Pharmacogn. Res., 2025; 17(1):173-184.
https://www.phcogres.com

Original Article

Design and Evaluation of Novel *in situ* Gel Forming Ocular Drug Delivery System of Kaempferol for Sustain Pharmacological Response against Cataract

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ABSTRACT

Aim: Cataract is an eye disease in which the lens of eyes becomes cloudy. It is a major source of blindness globally. As per the reports published by WHO, around 161 million people are visually compromised worldwide. No clinically proven drug is available to date for the cataract treatment and surgery is the only option left for the management of cataract Treatments other than surgery are just prevention based. **Background:** A major setback for the development of ocular medications is the poor bioavailability and low therapeutic response of available conventional ophthalmic solutions in the treatment of cataract due to the instant precorneal removal of the drug. Ophthalmic bioavailability of only 1-10% is generally attained and to overcome this problem frequent installation of the concentrated drug solution is required with increases the systemic absorption of the drug through the nasolacrimal absorption of the drug. The *in situ* gel forming systems are special drug dosage form that when instilled in the eye as a drop undergoes a transitional change from solution form to the gel with a change in its environmental pH. **Materials and Methods:** In the present study, Kaempferol ophthalmic gel was prepared using polymers such as Pectin and HPMC K4M as a pH-triggered gelling system to increase contact time and controlled release, to decrease the rate of administration and upsurge the therapeutic efficacy of the drug. Formulation development involved selection of right polymers from plethora of polymers such as HPMC k4m, Pectin, Carbopol and tween 80 in different compositions. The required quantity of drug (1%) soluble in ethanol was poured onto the polymeric solution and proper mixing was done. To evaluate the efficacy of the formulation developed, various methods were employed-clarity, pH, estimation of gelling capacity, gelling strength, viscosity, *in vitro* cumulative percent drug release. The composition that satisfies all the above-mentioned parameters, was selected as the optimized formulation and this formulation was used in the pharmacological evaluation of the drug. **Results:** The evaluation of the anti-cataract activity of Kaempferol was done by using the sodium selenite-induced cataract model in Wistar rat pups.

Keywords: Cataract, *In situ* gelling, Kaempferol, Ocular tension, Sustained Release.

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Received: 08-10-2024;
Revised: 13-11-2024;
Accepted: 03-12-2024.

INTRODUCTION

Cataract cause blindness by eye lens cloudiness.[1,2] Blindness can be broadly classified into "fixable" and "non-fixable". Out of about 18 million people around the world, 48% become blind due to age related cataract.[3] Eye lens in its normal arrangement is characterized by its crystalline nature that allows a clear passage of light.[4] The presence of special fiber proteins makes the eye lens transparent. Any change in this alignment can lead to lens opacity or cataract. Cataract can be categorized into several kinds based on its appearance and locations. These include nuclear cataracts, congenital cataracts and cortical cataracts. The major causes of cataract include Posterior smoking, UV radiation exposure and alcohol consumption.[5-7] Other factors may include factors like genetic and nutritional diabetes mellitus[8-12] Occurrence of cataract in patients with diabetes mellitus is 2-5 times more than normal people. Some common cataracts in diabetic patients include the subcapsular cataract, anterior subcapsular cataract and traumatic cataract.[4] Currently there is no cure for cataract, leaving surgery the only approach to manage cataract. However, some prevention-based treatments are claimed but still remain disputed.[1,2] Eye drops are the most common available

DOI: 10.5530/pres.20251969

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ophthalmic preparations. A major drawback of conventional eye drops is their poor availability at the site of action (<5%) after topical administration.[13] The release of ophthalmic preparations from the eye is due to protein binding, nasolacrimal drainage, systemic absorption, tear damage, enzymatic degradation, Blood Retinal Barrier (BRB) and complex penetration barriers.[13] To overcome this problem, ophthalmic preparations are instilled in higher concentrations. The instillation of these preparations in higher concentration results in ocular and systemic side effects.

To improve the therapeutic efficacy and duration of contact of eye drops, more recent methods have been devised for their manufacture. Using an *in situ* gel forming technology, fluid preparations are made into gel under physiological circumstances. These innovative medication delivery methods are administered into the eyes in the form of eye drops that immediately gelation the eyes on contact. Using Pectin and HPMC K4M polymers as a gelling system to increase contact time, controlled release, and lower the rate of administration in the *in vivo* systems, the current study aimed to develop a pH triggered *in situ* gel forming system where Kaempferol's effect against cataract was evaluated.

MATERIALS AND METHODS

Sigma Aldrich provided the kaempferol, sodium selenite, pectin, and HPMC K4M. Shiva Institute of Pharmacy lab provides all other analytical grade substances.

Preparation of Formulation

Selection of polymers

A list of the different compositions of the polymers was prepared based on literature review and the composition satisfying maximum required parameters was selected as the main formulation base.

Selection of buffers

The pH values of 6.0, 7.0, and 7.4 were used to access the various gelling capacity polymer compositions that were chosen. In order to facilitate formulation, the buffer with the highest gelling capacity was used.

Preparation of in situ gelling systems

For 20 min, at 121°C and 15 psi of pressure, all of the polymers were sterilized in an autoclave. Next, the necessary amount of phosphate buffer was sprinkled on top to dissolve them. A clear solution was formed by constantly stirring the mixture. The solution was stirred after adding benzoalkonium chloride and letting it hydrate for the entire night. After dissolving the drug's weight in one milliliter of ethanol, the polymer solution was combined with the medication until a homogenous solution was achieved. The developed formulation was filled in sterile glass vials under aseptic conditions sealed with aluminum caps.[14] All the above procedures were done under laminar air flow chamber to avoid contamination.

Pre-Formulation Study

Differential Scanning-Calorimetry (DSC)

Formulation DSC was done. The sample was thoroughly dried to avoid any damage to the equipment. Mixture of polymers and Kaempferol were weighed in the ratio 1:1:1. 5 mg, placed in the aluminum pan and was hermetically sealed. The sample was then scanned at a constant range of 10°C/minute over a temperature range of 50 to 310°C. The respective thermo-gram was then recorded.[15,16]

Physical stability of Kaempferol

The stability and compatibility of the Kaempferol was estimated by UV spectrophotometer. Kaempferol was mixed with the polymers (HPMC and pectin) in equal ratios in a petri plate and then stored at the accelerated degradation chamber (stability chamber) at the relative humidity of 70% and about 45°C temperature for 1 month. During this period, the sample was regularly observed for any change in its color or physical appearance.[16,17]

Assay of Kaempferol concentration in physical stability sample

After the physical stability studies, change in the concentration of Kaempferol was assessed by comparing the prepared sample with the standard sample on UV Spectrophotometer. 300 mg of the sample was taken in 10 mL of methanol. A solution of 1% concentration of Kaempferol was formed and a standard solution

Table 1: Different dose groups.

