69
5.	120	40.54 \pm 2.35
6.	180	49.72 \pm 1.72
7.	240	59.49 \pm 1.31
8.	300	65.37 \pm 2.40

9.	360	71.13±2.16
10.	420	82.89±1.33
11.	480	88.94±2.85

Stability studies over 30 days at $40 \pm 2^\circ\text{C} / 75 \pm 5\%$ RH showed that formulation F4 maintained physical integrity and drug content, confirming its stability.

Stability Studies

Table No. 11: Stability Study of Optimized Batch (F4) at $40 \pm 0.5^\circ\text{C}; 75 \pm 5\%$ RH condition

Time Interval (Days)	Visual Appearance	Clarity	pH	Viscosity (cps)	Drug Content (%)
0	Cloudy	Turbidity	5.34	2924	90.69
7	Cloudy	Turbidity	5.68	2975	90.78
15	Cloudy	Turbidity	5.91	3062	90.66
30	Cloudy	Turbidity	6.27	3121	90.71

Kinetic Modelling

Release kinetics for batch F4 best fit the Higuchi model ($R^2 = 0.9844$), indicating diffusion-

controlled release. Korsmeyer-Peppas model ($R^2 = 0.9821$) supported a non-Fickian release mechanism.

Table No. 12: Release Kinetic Model Fitting

Model	Zero Order	First Order	Higuchi Model	Korsmeyer-Peppas	Hixon-Crowell
(R^2)	0.9659	0.9778	0.9844	0.9821	0.9659

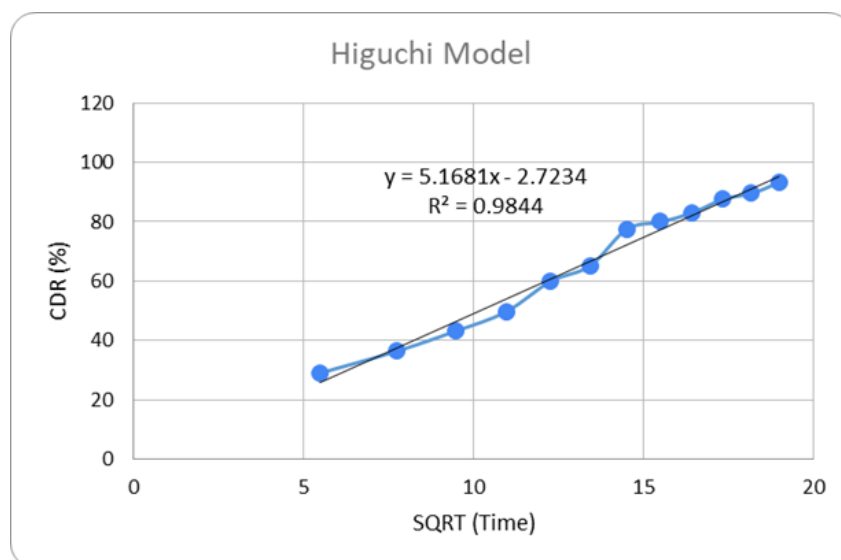


Figure No. 8: Higuchi Kinetic Model

Antifungal Activity

In-vitro antifungal testing against *Candida albicans* demonstrated superior activity of the

optimized formulation (KTZF4) over the marketed gel, particularly at $30 \mu\text{g/mL}$. This confirms the potential of the developed formulation as an effective ocular antifungal agent.

Table no. 13: Antifungal activity of gel formulations against Candida albicans

Sample	Zone of inhibition (mm)
--------	-------------------------



	10µg/ml	20µg/ml	30µg/ml
Marketed ketoconazole Gel	14.56±0.20	19.85±0.15	22.12±0.13
Ketoconazole Gel (KTZF4)	15.64±0.11	20.36±0.65	23.65±0.15



A

B

Candida Albicans

Figure no. 9: Zone of Inhibition by antifungal drug

4. CONCLUSION

In the present study, efforts were made to develop a thermoreversible in-situ ocular gel of Ketoconazole using cost-effective and pharmaceutically acceptable excipients. The formulation was optimized through 3^2 factorial design, employing Poloxamer 407 as the thermoresponsive polymer and HPMC as a viscosity enhancer. The combination of these excipients was selected based on their critical functionality in enhancing gelation behavior, ocular retention, and sustained drug release. Among all formulations, Batch F4 emerged as the most robust, exhibiting desirable gelation temperature (37°C), acceptable gelling time (93 seconds), high drug content (93.45%), optimal viscosity (3004 cps), and strong antifungal activity. The optimized formulation demonstrated a sustained drug release for up to 8 hours, following Higuchi diffusion kinetics, and maintained stability over 30 days under accelerated conditions. The method of formulation

was simple, reproducible, and scalable, making it suitable for industrial application. Compared to commercially available ocular gels, the developed system offers the advantage of improved bioavailability, patient compliance, and targeted antifungal therapy. The study thus concludes that KTZF4 in-situ gel can serve as a promising ophthalmic drug delivery system for effective management of fungal eye infections.

REFERENCES

1. Gaudana R, Ananthula HK, Parenky A, Mitra AK. Ocular drug delivery. *AAPS J.* 2010;12(3):348–360.
2. Barar J, Javadzadeh AR, Omidi Y. Ocular novel drug delivery: impacts of membranes and barriers. *Expert Opin Drug Deliv.* 2008;5(5):567–581.
3. Ludwig A. The use of mucoadhesive polymers in ocular drug delivery. *Adv Drug Deliv Rev.* 2005;57(11):1595–1639.

