

FORMULATION DEVELOPMENT AND EVALUATION OF PH RESPONSIVE IN-SITU GEL FORMULATIONS OF LOMEFLOXACIN HYDROCHLORIDE**Ankit Singh, Sunil Ahirwar*, SatkarPrassad****RKDF School of Pharmaceutical Sciences, BHABHA University, Madhya Pradesh, India***Corresponding Author's E mail:sunilahirwar687@gmail.com

Received 4 Sept. 2025; Revised 9 Sept. 2025; Accepted 8 Oct. 2025, Available online 15 Oct. 2025



Cite this article as: PatelS, AhirwarS andPrasadS.Formulation development and evaluation of pH responsive in-situ gel formulations of lomefloxacin hydrochloride. Asian Journal of Pharmaceutical Education and Research. 2025; 13(4):97-118.

<https://dx.doi.org/10.38164/AJPER/14.4.2025.97-118>

ABSTRACT

Conventional ophthalmic solution often eliminate rapidly after administration, which cannot provide and maintain an adequate concentration of the drug in the precorneal area. A major problem in ocular therapeutics is the attainment of optimal drug concentration at the site of action, which is compromised mainly due to precorneal due to loss factor resulting in only a small fraction of the drug being ocularly absorbed. The effective dose administered ophthalmically may be altered by increasing the retention time of medication into the eye by using an in situ gel – forming system. This study aimed to develop an ophthalmic delivery system for the antibacterial drug 'Lomefloxacin HCL' using pH-induced in situ gellation. Carbopol 940 was used as the gelling agent, along with HPMC E50LV and HPMC E4M as viscosity enhancing agents. The formulations were sterilized and evaluated for in vitro gelling capacity, rheological study, and percentage drug release. The developed formulations provided sustained drug release over 8 hours and were tested in albino rabbits, showing no changes in pH, drug content, or clarity. The developed system may be a valuable alternative to conventional methods, allowing for better drug concentration and ocular absorption.

Keywords: pH induced insitu gel, Lomefloxacin HCL, Carbopol 940, HPMC E50LV, HPMC E4M.

INTRODUCTION

Ophthalmic drug delivery is a complex and challenging task due to the eye's unique anatomy and biochemistry. Formulators must navigate the protective barriers of the eye without causing permanent tissue damage. Current methods, such as solutions, suspensions, and semisolids, have been criticized for their efficiency. Eye drop dosages are easy to instill but have drawbacks, as most of the medication is diluted in the tear film and drained away. This result in a large and unpredictable dose of medication and subsequent absorption may lead to undesirable side effects. This work aims to develop a pH-induced in-situ gel as an ophthalmic drug delivery system. In situ gels are made from polymers that exhibit phase transition due to environmental changes, and can be easily administered by dropping a

solution into the eye's conjunctiva sac. This delivery system has an ease of administration similar to an ophthalmic solution and a long retention time due to gel formation^{1,2}.

MATERIALS AND METHODS

Materials

The study used Lomefloxacin hydrochloride as a gift sample from Ipca Laboratories Ltd., HPMC E50LV and E4M from Colorcon Asia Pvt. Ltd., all other analytical grade chemicals and reagents. Instruments used included UV–Visible spectrophotometer (UV-1700, Shimadzu Corporation, Japan), a weighing balance (Model XB120A, Presica Instruments Ltd., Switzerland), an overhead stirrer (Remi Motors Ltd., Mumbai, India), a pH meter (pH Tutor, Eutech Instruments, Singapore), and a rheometer (Model DV-E, Brookfield Viscometer, USA).

Methods

Analytical method validation of Lomefloxacin Hydrochloride by UV-spectrophotometric

A Spectrophotometric method was developed for estimating Lomefloxacin Hydrochloride in Simulated Tear Fluid (STF). A standard stock solution was prepared by dissolving 100 mg of Lomefloxacin Hydrochloride in 100 ml of STF, and a working standard solution was prepared by adding 1-12 µg/ml of STF to the stock solution^{4,5}.

Preparation of pH induced in-situ gelling system

pH-sensitive polymers, such as carbomer derivatives and carbopol, are known to generate aqueous solutions in their unionized state. At physiological pH 7.4, these polymers undergo reversible ionization to create a stiff gel network that swells and creates huge aqueous holes. Carbopol 940 was therefore chosen to create the pH-induced in-situ gelling system. The proposed work was split into two halves because this requires optimization of the polymer ratio.

- Polymer ratio optimization
- Including active compounds in a polymer ratio that is optimal.

Optimization of polymer ratio for preparation of in-situ gelling system

Firstly, the Acetate buffer of pH 4 and 5 were prepared. Two sets of, each with five beakers was filled with acetate buffer of pH 4 and 5, respectively. Different concentration of Carbopol 940 from 0.1 % to 0.5 % was sprinkled to the beakers containing buffer solution of respective pH and allows hydrating overnight. Later the solution containing in the beakers were stirred with an overhead stirrer. These polymers were evaluated for clarity, gelling capacity and viscosity at physiological (pH 7.4) as well as

nonphysiological (pH 4 & 5) condition by using Brook Field Viscometer (DV-E Rheometer). These were carried out to get optimum polymer concentration⁶.

Incorporation of Lomefloxacin HCL in optimized formulation

Results from method 2 reveal that the formulations CH 11 (0.3 % Carbopol 940 and 1.5 % HPMC E50LV) and CH 15 (0.4 % Carbopol 940 and 1.5 % HPMC E50LV) showed good gelling capacity and desire viscosity. Results from method 3 reveal that the formulations CH 21 (0.2 % Carbopol 940 and 0.4 % HPMC E4M) and CH 24 (0.3 % Carbopol 940 and 0.4 % HPMC E4M) showed good gelling capacity and desire viscosity. These four formulations were selected as those had satisfactory attributes of gelling capacity and desired viscosity at physiological (pH 7.4) as well as non-physiological (pH 5) conditions. The detail data of the prepared formulations for pH induced in-situ gelling system of Lomefloxacin HCL are given in Table 12⁷.