Sl. No.	Groups	No. of animals	Treatment
1.	Normal Control Group	6	Vehicle
2.	Disease control	6	Sodium selenite (30 µ/kg) only once for cataract induction only then vehicle treatment for 15 days.
3.	Test Control 1	6	20 µl of 1% Kaempferol
Total		18	

of 1% Kaempferol was prepared on the other hand. Concentrations of both the samples were compared by UV spectrophotometry. Any change in the concentration of Kaempferol was noted down.[16]

Estimation of λ_{max} of Kaempferol

Kaepferol (100 ppm) was prepared in methanol. Wavelength range of 200-400 nm region was selected for scanning λ_{max} in UV spectrophotometer.[16]

Evaluation of Formulations

Visual appearance and Clarity

To ensure clarity, every prepared formulation was positioned against a black and white backdrop.[16]

pH Measurement

An ophthalmic formulation's pH should fall within a certain range to ensure formulation stability and prevent application site discomfort. The pH range for ophthalmic preparations is between 5.5 and 7.4. A pH meter that had been calibrated was used to determine the formulation's pH.[16]

Viscosity

A Brookfield DV III programmable viscometer was used to assess the formulation's rheological characteristics. With spindle number 62, the generated formulation was poured into the tiny adapter of the Brookfield DV III programmable viscometer, and the shear rate was adjusted to 4. The viscosity was computed using the average of the two values. After pouring the mixture into an ointment jar, simulated lachrymal fluid was added to elevate the pH to 7.4. The procedure was repeated times and the readings were noted down.[16]

Gelling capacity and gelling strength

The formulation's viscosity should be such that it quickly turns into gel when injected into the eye. All formulations' gelling capabilities were shown as + (gel forms in 60 sec and dissolves quickly), ++ (gel forms in 60 sec and stays stable for 3 hr), and +++ (gel forms in 60 sec and stays for 6 hr).[16]

Determination of Drug Content

By diluting 100 µL of the formulation to 10 mL of ethanol, the drug concentration of the final formulation that was chosen was ascertained. Using a UV visible spectrophotometer, an aliquot of mL was collected, and the concentration was measured at a wave length of 390 nm.[16]

Cumulative drug release study

For *in vitro* release testing of the formulation, Franz diffusion chamber was used. 1 mL of formulation was poured in the simulated tear solution (7 mL) to convert the formulation into

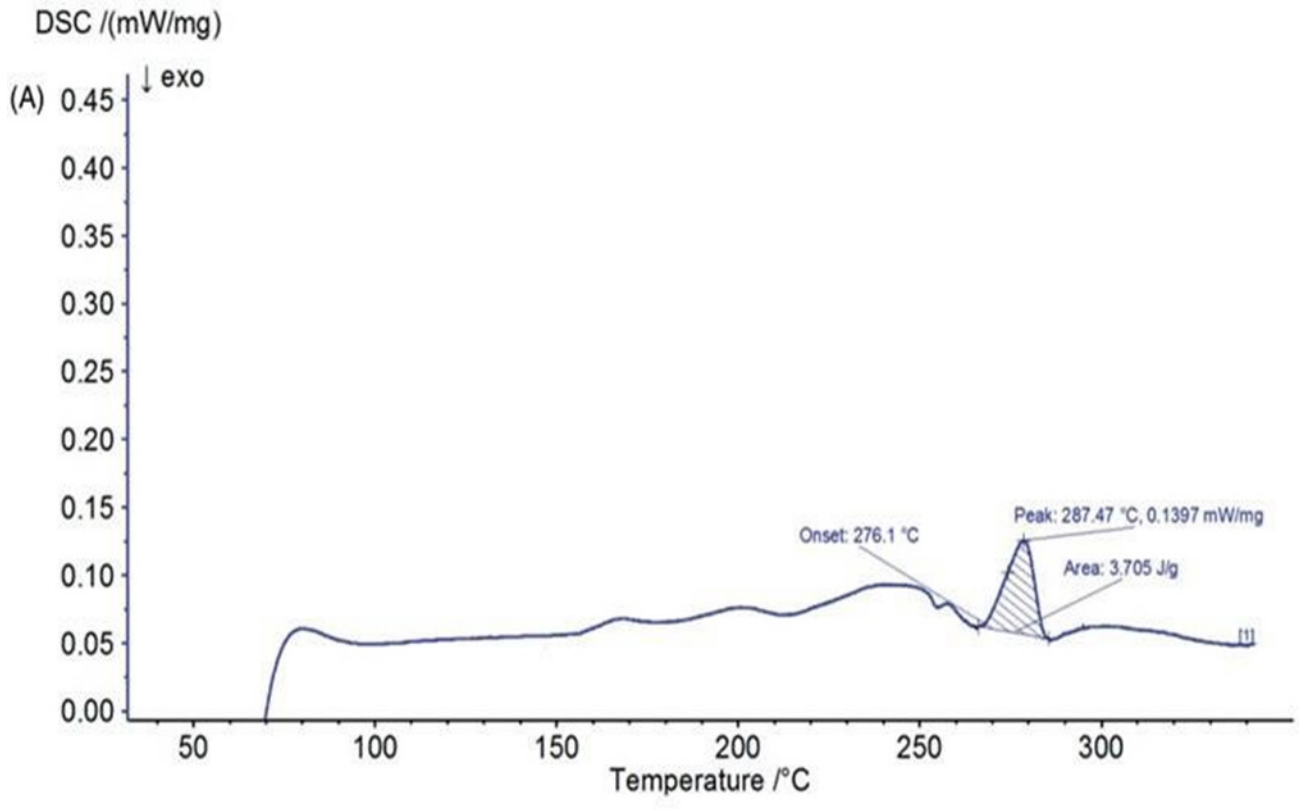

Figure 1: DSC Thermogram of Kaempferol Pure.