4. Gupta H, Jain S, Mathur R, Mishra P, Mishra AK. Sustained ocular drug delivery from a temperature and pH triggered in-situ gel system. *Drug Deliv.* 2007;14(8):507–515.
5. Almeida H, Amaral MH, Lobão P, Lobo JMS. In-situ gelling systems: a strategy to improve the bioavailability of ophthalmic pharmaceutical formulations. *Drug Discov Today.* 2014;19(4):400–412.
6. Dumortier G, Grossiord JL, Agnely F, Chaumeil JC. A review of poloxamer 407 pharmaceutical and pharmacological characteristics. *Pharm Res.* 2006;23(12):2709–2728.
7. Makwana SB, Patel VA, Parmar SJ. Development and characterization of in-situ gel for ophthalmic formulation containing ciprofloxacin hydrochloride. *Res Pharma Sci.* 2016;6:1–6.
8. Shah DN, Yau R, Lasco TM. Antifungal therapy for ocular fungal infections. *Clin Microbiol Rev.* 2014;27(3):511–536.
9. Vengurlekar P, Patel D, Patel M. Formulation and evaluation of ketoconazole ophthalmic in-situ gel. *J Chem Pharm Res.* 2011;3(2):464–470.
10. Pathak K, Keshri L. Development and characterization of ketoconazole loaded ocular in-situ gel for sustained antifungal activity. *Indian J Pharm Educ Res.* 2019;53(4):S609–S617.
11. Qian Y, Xu W, Xu X, et al. Preparation and evaluation of in-situ gel-based systems containing posaconazole for ocular delivery. *Drug Dev Ind Pharm.* 2017;43(4):649–656.
12. Cho WK, Park JH, Kim YS, et al. Poloxamer–HPMC-based thermo-sensitive ophthalmic in-situ gel for sustained release of timolol maleate. *Pharmaceutics.* 2021;13(9):1336.
13. Akhlaq M, Rasool N, Ansari TM, et al. Comparative study of citric acid as a buffering and chelating agent in ophthalmic formulations. *Pak J Pharm Sci.* 2019;32(2):661–667.
14. Nair AB, Kumria R, Harsha S, et al. In-situ gel formulations for ocular drug delivery. *Drugs Future.* 2010;35(8):625.
15. Kumar S, Haglund BO. pH-sensitive in situ gelling ophthalmic drug delivery system. US Patent 20060182763A1. 2006.
16. Srividya B, Cardoza RM, Amin PD. Sustained ophthalmic delivery of ofloxacin from a pH triggered in situ gelling system. *J Control Release.* 2001;73(2-3):205–211.
17. Dumortier G, Grossiord JL, Agnely F, Chaumeil JC. A review of poloxamer 407 pharmaceutical and pharmacological characteristics. *Pharm Res.* 2006;23(12):2709–2728.
18. Almeida H, Amaral MH, Lobão P, Lobo JMS. In situ gelling systems: a strategy to improve the bioavailability of ophthalmic pharmaceutical formulations. *Drug Discov Today.* 2014;19(4):400–412.
19. Bodmeier R, Chen H. Preparation and characterization of microspheres containing the anti-inflammatory drug, indomethacin, dispersed within a poloxamer 407 gel. *Int J Pharm.* 1989;57(2):115–124.
20. Dumortier G, Grossiord JL, Agnely F, Chaumeil JC. A review of poloxamer 407 pharmaceutical and pharmacological characteristics. *Pharm Res.* 2006;23(12):2709–2728.
21. Qian Y, Xu W, Xu X, et al. Preparation and evaluation of in-situ gel-based systems containing posaconazole for ocular delivery. *Drug Dev Ind Pharm.* 2017;43(4):649–656.
22. Rathapon Asasutjarit, et al. Mucoadhesive properties of HPMC-based polymeric films for buccal drug delivery. *AAPS PharmSciTech.* 2014;15(5):1327–1339.
23. Cho WK, Park JH, Kim YS, et al. Poloxamer–HPMC-based thermo-sensitive ophthalmic in-



- situ gel for sustained release of timolol maleate. *Pharmaceutics*. 2021;13(9):1336.
24. Patel H, Panchal DR, Patel U, et al. In-situ gel forming system for ophthalmic drug delivery of ciprofloxacin hydrochloride. *Int J Pharm Investig*. 2013;3(1):30–36.
25. Akhlaq M, Rasool N, Ansari TM, et al. Comparative study of citric acid as a buffering and chelating agent in ophthalmic formulations. *Pak J Pharm Sci*. 2019;32(2):661–667.
26. Nair AB, Kumria R, Harsha S, Attimarad M, Al-Dhubiab BE. In situ gel formulations for ocular drug delivery. *Drugs Future*. 2010;35(8):625.

HOW TO CITE: Shubham Durgawale*, Design, Development and Analysis of In-Situ Gel of Ketoconazole for Sustained Ocular Delivery, *Int. J. of Pharm. Sci.*, 2025, Vol 3, Issue 8, 573-586. <https://doi.org/10.5281/zenodo.16750877>