Table 1: Contents of formulations

Sr. No.	Ingredients	Concentrations (% w/v)			
		CHL 11	CHL 15	CHL 21	CHL24
1	Lomefloxacin HCL	0.3	0.3	0.3	0.3
2	Carbopol 940	0.3	0.4	0.2	0.3
3	HPMC E50LV	1.5	1.5	—	—
4	HPMC E4M	—	—	0.4	0.4
5	Sodium Chloride	0.9	0.9	0.9	0.9
6	Benzalkonium Chloride	0.01	0.01	0.01	0.01
7	Acetate Buffer (pH 5) up to	100	100	100	100

Preparation of pH induced hydrogel formulations

The buffer salts were dissolved in 50 ml of purified water; HPMC (E50LV / E4M) was added to hydrate. Carbopol 940 was sprinkled over this solution and allowed to hydrate overnight. The solution was stirred with an overhead stirrer. Lomefloxacin Hydrochloride was dissolved in small quantity of

water, Benzalkonium Chloride (Preservative) and Sodium chloride (Isotonocity adjusting agent) was added to this solution; the drug solution was added to the polymer solution under constant stirring until a uniform solution was obtained. Purified water was then added to make up the volume to 100ml. Formulation pH was adjusted to pH 5 with the help of 0.5 M Sodium Hydroxide. This solution was filtered through 0.2 μ m filter paper. The optimized formulations were sterilized in an autoclave at 121° C and 15 psi for 15 minutes⁸⁻¹⁰.

Evaluation of prepared in-situ gelling system

Visual appearance and clarity

Visual appearance and Clarity was done under fluorescent light against a white and black back ground for presence of any particulate matter^{9,10}.

pH

The pH of the prepared in-situ gelling system after addition of all the ingredients was measured using pH meter¹¹.

Drug content analysis

Drug content analysis of prepared in-situ gelling systems was carried out using Spectrophotometric method. The assay of these formulations was carried out by pipetting 0.1 ml of all four optimized formulations, and it was diluted up to 100 ml of Simulated Tear Fluid (pH 7.4). The absorbance was measured at 281.5 nm using UV-Visible spectrophotometer^{12,13}.

In-vitro gellation

The Gelling capacity of the formulations containing different ratio of Carbopol 940 and HPMC (E50LV / E4M) was evaluated. It was performed by placing a drop of polymeric solution in vials containing 1 ml of Simulated Tear Fluid, freshly prepared and equilibrated at 34°C, and visually assessed the gel formed and time for gellation as well as time taken for the gel formed to dissolve. The Composition of Simulated Tear Fluid was Sodium chloride (0.670 g), Sodium Bi Carbonate (0.2 g), Calcium Chloride dihydrate and bi-distilled water quantity sufficient up to 100 g. Physiological pH (7.4 $\pm$ 0.2) was adjusted by adding the required amount of 0.1 N HCL^{14,15}.

Interaction studies

Prepared in-situ gel formulations were tested for the intactness of drug in the various formulations by comparing with pure drug. These were done to ensure that the therapeutically active drug has not undergone any change after it has been subjected to processing steps during preparation of in-situ gelling systems. Taking IR spectra using KBr method did these studies¹⁶.

Sterility testing

Sterility testing were intended for detecting the presence of viable form of microorganisms and were performed for Aerobic and Anaerobic bacteria and fungi by using Fluid Thioglycolate Medium and Soyaban Casein Digest medium, respectively as per the Indian Pharmacopoeia. The sterile formulations were taken into laminar airflow. By the help of sterile formulation was removed from the vials. This solution was passed through the membrane filter of 0.45 μ m size with the help of vacuum pump. After filtration, the filter paper was removed from funnel and it was cut into two half. One half was dropped in bacterial media (Fluid Thioglycolate) and the other half was dropped in the fungal media (Soyaban Casein Digest). The media were kept for incubation for 7 days at 37°C. Both the media were observed every day for any microbial contamination and compared with a positive and negative control¹⁷.

Rheological studies

Rheological properties of the prepared in-situ gelling systems under the different Shear rates (2, 4, 6, 10, 20, and 30 rpm) were measured at nonphysiological (pH 5 and 25°C) and physiological condition (pH 7.4 and 34°C), respectively. The hierarchy of the shear rate was reversed, and the average of two reading was used to calculate the viscosity^{18,19}.

Comparative in-vitro release studies with marketed formulation

In-vitro drug release from the formulations was studied by the diffusion process. Here the pH of the Lacrimal fluid and the blinking rate of the eye were taken into consideration and were simulated. The in-vitro release of Lomefloxacin HCL as pure drug well as from the prepared formulations was studied through cellophane membrane using diffusion cell. The cellophane membrane was soaked overnight in the receptor medium (Simulated Tear Fluid, pH 7.4). It was tied to one end of a glass diffusion cell. 100 ml of receptor medium was taken in the 200 ml beaker. The diffusion cell was filled with 2 ml of the formulation and suspended in 100 ml of receptor containing beaker by assuring that the membrane was just touched the receptor medium surface. The whole assembly was transferred on magnetic stirrer and was maintained at 34°C $\pm$ 1°C and 22 rpm. The drug samples (1 ml) were withdrawn at the interval of 30 minutes from receptor medium and replaced by equal volumes of the receptor medium. The samples were diluted with appropriate receptor medium and analyzed by a UV-Visible spectrophotometer at 281.5 nm using receptor medium as a blank²⁰⁻²².

Pharmacokinetic release studies

All the optimized formulations were subjected to study the release kinetics of it. So the best fit kinetic model was determined for the optimized formulations using analysis software PCP – Disso V2²⁰⁻²³.

Antimicrobial efficacy studies

The Antimicrobial efficacy studies were carried out to ascertain the biological activity of the optimized formulations. *Staphylococcus Aureus*, *Pseudomonas Aeruginosa* and *E.coli* were used as the test organisms. These were determined by Agar diffusion test employing Cup-Plate method³⁸. A layer of nutrient agar (20 ml) seeded with the test microorganisms (0.2 ml) were allowed to solidify in the petri dishes. Cups were made on the solidified agar layer with the help of sterile borer. Then the volume of the formulations containing equivalent amount of drug was poured into the cups. After keeping the petri dishes at room temperature for 4 hours, the plates were incubated at 37°C for 24 hours. The zones of inhibitions were measured around the cups. The entire operation except the incubation was carried out in a laminar airflow unit²⁴.

Ocular irritancy studies

In developing a novel ophthalmic delivery system, an injury to the eye was taken into consideration. Since, eye being a sensitive, most delicate and yet most valuable of the sense organs, the injuries to the Cornea, Conjunctiva, and Iris were measured according to Draize test. According to the Draize test, the amount of the test substance applied to the eye is normally 100 µl placed into the lower cul-de-sac with observation of the various criteria made at a designated required time interval of 1hr, 24 hrs, 48 hrs, 72 hrs, and 1 week after administration. A total four albino rabbits (male) weighing 1.5-2 kg was used for the present study. The sterile formulations were instilled twice a day for a period of 7 days. Rabbits were observed periodically for redness, swelling, watering of the eye. The evaluation was made according to the Draize test protocol²⁵.