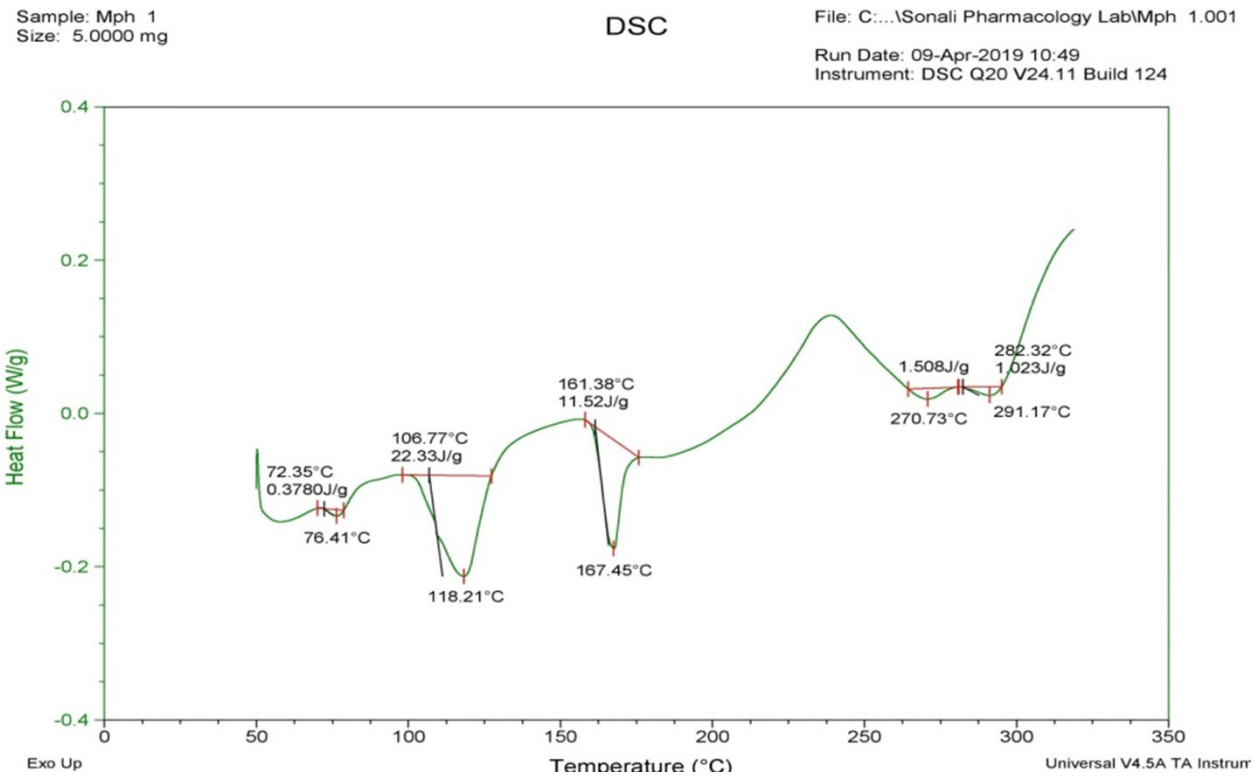

Figure 2: DSC thermogram of Kaempferol, Pectin and HPMC in a mixture of equal ratios.

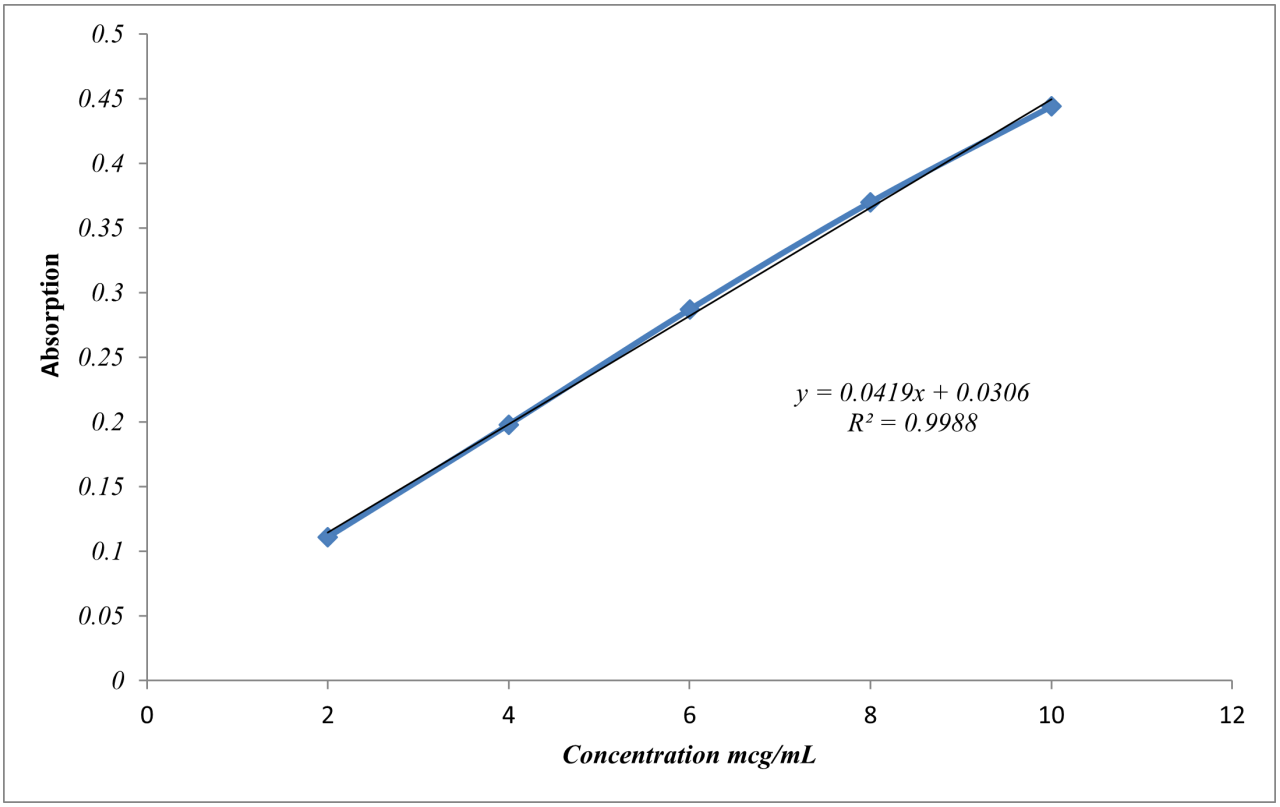

Figure 3: Standard curve of Kaempferol in ethanol+water solvent.

gel. The gel prepared was pipetted out carefully from the acceptor compartment and placed in the donor compartment of the apparatus. A dialysis membrane was placed between the donor and the receptor compartment to separate the test product (gel) from the collection medium (phosphate buffer pH 7.4) filled in the receptor compartment. The temperature of the receptor chamber was maintained at 37°C. The magnetic beads were placed into the receptor chamber and rpm was set at 30. Sample was collected at different time variables and absorbance was measured at UV Spectrophotometer.[16,18-20]