Accelerated stabilities studies

Stability is defined as the extent, to which a product retains with in specified limits and throughout its period of storage and use i.e., shelf life. Stability studies were carried out on optimized formulations according to International Conference on Harmonization (ICH) guidelines. A sufficient quantity of formulations in previously sterilized vials was stored in desiccators containing a saturated solution of sodium chloride, which gives a relative humidity of 75±5 %. The desiccators were placed in a hot air oven maintained at a temperature 40°C±0.5°C and at room temperature. Samples were withdrawn at 7 days interval for 42 Days. The logarithms of percent drug remaining were calculated and plotted against time in days. It was also analyzed for visual appearance, clarity, and pH^{26,27}.

RESULTS

Estimation of Lomefloxacin Hydrochloride by Spectrophotometric Method

A simple Spectrophotometric method for estimation of Lomefloxacin Hydrochloride was developed in Simulated Tear Fluid, which exhibited $\lambda_{\max}$ at 281.5 nm in Beer's range of 1-12 $\mu\text{g/ml}$ (Figure 1 & 2, and Table 1).

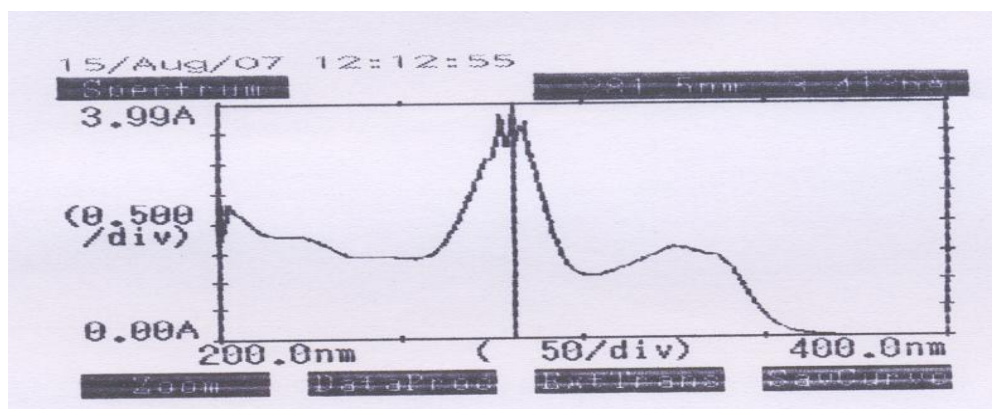


Figure 1: Spectrum of Lomefloxacin HCL.

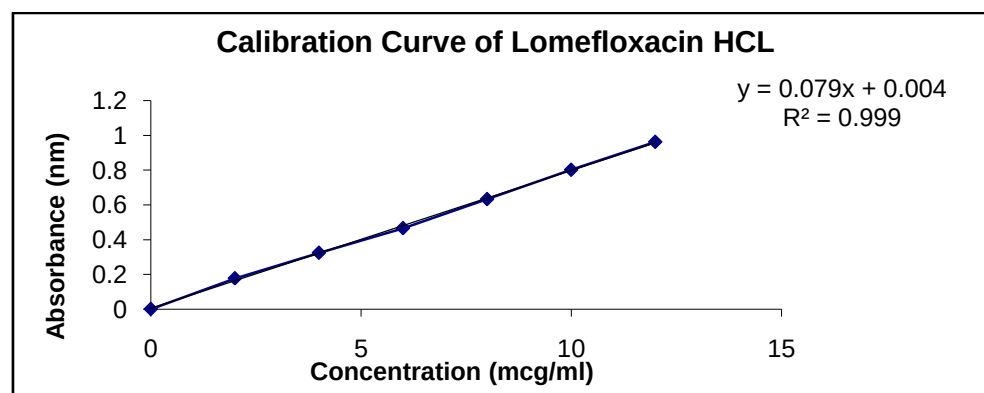


Figure 2: Calibration curve of Lomefloxacin HCL in STF

Preparation of pH induced in-situ gelling system

Optimization of polymer ratio for preparation of in-situ gelling system

Polymer like, Carbopol 940 were chosen for preparation of pH induced in-situ gelling systems. Formulations containing different concentration of Carbopol 940 (0.1-0.5 %) were prepared in different nonphysiological condition (like, pH 4 & pH 5), in order to identify the pH, clarity and Gelling capacity (Table 2).

Table 2. Viscosity and gelling capacity of different concentrations of carbopol 940.

Formulation Code	Concentration of Carbopol 940 (% w/v)	Viscosity (cps ay 20 rpm)			Gelling Capacity
		pH 4	pH 5	pH 7.4	
CP1	0.1	0.23 ^b	0.52 ^b	2.88	-
CP2	0.2	0.52 ^a	3.04 ^b	7.36	+
CP3	0.3	2.31 ^a	12.09 ^b	35.14	++
CP4	0.4	4.51 ^a	47.89 ^b	79.74	++
CP5	0.5	10.64 ^a	108.62 ^b	259.18	+++

Where, - is no gellation; + is gels after few minutes, dissolve rapidly; ++ is gellation immediate, remain for few hours; +++ is gellation immediate but for extended periods; a, is Translucent; b, is Transparent

As observed during practical work that Carbopol solution with lower concentration of it, viscosity of gels formed after gellation at pH 7.4 was very low and at higher concentration of it, viscosity of gels formed was very high. One more problem was found that as Carbopol concentration increase, the pH of the formulation became acidic. Another problem was observed that as Carbopol concentration increases, the solution became translucent at pH 4 but at pH 5 it was clear. Hence for further procedure, formulation pH was selected as pH 5. Form the above observations; Carbopol cannot be used alone for preparation of in-situ gels. Hence it was decided to take the help of polymer, which increases the viscosity without compromising the gelling capacity of Carbopol 940. Formulations containing different concentration of Carbopol 940 (0.1-0.4 %) and HPMC E50LV (0.5-2 %) were prepared in different nonphysiological condition (pH 5), in order to identify the pH, clarity and Gelling capacity (Table 3).