Sterility Study

In order to perform the sterility test in accordance with the USP standard procedure, 7.25 grams of FTM or SCDM were dissolved in 250 mL of filtered water with the aid of fluid thioglycolate medium and soyabean-casein digest medium. This underwent wet heat sterilization in an autoclave set at 121°C for 20 min while maintaining 15 pounds of pressure. Sterilized formulations (1 mL) were added to 9 mL of sterilized media, both of which were kept under laminar airflow in an aseptic room. The media were then incubated for one day at different temperatures (FTM at 34±1°C in a bacteriological incubator and SCDM at 23±1°C in a fungal incubator). The test tubes were examined a day later. The next day, 10 g of SCDM and 5 g of agar were dissolved in 250 mL of filtered water to create 12 plates of SCDM in 2% w/v of agar. After autoclaving, the medium was plated. Using a wire loop, 4 plates were infected with solutions from FTM test tubes, 4 plates were inoculated with solutions from SCDM test tubes, and 4 plates were left blank. After that, each plate was incubated at 34±1°C. For three days, the plates were examined every 24 hr.[16]

Table 2: Cataract Grading.

Grade No.	Observation
0	Normal clear lens.
1	Initial sign of posterior sub-capsular or nuclear opacity involving tiny scatters.
2	Slight nuclear opacity with swollen fibers or posterior sub-capsular scattering foci.
3	Diffuse nuclear opacity but not involving lens cortex.
4	Partial nuclear opacity.
5	Mature dense opacity involving entire lens.

Kinetics Modeling on Release Mechanism

The *in vitro* data result was examined by fitting the acquired data into several models, some of which are shown below. And this is done in order to get the optimized formulation's best-fitting kinetic model for *in vitro* drug release.[21,22]

- Zero order kinetic model.
- First order kinetic model.
- Korsmeyer-peppas model.
- Hixon-crowell model.
- Higuchi's model.

The result indicated that zero order fits best with high correlation for the optimized batch. We found faster release initially that may be the drug that is present in space or outside the gel matrix which initially diffuse very quickly. Both the nature and the polymers used can control the release of the drug.

Table 3: Formulation in Citrate Phosphate Buffer (50 mL).

Ingredients	F1	F2	F3	F4
Buffer (PH-6.0)	50 mL	50 mL	50 mL	50 mL
Pectin	3%	3%	3%	3%
Sodium methyl cellulose	-	-	0.5%	1%
HPMC K4M	0.5%	1%	-	-
Benzalkonium chloride	0.01%	0.01%	0.01%	0.01%

Table 4: Formulation prepared in Water (100 mL).

Ingredients	F5	F6	F7	F8
Water	100 mL	100 mL	100 mL	100 mL
Carbopol940	0.5	0.3	-	-
Citric acid	0.407	0.407	0.407	0.407
Disodium hydrogen phosphate	1.125	1.125	1.125	1.125
NaOH	0.1	0.1	0.1	0.1
Tween 80	0.5	0.5	0.5	0.5
Benzalkonium chloride	0.01%	0.01%	0.01%	0.01%

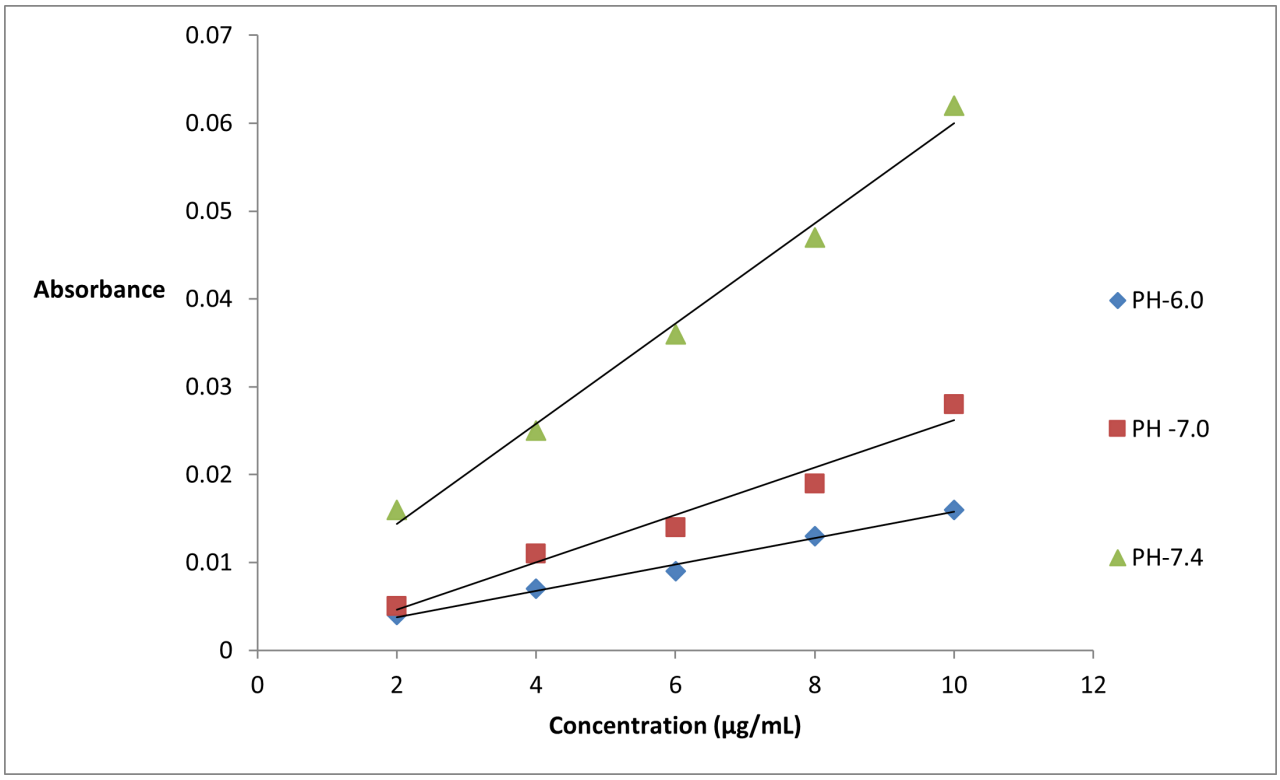

Figure 4: Concentration of the drugs in different PH with respect to the absorbance.

Table 5: Clarity, pH, Gelling capacity and strength.