Table 3 Viscosity and gelling capacity of different concentrations of Carbopol 940 and HPMC E50LV and Carbopol 940 and HPMC E4M.

Formulation Code	Concentration of Carbopol/HPMC E50LV (%w/v)	Concentration of Carbopol/HPMC E4M (%w/v)	Viscosity (cps at 20 rpm)		Gelling Capacity
			pH 5	pH 7.4	
CH1	0.1/0.5	-	0.98 ±	0.98 ±	-
CH2	0.1/1.0	-	4.88 ±	7.88 ±	+
CH3	0.1/1.5	-	26.58 ±	30.70 ±	+
CH4	0.1/2.0	-	53.0 ±	89.40 ±	++
CH5	0.2/0.5	-	2.60 ±	2.81 ±	-
CH6	0.2/1.0	-	6.84 ±	8.06 ±	+
CH7	0.2/1.5	-	29.05 ±	48.0 ±	++
CH8	0.2/2.0	-	66.60 ±	91.9 ±	++
CH9	0.3/0.5	-	4.22 ±	4.36 ±	-
CH10	0.3/1.0	-	12.38 ±	12.42 ±	+
CH11	0.3/1.5	-	33.13 ±	83.40 ±	++
CH12	0.3/2.0	-	85.90 ±	130.6 ±	+++
CH13	0.4/0.5	-	6.42 ±	7.69 ±	-
CH14	0.4/1.0	-	17.44 ±	21.28 ±	+
CH15	0.4/1.5	-	38.68 ±	85.50 ±	++
CH16	0.4/2.0	-	98.90 ±	147.30 ±	+++
CH17	-	0.1/0.2	0.5 ±	1.70 ±	-
CH18	-	0.1/0.4	4.92 ±	19.60 ±	+
CH19	-	0.1/0.6	42.80 ±	57.40 ±	++
CH20	-	0.2/0.2	4.78 ±	9.60 ±	+
CH21	-	0.2/0.4	42.70 ±	64.60 ±	++
CH22	-	0.2/0.6	102.80 ±	131.60 ±	+++
CH23	-	0.3/0.2	22.33 ±	76.90 ±	+
CH24	-	0.3/0.4	43.50 ±	63.20 ±	++
CH25	-	0.3/0.6	111.40 ±	145.9 ±	+++

Evaluation of prepared in-situ gelling system:**Evaluation of Visual appearance, Clarity, pH, and Drug Content**

All the prepared in-situ gelling systems were evaluated for preliminary steps such as Visual appearance, Clarity, pH, and Drug content. These formulations were transparent and clear. The pH of the formulations was found to be 5 ± 0.5 , and drug content was in between 99.38 % to 99.71% (Table 4).

Table 4. Preliminary evaluation of visual appearance, clarity, ph, and drug content.

Evaluation steps	CHL 11	CHL 15	CHL21	CHL 24
Visual Appearance	Transparent	Transparent	Transparent	Transparent
Clarity	Clear	Clear	Clear	Clear
pH	4.99 ± 0.15	4.97 ± 0.50	5.01 ± 0.12	4.98 ± 0.75
Drug Content	$99.71 \pm 1.25 \%$	$99.38 \pm 0.5 \%$	$99.43 \pm 0.25 \%$	$99.67 \pm 0.12 \%$

In-vitro gellation

Prepared in-situ gelling systems were evaluated for in-vitro gellation capacity. All the formulations were given satisfactory results (Table 5).

Table 5. Evaluation of gelling capacity.

Formulations	Gelling capacity
CHL 11	++
CHL 15	++
CHL 21	++
CHL 24	++

Interaction Studies

The prepared in-situ gelling systems were evaluated for interaction studies to ensure that there is no interaction occurred in between drug and polymers. For this conformation to stability of drug in the prepared formulations the IR spectra were taken and compared with that of pure drug. The result of these studies reveals that there were no definite changes obtained in the bands of drug with respect to pure drug (Fig. 3-4).

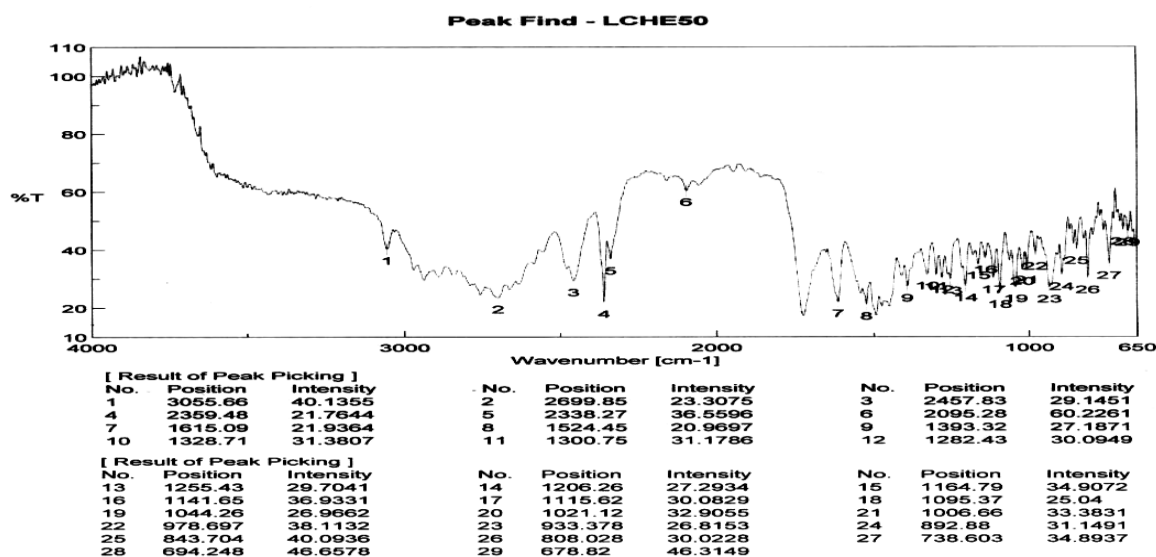


Figure 3: IR spectra of pure drug

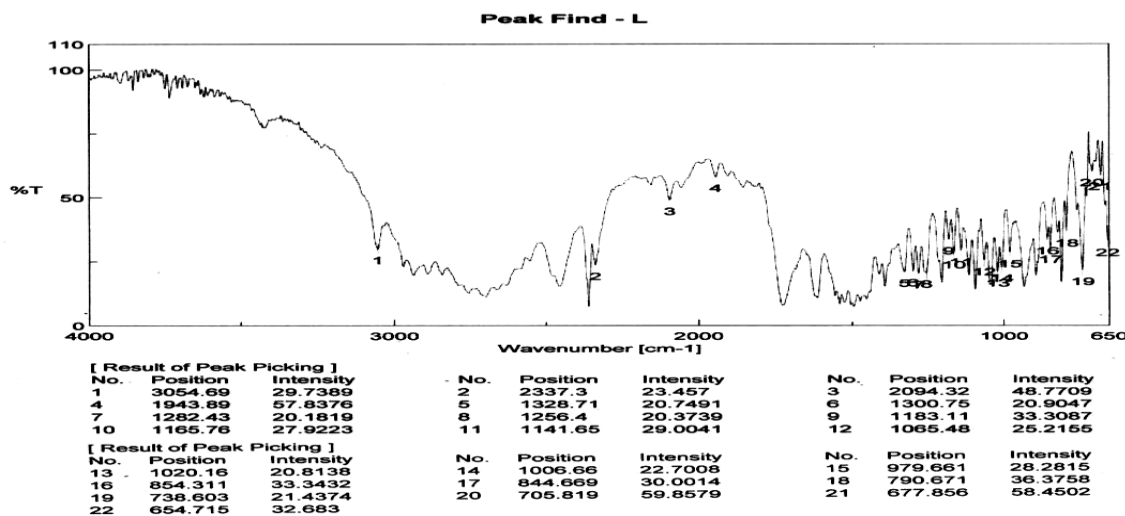


Figure 4: IR spectra of formulation LCHE50LV

Sterility Testing

All the prepared in-situ gelling systems were evaluated for the sterility. After 7 days of incubation the results showed that the no microbial growth was found in all formulations (Table 6).

Rheological Studies

For the development of optimum in-situ gelling system, two major prerequisites Viscosity and Gelling Capacity should be taken in consideration. Since the ocular shear rate is very high, ranging from 0.03 S^{-1} during inter-blinking periods to $4250\text{-}28,500 \text{ S}^{-1}$ during blinking, viscoelastic fluid with a viscosity

that is high under low shear rate condition and low under high shear rate condition, which is called Pseudoplastic fluid, is often preferred, so dynamic viscosity of formulations were 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. Results obtained reveals that the viscosity of these formulations all decreased as the shear rate increased, which showed the character of pseudoplastic fluid (Fig. 5 & 6).

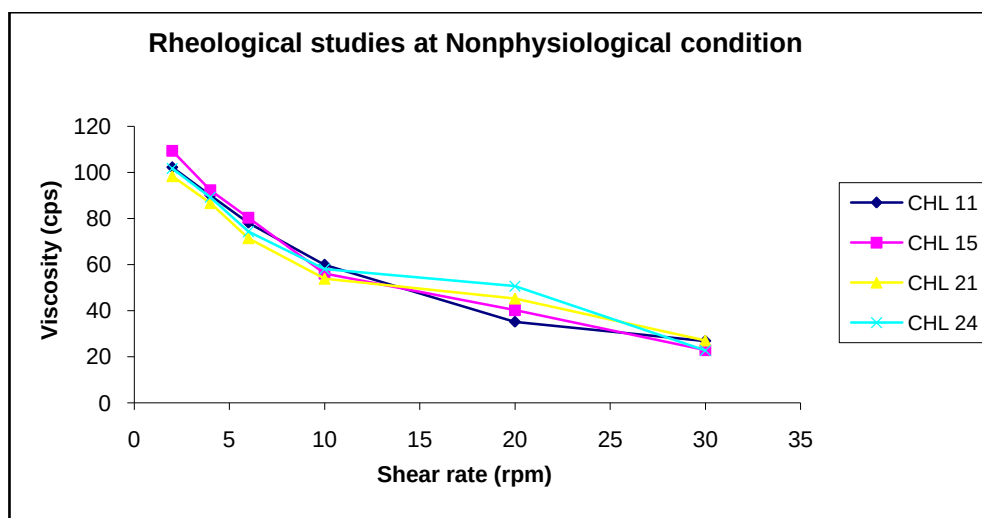


Figure 5 Rheological studies of formulations at nonphysiological condition (pH 5)

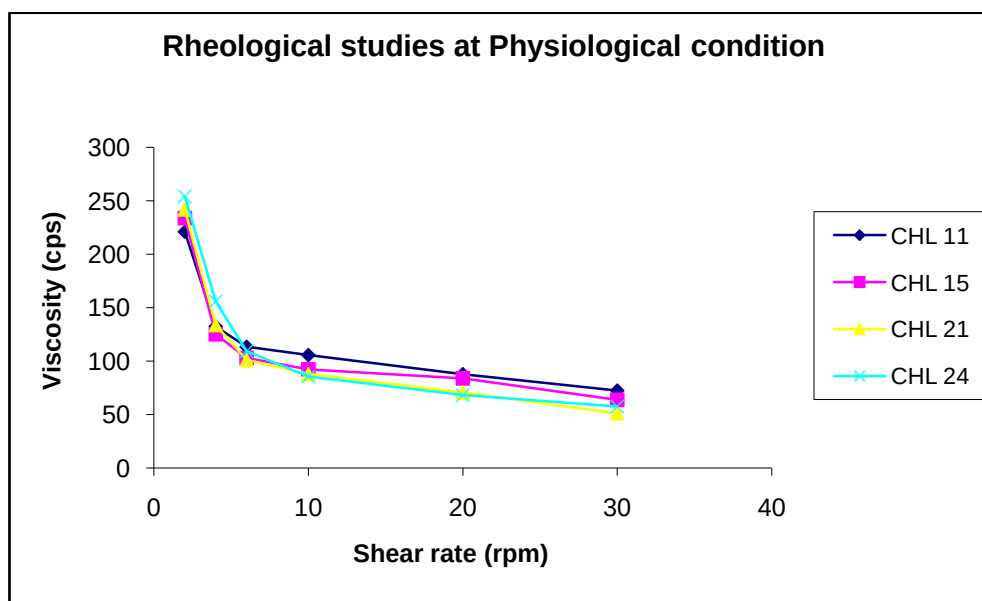


Figure 6. Rheological studies of formulations at physiological condition (pH 7.4)

5.3.6 In-vitro release studies

The in-vitro release of Lomefloxacin HCL as pure drug well as from the prepared formulations was studied through cellophane membrane using diffusion cell. The release studies of prepared in-situ gelling systems were carried out up to 8 hours, and that of pure drug was up to 2.5 hours. Shown in Tables 18-23 and Figures 11-16. In-Vitro Release of Marketed eye drops was done through Cellophane Membrane using diffusion cell. The release studies of marketed product were showed release up to 3 hours (Fig. 7).