Sl. No.	Formulation code	Temperature	Visual appearance	Clarity	PH	Gelling capacity	Gelling strength
1.	F1	25°C	Translucent	+	5.0	+	++
2.	F2	25°C	Translucent	+	5.2	+	++
3.	F3	25°C	Translucent	+	5.9	+	++
4.	F4	25°C	Translucent	+	6.2	+	++
5.	F5	25°C	Translucent	+	7.5	-	-
6.	F6	25°C	Translucent	+	7.5	-	-
7.	F7	25°C	Translucent	+	7.3	+	+
8.	F8	25°C	Translucent	+	7.5	+	+

*Gel formed within 60 sec - (+).

In vivo Animal Study

Animals required

There were 26 Wistar rat pups in total, weighing 13.00 g±1, with a relative humidity of 60%±5, a temperature of 25.3 C±3, and a 14 hr light/dark cycle. The rodents were fed a nutritional solution called VRK and were given unlimited access to RO water, and the air conditioning unit needed 10% exhaust from the air. The Institutional Animal Ethics Committee (SOP/IAEC/23/09) approved the protocol (SOP/IAEC/23/09) for the purpose of controlling and supervising animal studies, and it was followed strictly during all of the conducted experiments. The animals were kept under close observation for development, health, and ability to consume food for the whole research time in order to guarantee their overall wellbeing.

Model development

The animals were acclimatized to the laboratory conditions one week before initiation of the study and the health status was examined by veterinarian (Table 1). The induction of cataract was done in 9 days old Wistar rat pups weighing between 12 to 13 g by using sodium selenite through subcutaneous injection (30 micromole/kg body weight). Daily observation of the pups was done for any clinical sign and mortality. Dosing started after the confirmation of cataract, means animals in which cataract is visible are selected for dosing. All animals were divided into the

Table 6: **Viscosity.**

Formulation ID	Before gelling	After gelling
F1	432.7 cps	896.5 cps
F4	869.0 cps	1857 cps

*Both the F1 and F4 generation were found to have acceptable viscosities but we have selected F1 generation due its free-flowing properties.

different dose groups and Slit lamp analysis was carried out for 15 days.[23,24]

Cataract grading

A cataract grading table was formulated by observation of the male wistar rats as shown in Table 2.[24]

RESULTS

The final composition of Kaempferol decided to treat cataracts was then decided and is shown in Table 3 and Table 4.

From the above formulations the one which satisfy all the requirements to be a good *in situ* formulation was selected.

Pre-Formulation Result

DSC Studies

DSC was done by mixing of all the finalized polymers with the drug in equal proportions to find out any compatibility present (Figure 1). This data was then compared to the standard DSC thermogram of each polymer and drug, any shift in the melting point peak seen will be considered as a sign of incompatibility. DSC Thermogram of HPMC k4m showed at 141.14°C. The DSC of pectin shows a peak at 137°C which is melting point of pure pectin.

Peak of plain Kaempferol is observed at 287.47°C.

There is no any drastic change in the peak of Kaempferol which was found at 282.32 (Figure 2) when compared to the peak of the pure Kaempferol. It means that there was no interaction between polymers and the Kaempferol. Thus, we can conclude that our polymers are compatible with the drug (Kaempferol). On the other hand, shifting of polymers peak are also observed that can be due to entrapment of drug molecules into the polymers.

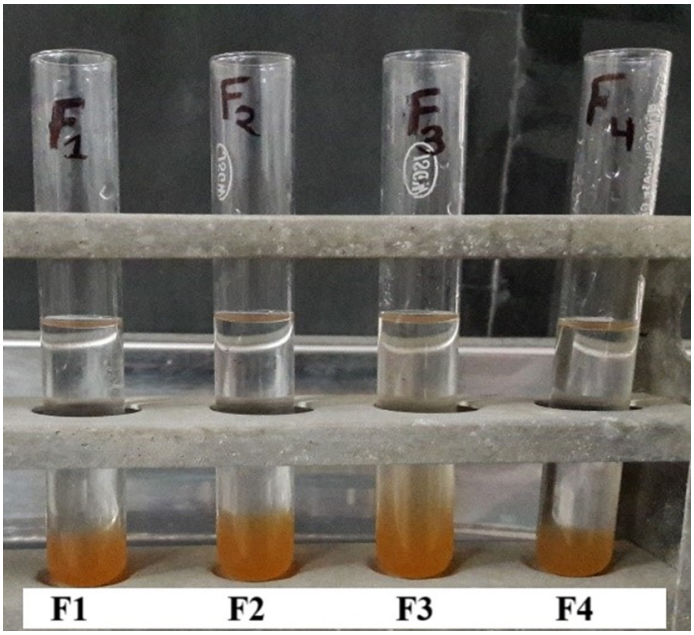

Figure 5: Gelling capacity of formulations in simulates tear solution.

Estimation of λ_{max}

Observation the λ_{max} of the Kaempferol by using hydro-alcoholic solvent and with the help of λ_{max} value we can find out estimate absorption and concentration of the sample. And λ_{max} of our sample was found at 390 nm.

Standard curve of Kaempferol

The standard curve of Kaempferol was obtained and represented in Figure 3.

Physical stability of Kaempferol

To find out any change (incompatibility) in the physical structure of polymers and Kaempferol we have performed physical stability study for 30 days. There were no abnormalities seen in the color and physical appearance. Hence, we concluded that there was neither any sign of physical incompatibility nor interactions between the polymers and the drug.

Table 7: **Observation table for cumulative percent drug release of 1% formulation.**

Sl. No.	Time hrs.	UV Absorption	Conc. in mcg per mL	Conc.in mcg per 2 mL	Cumulative conc.	cumulative conc. in 12 mL	% cumulative release
1.	0.5	0.072	1.04878	2.097561	2.097	25.164	5.0328
2.	1.0	0.094	1.585366	3.170732	5.267732	63.21278	12.64256
3.	2.0	0.086	1.390244	2.780488	8.04822	96.57863	19.31573
4.	3.0	0.064	0.853659	1.707317	9.755537	117.0664	23.41329
5.	4.0	0.086	1.390244	2.780488	12.53602	150.4323	30.08646
6.	5.0	0.132	2.512195	5.02439	17.56041	210.725	42.145

* There was about 42% of drug release that was reported after 5 hr.

Assay of Kaempferol

In the sample which was introduced to physical stability test, the drug content of Kaempferol was determined in triplicates (n=3) and was found to be 0.97±0.231% w/v and standard drug content was 1% w/v of Kaempferol.

Solubility study

Solubility of our drug was found very less at our selected pH (6.0) when compared to the other pH so there was a need to improve the solubility that was done by mixing our drug in a solvent (ethanol) in which drug get completely dissolved then this prepared solution was poured on the previously prepared base with continuous stirring as shown in Figure 4.