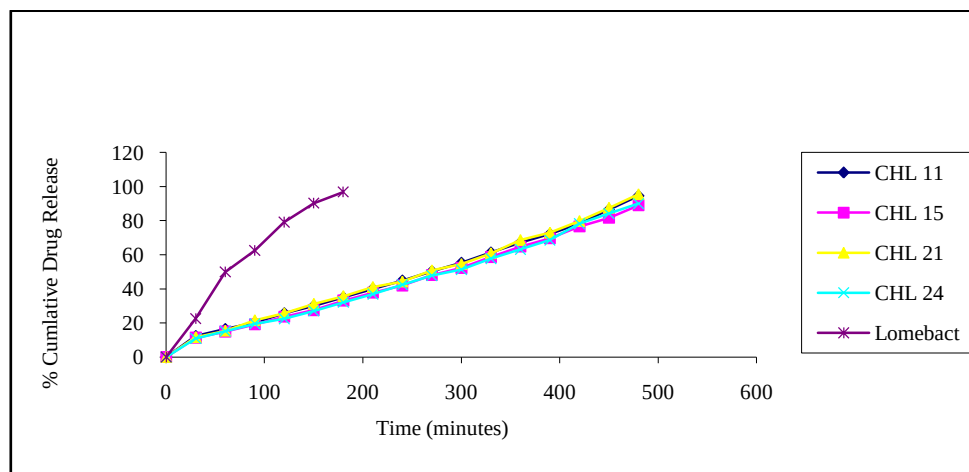


Figure 7: Comparative in-vitro release of marketed eye drop and prepared in-situ gels.

Pharmacokinetic Release Studies

The best fit kinetic model for the optimized formulation were the zero order and peppas model (Table 6), which suggest that the drug release was independent of the concentration and occurred by diffusion mechanism. The polymer can absorb a significant amount of water to form to elastic gel and at the same time, release the dissolved entrapped drug by diffusion through swollen regions of the gel. With a hydrophilic carbopol-HPMC gel, tear fluid would except to diffuse into the gel interior and leach out water soluble drug such as lomefloxacin HCL.

Table 6: Release Kinetics of Optimized Formulations.

Release type	Parameters	CHL 11	CHL 15	CHL 21	CHL 24
Zero order	R	0.9917	0.9936	0.9907	0.9939
	k	0.1973	0.1890	0.1986	0.1878
	t-test	29.881	34.017	28.207	34.990
First order	R	0.8581	0.9135	0.8528	0.9105
	k	-0.0041	-0.0036	-0.0042	-0.0036
	t-test	6.473	8.695	6.325	8.526
Matrix	R	0.9444	0.9355	0.9426	0.9307
	k	3.5462	3.3862	3.5689	3.3603
	t-test	11.127	10.258	10.933	9.857
peppas	R	0.9879	0.9834	0.9889	0.9825
	k	24.691	0.8180	0.9286	0.7778
	t-test	0.9635	21.019	25.792	20.446
Hixoncrowell	R	0.9422	0.9598	0.9376	0.9570
	k	-0.0010	-0.0009	-0.0010	-0.0009
	t-test	10.891	13.249	10.444	12.770
t-table at p 0.05 (two tails) DF =n-2		2.131	2.131	2.131	2.131

Antimicrobial Efficacy Studies

The optimized in-situ gelling formulations were showed antimicrobial activity when tested microbiologically by the Cup-Plate technique. Clear zones of inhibition were obtained in the case of all Formulations. The diameter of zone of inhibition produced by formulations against all test microorganisms is given in Table 7. The antimicrobial effect of the Lomefloxacin in prepared in-situ gelling systems is probably due to a fairly rapid initial release of the drug into the viscous solution

formed by dissolution of gel, followed by formation of a drug reservoir that permits the drug to be released to the target site relatively slowly.

Table 7: Antimicrobial Activity of In-situ gels.

Test Microorganisms	Diameter of the zone of inhibition produced by in-situ gels (mm)			
	CHL 11	CHL 15	CHL 21	CHL 24
Staphylococcus Aureus	26	25	26	23
Pseudomonas Aeruginosa	30	28	29	28
E.coli	26	24	25	24

Ocular Irritancy Studies

Prepared in-situ gelling systems were subjected for ocular irritancy studies. A total four albino rabbits (male) weighing 1.5-2 kg was used for the present study. The sterile formulations were instilled twice a day for a period of 7 days. Rabbits were observed periodically for redness, swelling, watering of the eye. The evaluation was made according to the Draize test protocol. All the formulations were found to be non-irritating with no ocular damage or abnormal clinical signs to the cornea, iris, and conjunctiva observed (Table 8).

Table 8: Ocular irritancy profile.

Eye Tissues	Cornea	Iris	Conjunctiva	Total
Score point	1.5	2	1.5	5

Accelerated Stabilities Studies

The accelerated stabilities studies were carried for prepared in-situ gelling systems. All the Formulations were analyzed for Visual appearance, Clarity, pH and Drug Remaining. 42 days studies reveal that there were no changes observed in Visual changes and Clarity. All the formulations showed slight changes in pH, but it were in acceptable limits (± 0.5). See Tables 29-32. Study of drug content

remaining in all formulations reveals that there were no definite changes observed for drug degradation (Tables 9 & 10).

Table 9: Stabilities Studies of Formulation CHL 11.