Clarity, pH, Gelling capacity and strength

Only some of the formulations have stable gel formation they are F1, F2, F3, F4 on the other hand there was no gelling properties were found in the F5 and F6 generations and in the remaining generations either gel formation was there but stability was an issue. By concluding all the data, we selected F1, F2, F3, F4 generations for further evaluation studies as shown in Table 5.

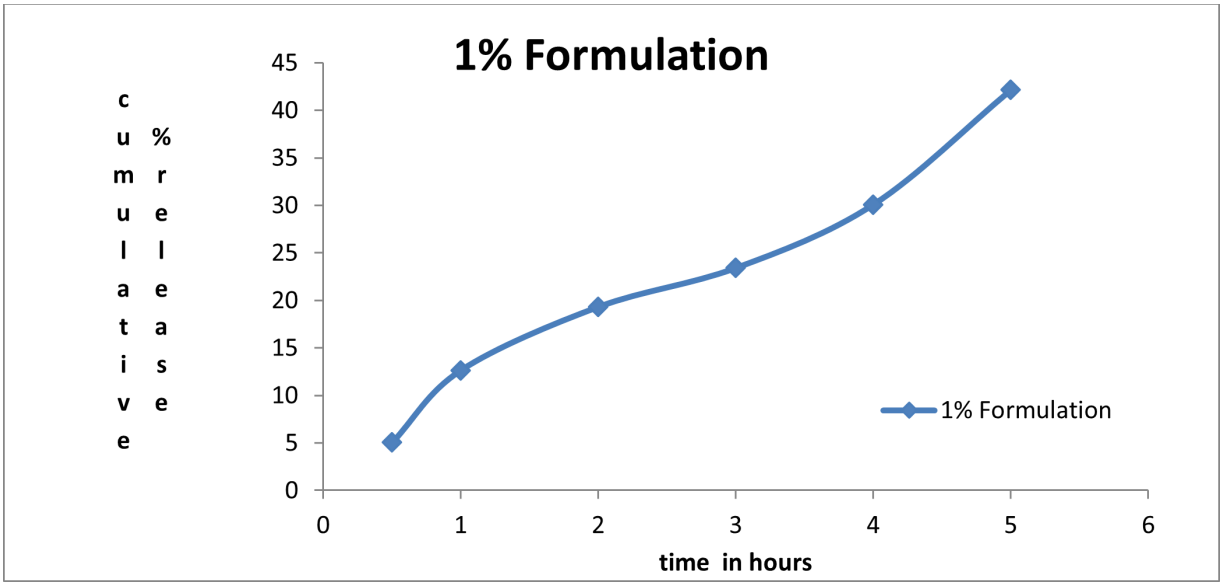

Figure 6: *In vitro* release profile of Kaempferol from an ophthalmic *in situ* gel.

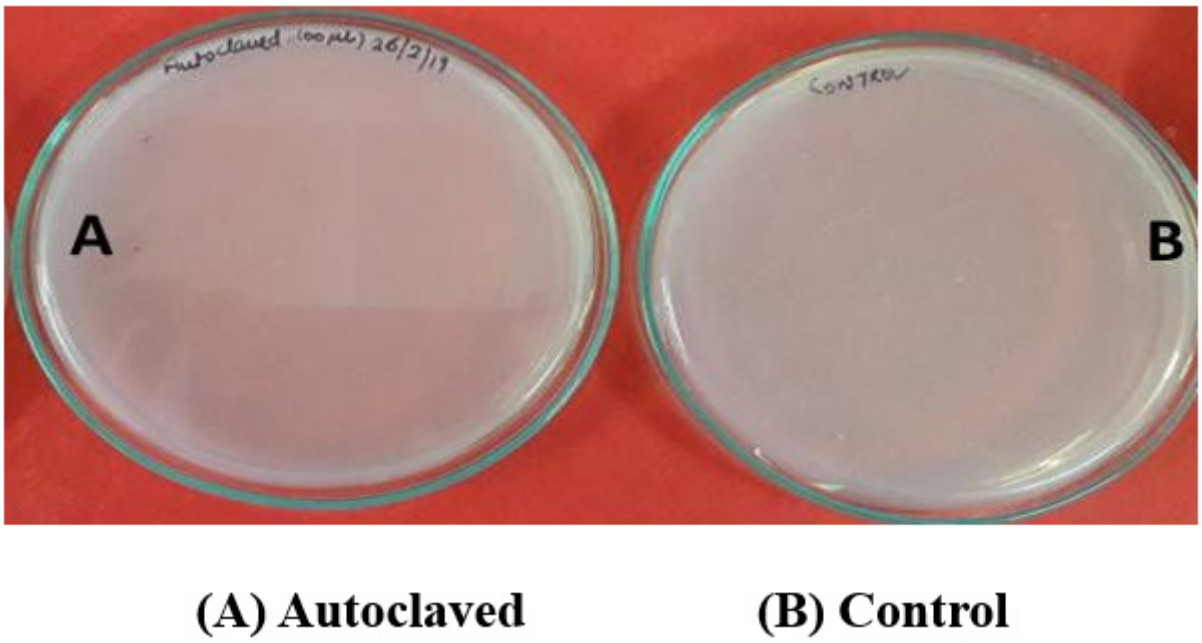

Figure 7: Sterility testing by wet sterilization method.

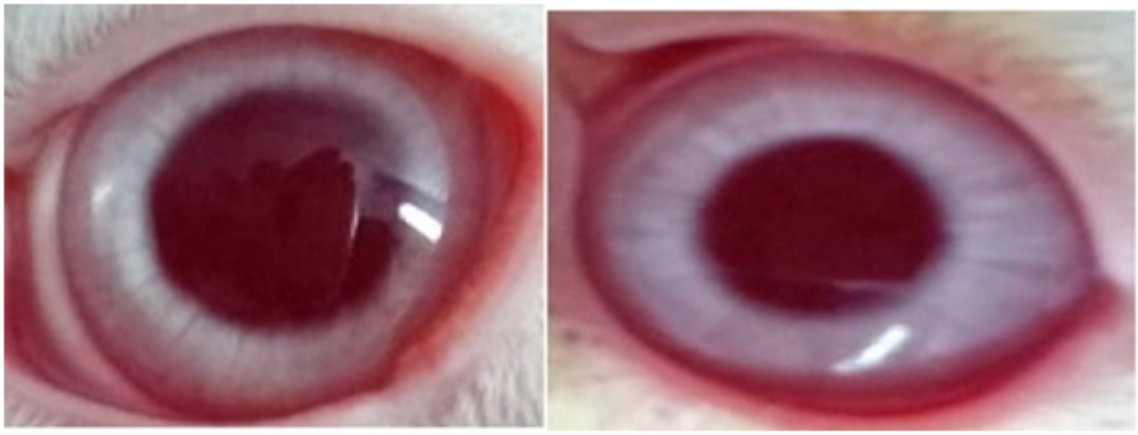

Figure 8: Eye Irritation Result (self).