Sr. No.	Formulation code	Numbers of Days	Visual Appearance		Clarity		pH	
			RT	40°C	RT	40°C	RT	40°C
1	CHL 11	0	Transparent	Transparent	Clear	Clear	4.99	4.99
2		7	Transparent	Transparent	Clear	Clear	5.01	4.97
3		14	Transparent	Transparent	Clear	Clear	4.99	4.98
4		21	Transparent	Transparent	Clear	Clear	4.98	4.99
5		28	Transparent	Transparent	Clear	Clear	4.98	4.97
6		35	Transparent	Transparent	Clear	Clear	4.99	5.01
7		42	Transparent	Transparent	Clear	Clear	5.01	5.00
8	CHL 15	0	Transparent	Transparent	Clear	Clear	4.98	4.98
9		7	Transparent	Transparent	Clear	Clear	4.99	5.01
10		14	Transparent	Transparent	Clear	Clear	4.97	4.99
11		21	Transparent	Transparent	Clear	Clear	5.02	5.02
12		28	Transparent	Transparent	Clear	Clear	5.03	4.98
13		35	Transparent	Transparent	Clear	Clear	5.01	5.03
14		42	Transparent	Transparent	Clear	Clear	5.02	4.98
15	CHL 21	0	Transparent	Transparent	Clear	Clear	4.99	5.00
16		7	Transparent	Transparent	Clear	Clear	5.03	4.96
17		14	Transparent	Transparent	Clear	Clear	5.00	4.99
18		21	Transparent	Transparent	Clear	Clear	4.98	4.98

19		28	Transparent	Transparent	Clear	Clear	4.97	4.98
20		35	Transparent	Transparent	Clear	Clear	4.99	4.99
21		42	Transparent	Transparent	Clear	Clear	5.01	4.98
22	CHL 24	0	Transparent	Transparent	Clear	Clear	5.02	5.02
23		7	Transparent	Transparent	Clear	Clear	5.04	4.99
24		14	Transparent	Transparent	Clear	Clear	4.99	4.97
26		21	Transparent	Transparent	Clear	Clear	4.97	5.01
27		28	Transparent	Transparent	Clear	Clear	4.99	4.99
28		35	Transparent	Transparent	Clear	Clear	4.99	5.00
29		42	Transparent	Transparent	Clear	Clear	4.98	4.97

Table 10: Stabilities Studies of Formulation CHL 11 and CHL 15.

Sr. No.	Numbers of Days	% Remaining	Drug (CHL 11)	% Remaining	Drug (CHL 15)	% Remaining	Drug (CHL 21)	% Remaining	Drug (CHL 24)
		RT	40°C	RT	40°C	RT	40°C	RT	40°C
1	0	99.79	99.79	99.43	99.42	99.47	99.46	99.65	99.65
2	7	99.72	99.63	99.41	99.37	99.42	99.41	99.64	99.62
3	14	99.68	99.52	99.46	99.34	99.40	99.38	99.56	99.59
4	21	99.53	99.46	99.35	99.31	99.43	99.35	99.55	99.54
5	28	99.49	99.31	99.29	99.26	99.39	99.28	99.55	99.52
6	35	99.48	99.28	99.23	99.14	99.36	99.12	99.52	99.46
7	42	99.42	98.97	99.24	99.01	99.23	98.94	99.53	99.41

DISCUSSION

The study aims to develop a "pH Induced In-Situ Gelling System of Antibacterial agent, Lomefloxacin HCL" for treating various eye bacterial diseases. This innovative approach aims to increase the pre-corneal residence time of drugs, improve patient compliance, and enhance therapeutic performance over conventional ocular dosage forms. The system's unique sol-to-gel transition property can enhance bioavailability and patient satisfaction.

Preparation of in-situ gelling systems:

The study focuses on the preparation of in-situ gelling systems using Carbopol 940 and HPMC E50LV & HPMC E4M. Carbopol 940's low viscosity and high pH increase led to the use of HPMC to decrease its concentration without compromising its gelling capacity. Different viscosity grades were combined with Carbopol 940 to optimize concentrations. Four formulations viz. CH 11 (0.3 % Carbopol 940 and 1.5 % HPMC E50LV), CH 15 (0.4 % Carbopol 940 and 1.5 % HPMC E50LV), CH 21 (0.2 % Carbopol 940 and 0.4 % HPMC E4M) and CH 24 (0.3 % Carbopol 940 and 0.4 % HPMC E4M) were selected based on viscosity and gelling capacity, and the drug was incorporated into these optimized formulations.

Evaluation of prepared in-situ gelling systems:

A Spectrophotometric method was developed to estimate Lomefloxacin HCL, a fluoroquinolone agent used to treat eye diseases like conjunctivitis. The absorption maxima were obtained at 281.5 nm using a UV spectrophotometer. The optimized in-situ gels were evaluated for visual appearance, clarity, pH, and drug content. All formulations were found transparent and clear, with a pH within 5 - 0.5 and drug content within 99.38-99.71%. The formulations had a pseudoplastic character, allowing for easy instillation into the eye as a liquid and rapid sol-to-gel transition.

In-vitro release of Lomefloxacin HCL was studied through diffusion cell using cellophane membrane for 8 hours, comparing it with the pure drug and marketed eye drop. Results showed sustained drug release over 8 hours, with no definite changes in bands observed. Sterility testing showed no microbial contamination and sterility. Antimicrobial efficacy was also found to be effective.

The formulations were tested for stability at room temperature and 40°C. The developed formulations are a viable alternative to conventional eye drops, as they are easily administered, decrease the frequency of administration, and prolong the precorneal residence time for higher bioavailability and

reduced systemic side effects. The "pH Induced In-Situ Gelling System of an Antiinfective drug (Lomefloxacin HCL) for Sustained Ocular Delivery" was a successful experiment.

CONCLUSION

This work aims to develop a pH-induced in-situ gel as an ophthalmic drug delivery system. A Spectrophotometric method was developed to estimate Lomefloxacin Hydrochloride in Simulated Tear Fluid using Carbopol 940 polymer. Formulations were evaluated for transparency, clarity, pH, and drug content. The formulations showed satisfactory in-vitro gelation capacity and sterility. The optimal formulation was found to be zero order and peppas, indicating drug release was independent of concentration. The formulations also showed antimicrobial activity and were non-irritating. Accelerated stabilities studies were conducted without changes in visual appearance, clarity, pH, or drug content.

References

1. Pal P, Sambhakar S and Paliwal S. Revolutionizing ophthalmic care: a review of ocular hydrogels from pathologies to therapeutic applications. *Current Eye Research*.2025; 50(1): 1-17.
2. Singh J and Nayak P. pH-responsive polymers for drug delivery: trends and opportunities. *Journal of polymer science*. 2023; 61(22): 2828-2850.
3. Peng X, Zhang T, Wu Y, Wang X, Liu R and Jin X. mPEG-CS-modified flexible liposomes-reinforced thermosensitive sol-gel reversible hydrogels for ocular delivery of multiple drugs with enhance synergism. *Colloids and Surfaces B: Biointerfaces*, 2023; 231: 113560.
4. Lin KT, Wang A, Nguyen AB, Iyer J and Tran SD. Recent advances in hydrogels: ophthalmic applications in cell delivery, vitreous substitutes, and ocular adhesives. *Biomedicines*.2021; 9(9): 1203.
5. Wang X, Li F, Liu X and Zhang H. Applications and recent developments of hydrogels in ophthalmology. *ACS Biomaterials Science & Engineering*. 2023; 9(11): 5968-5984.
6. Ourani-Pourdashti S, Mirzaei E, Heidari R, Ashrafi H and Azadi A. Preparation and evaluation of niosomal chitosan-based in situ gel formulation for direct nose-to-brain methotrexate delivery. *International Journal of Biological Macromolecules*. 2022; 213: 1115-1126.

7. Allam A, Elsabahy M, El Badry M and Eleraky NE. Betaxolol-loaded niosomes integrated within pH-sensitive in situ forming gel for management of glaucoma. *International Journal of Pharmaceutics*. 2021;598: 120380.
8. Laddha UD and Kshirsagar SJ. Formulation of nanoparticles loaded in situ gel for treatment of dry eye disease: In vitro, ex vivo and in vivo evidences. *Journal of Drug Delivery Science and Technology*. 2021; 61: 102112.
9. Shen T and Yang Z. In vivo and in vitro Evaluation of in situ Gel Formulation of Pemirolast Potassium in Allergic Conjunctivitis. *Drug Design, Development and Therapy*. 2021; 2099-2107.
10. Ranch KM, Maulvi FA, Koli AR, Desai DT, Parikh RK and Shah DO. Tailored doxycycline hyclate loaded in situ gel for the treatment of periodontitis: Optimization, in vitro characterization, and antimicrobial studies. *AAPS PharmSciTech*. 2021; 22(3): 77.
11. Reddy YN, De A, Paul S, Pujari AK and Bhaumik J. In Situ Nanoarchitectonics of a MOF hydrogel: A self-adhesive and pH-responsive smart platform for phototherapeutic delivery. *Biomacromolecules*. 2023; 24(4): 1717-1730.
12. Zhang J, Hurren C, Lu Z and Wang D. pH-sensitive alginate hydrogel for synergistic anti-infection. *International journal of biological macromolecules*. 2022; 222: 1723-1733.
13. Li Z and Yu D. Formulation and characterization of pH-responsive pickering emulsions stabilized by soy protein isolate/nicotinamide mononucleotide complexes for controlled drug release. *Industrial Crops and Products*. 2023; 203: 117158.
14. Yin H, Song P, Chen X, Xiao M, Tang L and Huang H. Smart pH-sensitive hydrogel based on the pineapple peel-oxidized hydroxyethyl cellulose and the hericiumerinaceus residue carboxymethyl chitosan for use in drug delivery. *Biomacromolecules*. 2021; 23(1): 253-264.
15. Luo Q, Hossen A, Sameen DE, Ahmed S, Dai J, Li S and Liu Y. Recent advances in the fabrication of pH-sensitive indicators films and their application for food quality evaluation. *Critical reviews in food science and nutrition*. 2023; 63(8): 1102-1118.
16. Li Q, Dong M, Han Q, Zhang Y, Yang D, Wei D and Yang Y. Enhancing diabetic wound healing with a pH-responsive nanozyme hydrogel featuring multi-enzyme-like activities and oxygen self-supply. *Journal of Controlled Release*. 2024; 365: 905-918.

17. Wu H, Chen X, Tan R, Luo Y, Hu Y, Li Y and Kang W. Controllable regulation of emulsion stability by a pH-responsive zwitterionic/anionic surfactant system. *Fuel*. 2022; 312: 122921.
18. Ahmadi M, Panahi F, Bahri-Laleh N, Sabzi M, Pareras G, Falcone BN and Poater A. pH-responsive gelation in metallo-supramolecular polymers based on the protic pyridinedicarboxamide ligand. *Chemistry of Materials*. 2022; 34(13): 6155-6169.
19. Xie X, Lei H and Fan D. Antibacterial hydrogel with pH-responsive microcarriers of slow-release VEGF for bacterial infected wounds repair. *Journal of Materials Science & Technology*. 2023; 144: 198-212.
20. Zheng J, Zhang Y and Zhang S. Sustained release of azithromycin from lipid liquid-crystalline nanoparticles laden in situ gel for the treatment of periodontitis: In vitro and efficacy study. *Journal of Biomaterials Applications*. 2022; 37(3): 482-492.
21. He J, Zhang Z, Yang Y, Ren F, Li, J, Zhu S and Chu D. Injectable self-healing adhesive pH-responsive hydrogels accelerate gastric hemostasis and wound healing. *Nano-micro letters*. 2021; 13(1): 80.
22. Masood N, Razaque G, Shahwani GM, Shirazi J, Nawaz H, Masood M, and Tariq H. Formulation and In Vitro Characterization of Xanthan Gum/Eudragit Controlled Release Hydrogel Using Metformin as a Model Drug. *Pak-Euro J. Med. Life Sci*. 2022; 5: 81-92.
23. Berillo D, Zharkinbekov Z, Kim Y, Raziyeveva K, Temirkhanova K and Saparov A. Stimuli-responsive polymers for transdermal, transmucosal and ocular drug delivery. *Pharmaceutics*. 2021; 13(12): 2050.
24. Cai C, Wang T, Han X, Yang S, Lai C, Yuan T and He N. In situ wound sprayable double-network hydrogel: Preparation and characterization. *Chinese Chemical Letters*. 2022; 33(4): 1963-1969.
25. Fang W, Yang L, Chen Y and Hu Q. Bioinspired multifunctional injectable hydrogel for hemostasis and infected wound management. *Acta Biomaterialia*, 2023; 161: 50-66.
26. Muthoni A, Anyango A and Wanjala VH. Mucilage-Based Nanocarriers for Targeted Cancer Therapy—Design, Functionalization, and Therapeutic Potential. *Drug Development and Industrial Pharmacy*, (just-accepted). 2025; 1-36.

27. Patil RS and Sancaktar E. Fabrication of pH-responsive polyimide polyacrylic acid smart gating membranes: Ultrafast method using 248 nm krypton fluoride excimer laser. *ACS Applied Materials & Interfaces*. 2021; 13(21): 24431-24441.
28. Chen Y, Lee JH, Meng M, Cui N, Dai CY, Jia Q and Jiang HB. An overview on thermosensitive oral gel based on poloxamer 407. *Materials*. 2021; 14(16): 4522.