Table 8: Kinetic Model fitting for an optimized batch F1-1%.

Kinetic models	Regression coefficient (r)
Zero order	0.9717
First Order	0.9581
Korsmeyer-peppas model	0.8333
Hixon-crowell model	0.9665
Higuchi model	0.9535

Gelling capacity

Gelling capacity was found as Figure 5.

Viscosity

Viscosity of the *in situ* gel formulation is a major parameter as shown in Table 6.

Observation table for cumulative percent drug release of 1% formulation

The observation of the drug release was observed and shown in Table 7.

Figure 6 displays the cumulative percentage of Kaempferol release in the simulated tear fluid as a function of time. Tables 5 and 6 reveal the release statistics. Conditions for drug release *in vitro* could differ significantly from those in the eye. But the *in vitro* findings made it abundantly evident that the improved gel could hold the medication for an extended amount of time.

Determination of drug content

Three times (n=3), the drug content of kaempferol was measured and found to be 0.41±0.075% w/v; the standard drug content was 1% w/v.

Sterility testing by using wet heat sterilization method

Sterility is one of the most vital requirement for an opthalmic preparation to determine the absence of viable microorganisms that may harm the patient's eye. Wet sterilization method was found to be very efficient to for the sterilization of the formulation. There was no microbial growth observed in the sterilized opthalmic *in situ* gels when compared to the control one. Results of the wet heat sterilization are shown in Figure 7 based on these observations, it was concluded that autoclaving of polymers could be done to achieve the sterility (Figure 7).

Kinetics modeling on release mechanism

Kinetic Model fitting for an optimized batch F1-1% (Table 8).

The results indicated that the zero order models was best fitted model with high correlation for the optimized batch the faster release initially indicated that that some of the drug present in the solution was present outside the gel matrix that initially diffuses quickly. The release of the drug from the gel is controlled by both the nature and the concentration of the drug and polymers used.

Eye irritation study on rabbit eye

This study was done to check any harm produced by our drug and to ensure that safety of drug due prolonged used. There was no any abnormality was observed in the eye of the treated group no any sign of redness, conjunctival damage, swelling, aqueous flare, vascularization, and excessive tear production was observed as compared to the normal as shown in Figure 8.

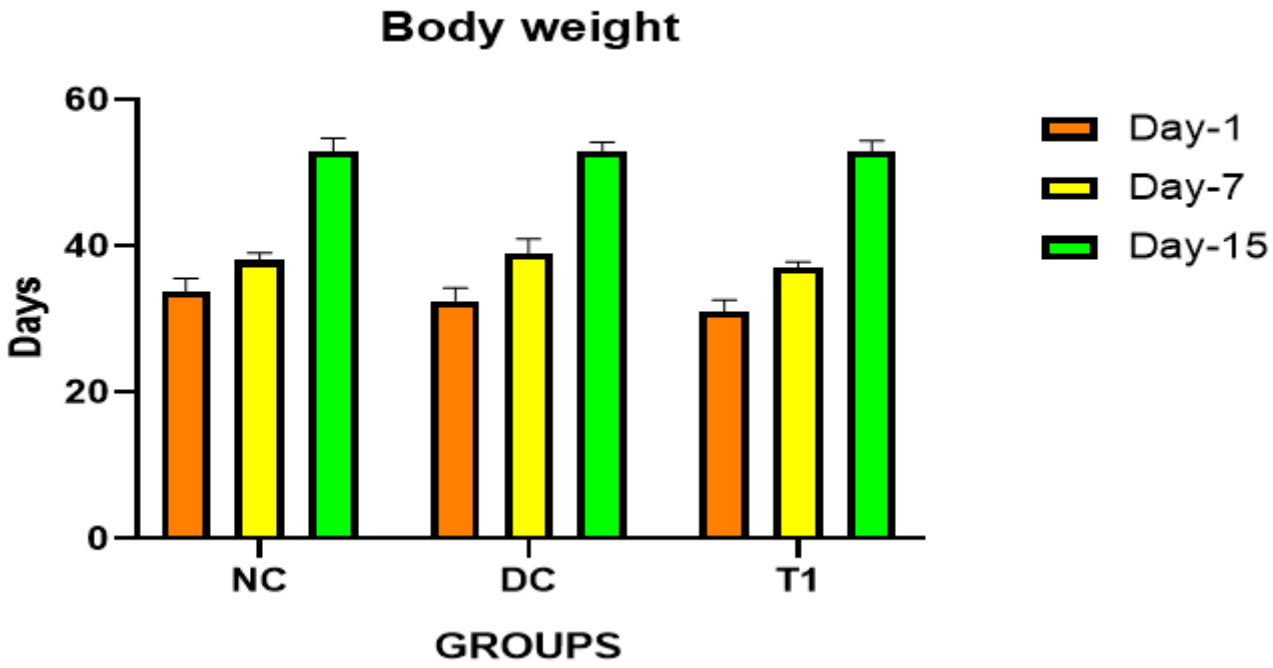

Figure 9: Graph showing weekly body weight.

Table 9: Results of pharmacological evaluations.

Sl. No.	Treatment	Days		
		1	7	15
1	Normal control	1.722401	1.095445	1.788854
2	Disease control	1.760682	1.966384	1.169045
3	Test control-1%	1.602082	0.894427	1.414214

Data shown as mean ±SEM (n=6).

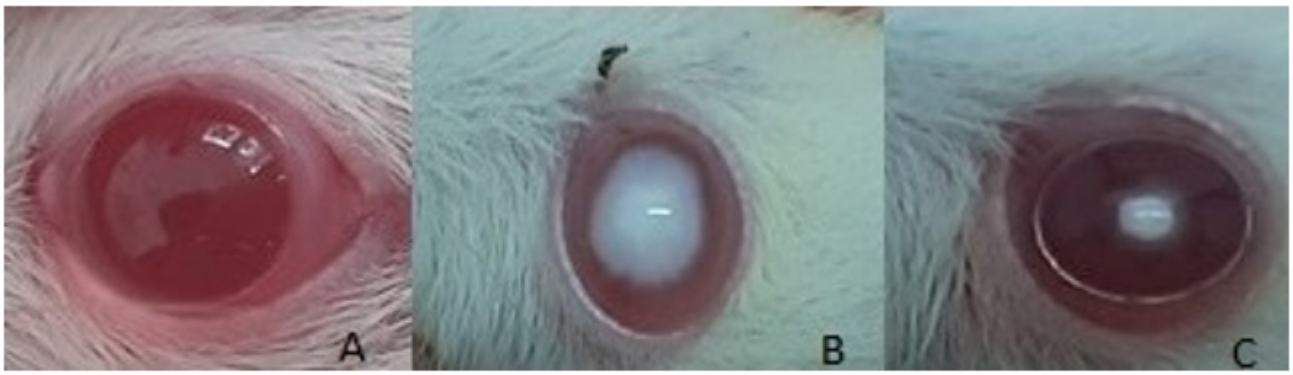

Figure 10: Photographic data of anticataract study result (self).

Table 10: Data Of Anticataract Study Result.

Group ID	Cataract Grading	
	Right eye	Left eye
NC	0	0
DC	5	5
T1-1%	3	3

RESULTS

Weekly body weight of experimental animals

The weekly body weight of all groups of animals was noted and is shown in Figure 9.

The result is shown in Table 9.

Pictographic data of anticataract study result

The 1% test formulation was found to depict the protective action against the cataract progression when compared to the normal eye and disease eye (Figure 10).

The result of anticataract study is shown in Table 10.

DISCUSSION AND RESULTS

Pre-formulation study

Before the selection of the final composition of the base we have performed various pre-formulations studies in order to find out the compatibility between the drug and our polymers. We have prepared each composition in three different pH buffers, and the buffer in which the gelling capacity was observed was selected. After that we have done the Differential Scanning Calorimetry (DSC) study to find out any incompatibility that can cause any change in the drugs physical or chemical property. As our result of DSC study, we find out some signs of in-compatibility between the used polymers that can be due to entrapment of the drug into the polymers but our drug was remained intact or we can say there were no any sign of the incompatibility between the drug and the polymers. And to further ensure this that our drug was not affected be performed stability study by mixing our drug with the polymers and then placed in an accelerated degradation condition or we can say in the stability chamber and then assay of Kaempferol was performed, then from the reported results we concluded that there was no any interaction between the Kaempferol and polymers. As pre-formulation study we performed various other studies like - estimation of lambda max, preparation of standard curve solubility study.

Formulation development and evaluation

All the selected compositions were further evaluated through the parameters like gelling capacity, gelling strength, clarity, pH, *in vitro* cumulative drug release study and sterility etc. The formulation which satisfies all above parameters was selected as our final formulation. The optimized formulation shows extended *in vitro* release of upto approximately 42% within 5 hr and found to follow zero order kinetics. The final formulation was prepared in two concentrations 1% and 2%. The dose was selected on the basis of pilot study.

Pharmacological evaluation of cataract

The prepared formulation showed marked decrease in cataract progression and the prepared formulation founds to be compatible with the eye because there was no any clinical abnormality was observed. All the normal control lenses in group 1 were clear. In group 2 (disease group all rats developed cataracts (grade 5-grade 6), whereas in group 3 (treatment group) developed cataracts (grade 3-grade 4). The presence of oxidative stress in selenite cataract development and its prevention by Kaempferol support the possibility that by instilling Kaempferol in the eye can help to prevent human senile cataract.

CONCLUSION

The evaluation of an experiment designed to demonstrate novel *in situ* gel forming ocular drug delivery system of Kaempferol for sustained pharmacological response against cataracts has demonstrated promising results. This system offers a new approach to enhance drug bioavailability and prolonging drug retention time in the ocular cavity, overcoming the limitations of conventional eye drops.

In conclusion, the novel *in situ* gel forming system for Kaempferol presents a viable and efficient therapeutic option for cataract management. Furthermore, deeper studies and clinical trials are required to get an estimate of how effective the drug is. However, this system holds promise as a sustained ocular drug delivery platform, providing an improved therapeutic outcome and convenience for patients suffering from cataracts.

ACKNOWLEDGEMENT

This work is my wonderful start to my journey in Research in Pharmacology. During this time, I would highly thank and appreciate all my students that with their sheer dedication and hard work, without which this research would have been taken longer. Now to properly acknowledge everyone that has contributed their efforts and hard work in this project.

With pleasure, I would like to thank Ms. Arushi for all the formulation preparation, Gobind Singh for preparation of all the doses, Sumiran Negi for animal handling and Vishal Thakur for animal dosing and other students too for their unconditional support and invaluable suggestions throughout this project.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

HPMC: Hydroxypropyl methylcellulose; **UV:** Ultraviolet; **SCDM:** Soyabean Casein Digest Medium; **FTM:** Fluid thioglycolate Medium; **USP:** Unites States Pharmacopoeia; **VRK:** Vaccinia Related Protein Kinases; **DSC:** Differential Scanning Calorimetry.

SUMMARY

This project work aims to understand the effects of Kaempferol and its potential pharmacological use in the treatment of Cataracts. The formulation used during this project is aimed to provide sustained release of the drug, enhancing its therapeutic efficacy and prolonging its pharmacological action in the eye and providing relief. This system involves giving the drug via ocular route thereby, improving drug retention time and bioavailability. By ensuring controlled and sustained drug delivery, the formulation seeks to address the limitations of conventional cataract treatments, potentially offering a more effective, long-lasting solution for managing the disease. Evaluation parameters included drug release profile, *in vitro* and *in vivo* performance, and therapeutic response against cataract progression. This research focuses on developing and evaluating an *in situ* gel-forming ocular drug delivery system for Kaempferol, designed to provide a sustained therapeutic effect for cataract treatment. The gel is formulated to transition from a liquid to a gel upon administration into the eye, allowing for prolonged drug retention and enhanced bioavailability. This novel approach aims to overcome the challenges of conventional eye treatments, such as poor drug absorption and short residence times, by ensuring a controlled and extended release of Kaempferol. Comprehensive *in vitro* and *in vivo* studies were conducted to assess the system's drug release behaviour, stability, and its efficacy in reducing cataract progression. The findings suggest that this system could offer a more efficient and long-lasting solution for cataract management.

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Cite this article: Chaudhuri A, Gauttam VK, Arushi, Negi S, Singh G, Thakur V, *et al*. Design and Evaluation of Novel *in situ* Gel Forming Ocular Drug Delivery System of Kaempferol for Sustain Pharmacological Response against Cataract. Pharmacog Res. 2025;17(1):173-84.